(*Z*)-3-*p*-Tolylsulfinylacrylonitrile as a Chiral Dienophile: Diels−Alder Reactions with Furan and Acyclic Dienes

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The behavior of (*Z*)-3-*p*-tolylsulfinylacrylonitrile (**1**) as a chiral dienophile has been evaluated from its reactions with furan and acyclic dienes. Electrostatic interactions of the cyano group with the sulfinyl one restrict the conformational mobility around the C−S bond, thus controlling the π−facial selectivity, which is almost complete in all cases, the approach of the diene from the less-hindered face of the dienophile (that bearing the lone electron pair) in the predominant rotamer being the favored one. The regioselectivity is also completely controlled by the cyano group. Additionally, the reactivity of compound **1** as well as its *endo*-selectivity are both higher than those observed for the corresponding (*Z*)-3-sulfinylacrylates, thus proving the potential of sulfinylnitriles as chiral dienophiles.

Introduction

The sulfinyl group has become one of the most interesting chiral inductors in asymmetric Diels−Alder reactions due to its ability to differentiate between diastereotopic faces of neighboring double bonds. It drew the attention of many researchers, whose contributions have been collected in many excellent reviews.[1] The poor results obtained from vinyl sulfoxides—a rather low reactivity and only a moderate stereoselectivity[2]—were substantially improved by incorporating further activating groups to the double bond, which increases the reactivity and simultaneously restricts the conformational mobility around the C−S bond, hence improving the stereoselectivity of the dienophile. In this sense, many electron-withdrawing groups have been incorporated to vinyl sulfoxides, alkoxycarbonyl ones being the most widely used. The interest of (*Z*)-3-sulfinylacrylates, clearly the most frequently used sulfinyl dienophiles, derives from the fact that the adducts resulting from their cycloadditions with cyclopentadiene and furan can be used as chiral building blocks in the synthesis of a number of natural products. Thus, bicyclic sesquiterpenes[3] were prepared from the adducts resulting from the reaction of the *p*-tolylsulfinylacrylates with cyclopentadiene. Nevertheless, the results obtained in the Diels−Alder reaction showed the rather low reactivity—they were unable to react with furan even under forced conditions—and moderate *endo*-selectivity of these sulfoxides as dienophiles.[2] Therefore the search of more reactive sulfinyl derivatives was undertaken. In this context, pyridylsulfinyl derivatives exhibited a higher reactivity toward cyclopentadiene,[4] and their *endo*-adducts were transformed into precursors of the Ohno's lactone.[5] They were able to react with furan[6] and substituted furans[7] yielding mixtures of the four possible adducts (Scheme 1) with low *endo*/*exo* selectivity in the presence of Et_2AlCl (<2:1). It became higher (ca. 4:1) in the absence of any catalyst, but the π-facial selectivity for the *endo* approach was clearly poorer (55:45, see Scheme 1).

Despite their moderate stereoselectivity, the interest of these reactions derives from the use of these furan adducts as building blocks in the synthesis of a number of natural products such as *C*-nucleosides,[8] methyl epishikimate,[9] pseudosugars,[10] and glyoxalase I inhibitors.[11]

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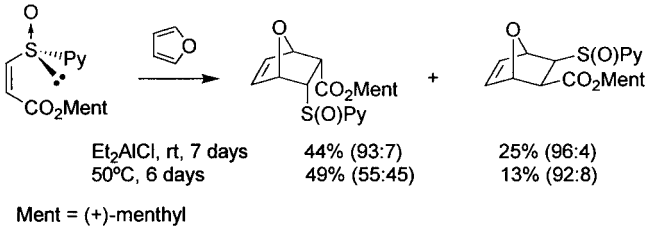
Scheme 1



The use of high pressures makes the reactions easier with furan derivatives[12] but the *endo/exo* selectivity remains moderate (ca. 42−68% de's), thus indicating that high presssures do not have a significant influence in the stereoselectivity.

All these results evidenced that the high synthetic interest of the adducts obtained from furan and (*Z*)-3-sulfinylacrylates was basically restricted by the low reactivity of these dienophiles and the moderate *endo/exo* selectivity of their Diels−Alder reactions. The nontrivial procedure required to prepare optically pure pyridyl sulfoxides is another disadvantage to the use of these dienophiles. The search for new, more readily prepared dienophiles, synthetically equivalent to (*Z*)-3-sulfinylacrylates but possessing higher reactivity and stereoselectivity, became an interesting challenge. Recently we have reported the synthesis of (*Z*)-3-*p*-tolylsulfinylacrylonitrile (**1**) and its dienophilic behavior with cyclopentadiene.[13] The results suggested that this easily obtained vinyl sulfoxide fulfilled all the expected requirements (higher reactivity and more stereoselectivity than the corresponding ester). In this paper we describe the reactions of **1** with dienes less reactive than cyclopentadiene, such as furan and acyclic dienes, which confirms the interesting dienophilic features of this vinyl sulfoxide.

Results and Discussion

The synthesis of the starting (*Z*)-3-sulfinylacrylonitrile (**1**) was easily performed by stereoselective conjugated addition of Et_2AlCN to alkinyl sulfoxides.[13] The results obtained in the Diels−Alder reactions of **1** with furan under different conditions are collected in Table 1. Treatment of **1** with 8 equiv of furan in refluxing CH_2Cl_2 for several days afforded the unaltered starting material. The addition of $ZnBr_2$ or Me_2AlCl as catalyst at room temperature allowed the formation of small amounts of the expected adducts. No improvement in the results was observed on increasing either the reaction time or the temperature. However, the use of furan as the solvent substantially improved the yields (although the reaction was never complete) affording ***endo*-2A** and ***exo*-2A** adducts, which could be isolated and characterized. Traces of compound ***endo*-2B** could also be detected (^{1}H NMR) in the crude mixture. Under these conditions (entry 1) the *endo/exo* ratio was 84/16 and the π−facial selectivity for the *endo*-approach was estimated as higher than 33 (**A/B** ratio).

As expected, the use of Lewis acids as catalysts shortened the reaction times, but it had no significant influence on both *endo/exo* and π-facial selectivities (entries 2−5), which were also slightly modified by a decrease in the reaction temperature.[14] In the case of the Diels−Alder reactions of **1** with cyclopentadiene[13] a complete reversion of the π-facial selectivity was observed by using BF_3 as the catalyst. Nevertheless, all attempts performed in order to extend this methodology at atmospheric pressure to the use of furan as the diene failed since they gave rise to the undesired hydrolysis of the cyano group of the starting dienophile into a carboxamido group as the major transformation.

Finally, the use of high pressures also increased the rate of reactions conducted in furan as the solvent, but the facial diastereoselectivity is slightly modified (entry 6), mainly if reactions are catalyzed by $ZnBr_2$ (entry 7). At 4 kbar no starting material was detected by NMR analysis of the crude material. Nevertheless, a small amount of **1** was isolated by flash chromatography, presumably due to a retro-Diels−Alder reaction during the purification stage.

The *endo* or *exo* character of the isolated adducts was established by ^{1}H NMR. The absolute configuration of compound ***endo*-2A** obtained as the major one in these reactions was unequivocally assigned by X-ray analysis. The sense of the high π-facial selectivity for the *endo* approach is the expected one from the results obtained with cyclopentadiene[13] and it can be attributed to the strong conformational polarization around the C−S bond induced by the cyano group. It determines that the sulfinyl oxygen adopts almost exclusively the conformation *s-trans*—in order to minimize the dipolar repulsion with nitrile[15]—arranging the *p*-tolyl group toward the upper **B** face (Scheme 2). This becomes so sterically congested that the diene approach is only possible from the less-hindered **A** face containing the lone electron pair. According to this proposal, which satisfactorily explains the stereochemistry of the major adduct, the *exo* approach of furan will also take place from the same face **A**, which allows us to assign compound ***exo*-2A** the structure shown in Table 1.

Important advantages can be inferred from the comparison of the results obtained from compound **1** with those from the corresponding sulfinyl esters. First, the reactivity of the *p*-tolylsulfinylnitrile is higher than that of pyridylsulfinylacrylates,[4,6,7] which, in turn, were more reactive than *p*-tolylsulfinylacrylates and unreactive in the presence of furan, as deduced from the reaction times required under similar conditions (compare Table 1 and

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(14) The scarce influence of the catalyst and the temperature in the *endo/exo* ratio suggested that it was the result of a thermodynamic control process through a retro-Diels−Alder reaction, which is a quite common feature of furan adducts. To verify this point, the reaction time was increased in several days in the reactions carried out without catalyst. Under these conditions, the *endo/exo* ratio decreased down to 2: 1. Additionally a diastereomerically pure sample of the major adduct ***endo*-2A** was maintained in furan for 2 days and the formation of a small amount of ***exo*-2A** (<10%) could be observed. This proves that retro-Diels Alder takes place but it is slower than the normal reaction. Therefore, we can conclude that the *endo/exo* selectivity must be slighly higher than that indicated in Table 1, but the existing ***exo*-2A** adduct is not exclusively derived from the retro-Diels−Alder but also from the direct formation through a Diels−Alder process.

(15) The assumption of this repulsion minimizing the conformational energy is supported by the relative arrangement of cyano and sulfinyl groups observed in the X-ray structure for adduct ***endo*-2A**. In the latter case, both groups adopt an eclipsed conformation such as in dienophile **1**.

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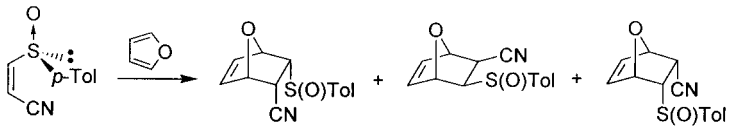
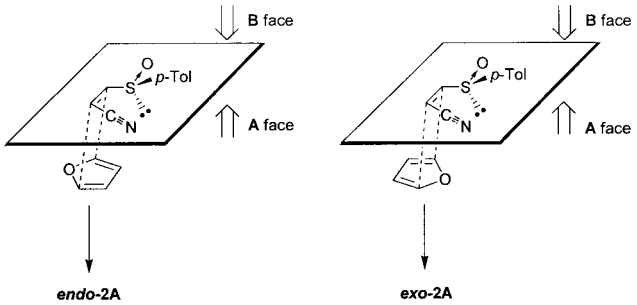
Table 1. Diels–Alder Reactions of 1 and Furan



entry	catalyst	conditions	pressure	***endo*-2A**×*bb*	***exo*-2A**[a]	***endo*-2B**[a]	*endo/exo*[b]	A/B[b]
1	—	rt, 2 d	1 bar	51	11	traces	84/16	>33
2	$ZnBr_2$	rt, 1 d	1 bar	42	13	traces	86/14	>33
3	$ZnBr_2$	0 °C, 7 d	1 bar	—[c]	—[c]	—[c]	85/15	>33
4	$ZnBr_2$	−20 °C, 3 d	1 bar	—[c]	—[c]	—[c]	87/13	>33
5	Me_2AlCl	rt, 1 d	1 bar	53	10	traces	87/13	>33
6	—	rt, 1 d	4 kbar	61	12	4	84/16	~25
7	$ZnBr_2$	rt, 13 h	4 kbar	55	16	6	78/22	10

[a] Isolated yield (%). [b] From integration of well-separated signals of the ^1H NMR spectrum of the crude mixture. [c] Not determined.

Scheme 2



Scheme 1). Second, the π-facial selectivity of compound **1** is almost complete, regardless the presence of a catalyst (Table 1), whereas it was poorer starting from pyridylacrylate, mainly in the absence of Lewis acids (Scheme 1). Finally, the *endo/exo* selectivity of the reaction was also higher for sulfinyldienophiles containing a cyano group than for those with an ester moiety.[13] Additionally, the synthesis of **1** is much easier than that of sulfinyl esters.

The lower *endo*-selectivity of the sulfinylacrylate with respect to its corresponding acrylonitrile **1** can be understood by assuming that steric interactions between the ester and sulfinyl groups distort the planarity of the former one. Such a distortion can also be responsible for the lower reactivity of the acrylate.

These good results prompted us to investigate the behavior of **1** with acyclic dienes, which had never been studied with 3-sulfinylacrylates, maybe due to their low reactivity. The results obtained in reactions with (*E*)-1-methoxy-1,3-butadiene (**3**) and piperylene (**4**) are collected in Table 2. When **1** reacted with an excess of 1-methoxy derivative **3** in the absence of a cosolvent, a complete transformation of the starting material was achieved after 4 days at room temperature (entry 1). By contrast, all attempts to perform the reaction of **1** with piperylene (**4**) at atmospheric pressure were unsuccessful even in the presence of different catalysts and working at high temperatures for long reaction times. The lower reactivity of **4** and the scarce solubility of **1** in this diene, which precludes its use as a solvent (the reactions were performed with 8 equiv of **4** in CH_2Cl_2 as the solvent) can account for this unsuccessful result. At a pressure of 4 kbar, 1-methoxy derivative **3** required shorter reaction times (entry 2) and piperylene evolved into the corresponding cycloadducts after 10 days at room temperature (entry 4). The π-facial selectivity for the *endo*-approach (**A/B** ratio) is very high and the regioselectivity complete (governed by the cyano group) with both dienes. The combined influence of high pressure and Lewis acid catalysis determines, as in the case of furan, a substantial decrease in the facial diastereoselectivity (entries 3 and 5). The *endo/exo* selectivity of the reactions with diene **3** was similar to the observed from furan, whereas it was clearly higher with diene **4**, even in the presence of $ZnBr_2$. In the presence of a boron catalyst no transformation was achieved, partially due to the fast polymerization of the diene under the reaction conditions.

Configurational assignment of compound ***endo*-5A** was unequivocally established by X-ray diffraction studies (Supporting Information). Results obtained in these reactions can also be easily rationalized by assuming the model proposed in Scheme 2, the approach of acyclic dienes from the less-hindered face of sulfinylnitrile **1** (in its electrostatically preferred conformation) being favored. Finally, we must remark that, as expected, the regioselectivity is controlled by the cyano group and is not affected by addition of the Lewis acid, which evidences that the relative magnitude of the coeficients at the dienophilic double bond must remain identical under both reaction conditions.

Finally, reactions with 3,4-dihydro-6-methoxy-1-vinylnaphthalene (**7**) (Dane's diene)[16] were also studied (Table 3). The interest of this diene, one of the most frequently used in the construction of the steroidal systems,[17] is related to the regioselectivity of their reactions, mainly to the role of the Lewis acid catalysts, which are able to invert it in many cases.[18]

In the absence of a catalyst, **1** reacted with 4 equiv of Dane's diene **7** in CH_2Cl_2–benzene, but the formation of

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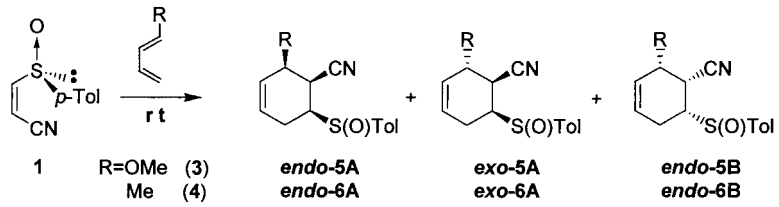
Table 2. Diels–Alder Reactions of 1 with Acyclic Dienes 3 and 4

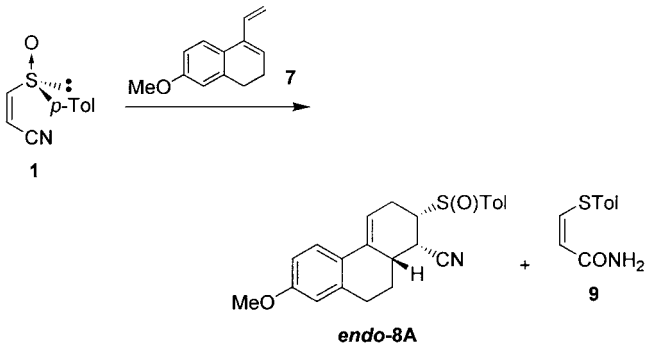


1 R=OMe (3) *endo*-5A *exo*-5A *endo*-5B
Me (4) *endo*-6A *exo*-6A *endo*-6B

entry	diene	catalyst	pressure	time (d)	product	*endo*-A[a]	*exo*-A[a]	*endo*-B[a]
1	**3**	—	1 bar	4	**5**	70	12	traces
2	**3**	—	4 kbar	3	**5**	70	9	5
3	**3**	$ZnBr_2$	4 kbar	3	**5**	63	13	16
4	**4**	—	4 kbar	10	**6**	70	5	traces
5	**4**	$ZnBr_2$	4 kbar	7	**6**	57	4	13

[a] Isolated yield (%).

Table 3. Diels-Alder Reactions of 1 and Dane's Diene 7



endo-8A

entry	diene equiv	catalyst	pressure	time (d)	*endo*-8A[a]	9
1	4	$ZnBr_2$	1 bar	7	50	12
2	2.5	—	4 kbar	7	60	—
3	2	$ZnBr_2$	4 kbar	3	84	4

[a] Isolated yield (%).

the adducts is extremely slow, the degree of transformation being very low even after long reaction times (27 days at room temperature). However, addition of $ZnBr_2$ led to a complete transformation of **1** after 7 days (Table 3, entry 1) yielding compound ***endo*-8A** as the only adduct, along with *β*-sulfenylacrylamide **9**, presumably resulting from the hydrolysis of cyano group of the dienophile with concomitant anchimeric assistance of the sulfinyl oxygen.[19] The configuration of this adduct was also determined by X-ray analysis (Supporting Information).

The use of high pressure makes the reaction easier by reducing the reaction times and the number of diene equivalents (entries 2 and 3), but the exclusive formation of the adduct ***endo*-8A** (no other adduct could be detected by ^1H NMR from the reaction crudes) was observed under all conditions. These results demonstrate that reactions of (*Z*)-3-*p*-tolylsulfinylacrylonitrile (**1**) with Dane's diene (**7**) are completely regio *endo* and *π*–facial selective, thus confirming that compound **1** is one of the best chiral dienophiles to be used with Dane's diene to build steroidal skeletons. Concerning the regioselectivity, which remains unaltered under all conditions, it seems to be controlled by the cyano group at the dienophile and the substituent at C-1 at the diene. Taking into account that the relative magnitude of the coeficients at dienophilic double bond is not altered by the Lewis acid (see before), the results indicated in Table 3 suggest that it is also the case for Dane's diene. This does not agree with those explanations attributing changes in regioselectivity only to the association of the methoxy group to the catalyst,[20] but it suggests that alterations of the dienophile must be mainly responsible for the changes in the regioselectivity.

As a conclusion we can state that the readily obtained (*Z*)-3-*p*-tolylsulfinylacrylonitrile (**1**) is a very efficient chiral sulfinyldienophile exhibiting some important advantages with respect to its corresponding sulfinylacrylate. The higher reactivity of the nitrile **1**, allowing its reactions with furan and acyclic dienes, as well as its higher *endo*-selectivity could be a consequence of the linear structure of the nitrile, which avoids the steric interactions between CO_2R and SOTol groups that distort the planarity in the case of the ester. The higher *π*-facial selectivity exhibited by **1** must be a consequence of the strong repulsion between the C≡N and S–O dipoles. These features make compound **1** an advantageous synthetic equivalent of sulfinylacrylate as a chiral dienophile.

Experimental Section

General Methods. Dienes, except Dane's diene (**7**), and Lewis acids are commercially available and were used without further purification. $ZnBr_2$ was flame-dried in the reaction flask before use. Flash chromatography was performed with silica gel 60 (230–400 mesh ASTM), and silica gel F 254 plates were used for preparative TLC. NMR spectra were determined in $CDCl_3$ solutions at 200 (or 300) and 50.3 (or 75) MHz for ^1H and ^{13}C NMR, respectively. *J* values are given in hertz. Yields are shown in Tables 1–3. Compound **1** was synthesized and purified according to procedure described in ref 13. To verify the optical purity of **1** to be used as the substrate in further reactions, it is necessary to check it by NMR using $Yb(hfc)_3$ as the LSR (substrate–LSR molar ratio 1:0.3). Reactions with piperylene were carried out with racemic **1**. High-pressure reactions were performed in 1.5 mL polyethylene sample vials in a Unipressequipment 101 LV 30/16 apparatus.

Diels–Alder Cycloadditions of 1 with Furan. Method i: Thermal Conditions. A solution of **1** (0.75 mmol) in an excess of furan (2 mL) was stirred at room temperature. When the reaction was completed (2 days at atmospheric pressure or 1 day at 4 kbar), the crude mixture was concentrated, and the residue was purified by flash chromatography (2:3 hexanes–ethyl acetate).

Method ii: In the Presence of $ZnBr_2$. To a solution of $ZnBr_2$ (337.8 mg, 1.5 mmol) in THF (0.4 mL), under argon at room temperature, was added a solution of **1** (143.5 mg, 0.75

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mmol) in furan (3 mL). When the reaction was completed (see Table 1), water (4 mL) was added, and the mixture was extracted with CH_2Cl_2 (3 × 4 mL). The organic layer was dried (Na_2SO_4) and concentrated.

Method iii: In the Presence of Me_2AlCl. To a solution of **1** (0.75 mmol) in furan (3 mL), under argon at room temperature, was added a 1.0 M solution of Me_2AlCl (900 μL, 0.9 mmol) in hexanes. The reaction mixture was stirred for 1 day at room temperature, poured into saturated aqueous sodium potassium tartrate (4 mL), and extracted with CH_2Cl_2 (3 × 4 mL). The organic layer was dried (Na_2SO_4) and concentrated.

(1*S*,2*R*,3*R*,4*R*)-3-[(*R*)-*p*-Tolylsulfinyl]-7-oxabicyclo[2.2.1]-hept-5-ene-2-carbonitrile (*endo*-2A). It was crystallized from hexanes−ethyl acetate (white solid): mp 105−107 °C; $[\alpha]^{20}_D = +24.6$ (*c* 1, $CHCl_3$); ^{1}H NMR δ 7.79 and 7.36 (AA′BB′ system, 4H), 7.03 (dd, 1H, J = 1.7 and 5.9), 6.80 (dd, 1H, J = 1.7 and 5.9), 5.45 (ddd, 1H, J = 1.1, 1.6 and 4.2), 5.35 (ddd, 1H, J = 1.0, 1.7 and 4.3), 3.76 (dd, 1H, J = 4.2 and 9.0), 3.03 (dd, 1H, J = 4.3 and 9.0), 2.43 (s, 3H); ^{13}C NMR δ 143.1, 139.0, 136.0, 135.9, 130.2, 125.7, 116.3, 81.1, 80.6, 66.0, 29.2, 21.4. Anal. Calcd for $C_{14}H_{13}NO_2S$: C, 64.84; H, 5.05; N, 5.40; S, 12, 36. Found: C, 64.69; H, 4.96; N, 5.04; S 11.84.

(1*R*,2*R*,3*R*,4*S*)-3-[(*R*)-*p*-Tolylsulfinyl]-7-oxabicyclo[2.2.1]-hept-5-ene-2-carbonitrile (*exo*-2A). It was crystallized from hexanes−ethyl acetate (white solid): mp 117−118 °C; $[\alpha]^{20}_D = -91.2$ (*c* 0.27, $CHCl_3$); ^{1}H NMR δ 7.80 and 7.34 (AA′BB′ system, 4H), 6.55 (dd, 1H, J = 1.6 and 5.9), 6.43 (dd, 1H, J = 1.6 and 5.9), 5.74 (t, 1H, J = 1.3), 5.40 (t, 1H, J = 1.3), 3.04 (d, 1H, J = 7.8), 2.54 (d, 1H, J = 7.8), 2.41 (s, 3H); ^{13}C NMR δ 143.1, 139.6, 137.0, 135.4, 130.2, 126.1, 117.9, 83.4, 79.1, 65.9, 31.0, 21.5; HRMS (FAB) 260.0755 $[M + H]^+$ ($C_{14}H_{14}NO_2S$ requires 260.0745). Anal. Calcd for $C_{14}H_{13}NO_2S$: C, 64.84; H, 5.05; N, 5.40; S, 12.36. Found: C, 64.41; H, 4.86; N, 5.17; S 12.44.

(1*R*,2*S*,3*S*,4*S*)-3-[(*R*)-*p*-Tolylsulfinyl]-7-oxabicyclo[2.2.1]-hept-5-ene-2-carbonitrile (*endo*-2B). It was crystallized from hexanes−ethyl acetate (white solid): mp 131−132 °C; $[\alpha]^{20}_D = +122.4$ (*c* 0.17, $CHCl_3$); ^{1}H NMR δ 7.69 and 7.42 (AA′BB′ system, 4H), 6.80 (dd, 1H, J = 1.6 and 5.8), 6.52 (dd, 1H, J = 1.6 and 5.8), 5.37 (ddd, 1H, J = 1.1, 1.9 and 4.2), 4.30 (dt, 1H, J = 1.3 and 4.2), 3.69 (dd, 1H, J = 4.2 and 8.7), 3.55 (dd, 1H, J = 4.2 and 8.6), 2.47 (s, 3H); ^{13}C NMR δ 143.6, 138.9, 136.7, 134.2, 130.6, 125.2, 116.2, 80.8, 79.5, 69.7, 31.5, 21.5; HRMS (FAB) 260.0751 $[M + H]^+$ ($C_{14}H_{14}NO_2S$ requires 260.0745). Anal. Calcd for $C_{14}H_{13}NO_2S$: C, 64.84; H, 5.05; N, 5.40; S, 12,36. Found: C, 64.07; H, 5.33; N, 5.14; S 12.35.

Diels−Alder Cycloadditions of 1 with Acyclic Dienes. Method i: Thermal Conditions. The reactions were carried out at room temperature and at 4 kbar from a solution of **1** (0.5 mmol) and an excess of diene (4 mmol) in CH_2Cl_2 (1 mL) or at atmospheric pressure from a mixture of **1** in 1.03 mL of (*E*)-1-methoxybutadiene (**3**) (5 mmol). When the reaction was completed (see Table 2), the crude mixture was concentrated, and the residue was purified by flash chromatography (4:5 hexanes−ethyl acetate).

Method ii: In the Presence of $ZnBr_2$. To a solution of $ZnBr_2$ (337.8 mg, 1.5 mmol) in THF (0.4 mL), under argon at room temperature, was added a solution of **1** (143.5 mg, 0.75 mmol) in CH_2Cl_2 (1 mL). The reaction mixture was stirred for 1 h at room temperature. Then the corresponding diene [6 mmol of piperylene (**4**) or 3 mmol of (*E*)-1-methoxybutadiene (**3**)] was added, and the mixture was kept at 4 kbar at room temperature. When the reaction was completed, the crude mixture was poured into water (4 mL) and extracted with CH_2Cl_2 (3 × 5 mL). The organic layer was dried (Na_2SO_4) and concentrated.

(1*R*,2*R*,6*S*)-2-Methoxy-6-[(*R*)-*p*-tolylsulfinyl]-3-cyclohexene-1-carbonitrile (*endo*-5A). It was obtained from reaction of **1** with (*E*)-1-methoxybutadiene (**3**). The residue was treated with 1:2 hexane−acetone, ***endo*-5A** remaining insoluble as a white solid [the yield can be increased by chromatographic purification of mother liquors (4:5 hexanes−ethyl acetate)]. It was crystallized from hexane−CH_2Cl_2 (white solid): mp 126−127 °C; $[\alpha]^{20}_D = +7.1$ (*c* 1, $CHCl_3$); ^{1}H NMR δ 7.62 and 7.39 (AA′BB′ system, 4H), 5.94 (ddt, 1H, J = 4.2, 10.3 and 2.1), 5.72 (m, 1H), 3.86 (m, 1H), 3.37 (s, 3H), 3.13 (dd, 1H, J = 2.8 and 5.6), 2.88 (ddd, 1H, J = 2.8, 6.1 and 10.5), 2.77−2.53 (m, 2H), 2.44 (s, 3H); ^{13}C NMR δ 143.2, 137.3, 130.3, 127.0, 126.3, 125.1, 115.1, 75.6, 59.5, 56.7, 30.5, 23.5, 21.5. Anal. Calcd for $C_{15}H_{17}NO_2S$: C, 65.43; H, 6.22; N, 5.09; S, 11.64. Found: C, 65.64; H, 6.05; N, 4.95; S,11.81.

(1*R*,2*S*,6*S*)-2-Methoxy-6-[(*R*)-*p*-tolylsulfinyl]-3-cyclohexene-1-carbonitrile (*exo*-5A). It was obtained (partially unpurified with ca. 3% of ***endo*-5A**) as a colorless oil from reaction of **1** with (*E*)-1-methoxybutadiene (**3**) and further chromatographic purification (4:5 hexanes−ethyl acetate). $[\alpha]^{20}_D = +82.5$ (*c* 0.9, $CHCl_3$); ^{1}H NMR δ 7.58 and 7.37 (AA′BB′ system, 4H), 6.09 (ddd, 1H, J = 2.4, 4.9 and 9.9), 5.87 (m, 1H), 3.92 (m, 1H), 3.21 (s, 3H), 3.11 (ddd, 1H, J = 3.2, 5.7 and 11.1), 2.97 (t, 1H, J = 3.0), 2.64 (dddt, 1H, J = 1.2, 10.9, 18.4 and 2.4), 2.58 (ddt, 1H, J = 2.0, 18.6 and 5.2), 2.43 (s, 3H); ^{13}C NMR δ 142.9, 137.5, 130.6, 130.2, 125.0, 123.3, 116.2, 74.2, 56.8, 56.2, 29.8, 22.3, 21.5; HRMS (FAB) 276.1055 $[M + H]^+$ ($C_{15}H_{18}NO_2S$ requires 276.1058).

(1*S*,2*S*,6*R*)-2-Methoxy-6-[(*R*)-*p*-tolylsulfinyl]-3-cyclohexene-1-carbonitrile (*endo*-5B). It was obtained from reaction of **1** with (*E*)-1-methoxybutadiene (**3**) and further chromatographic purification (4:5 hexanes−ethyl acetate). It was crystallized from 1:1 hexanes−ethyl acetate (white solid): mp 169−170 °C; $[\alpha]^{20}_D = +107.0$ (*c* 0.25, $CHCl_3$); ^{1}H NMR δ 7.58 and 7.36 (AA′BB′ system, 4H), 5.69 (br s, 2H), 4.16 (dd, 1H, J = 3.1 and 6.0), 4.00 (m, 1H), 3.49 (s, 3H), 2.86 (ddd, 1H, J = 3.0, 5.6 and 11.6), 2.42 (s, 3H), 2.29 (ddd, 1H, J = 3.2, 11.6 and 17.8), 1.54 (m, 1H); ^{13}C NMR δ 143.3, 137.6, 130.3, 127.8, 125.9, 125.3, 115.4, 75.5, 61.3, 57.0, 30.7, 22.6, 21.5; HRMS (FAB) 276.1052 $[M + H]^+$ ($C_{15}H_{18}NO_2S$ requires 276.1058). Anal. Calcd for $C_{15}H_{17}NO_2S$: C, 65.43; H, 6.22; N, 5.09; S, 11.64. Found: C, 64.55; H, 6.16; N, 4.88; S 11.63.

(1*S,2*R**,6*S**)-2-Methyl-6-[(*R*)-*p*-tolylsulfinyl]-3-cyclohexene-1-carbonitrile (*endo*-6A).** It was obtained from reaction of **1** with piperylene and further chromatographic purification (1:2 hexanes−ethyl acetate). It was crystallized from hexanes−ethyl acetate (white solid): mp 154−155 °C; ^{1}H NMR δ 7.58 and 7.35 (AA′BB′ system, 4H), 5.80 (ddt, 1H, J = 5.3, 10.1 and 2.8), 5.41 (m, 1H), 2.90 (ddd, 1H, J = 2.9, 7.0 and 10.1), 2.66 (dd, 1H, J = 2.8 and 5.3), 2.64−2.56 (m, 2H), 2.48−2.36 (m, 1H), 2.42 (s, 3H), 1.13 (d, 3H, J = 7.3); ^{13}C NMR δ 143.1, 137.9, 130.4, 129.5, 125.2, 124.9, 116.3, 62.0, 33.4, 32.3, 23.2, 21.6, 18.3; HRMS (FAB) 260.1101 $[M + H]^+$ ($C_{15}H_{18}NOS$ requires 260.1109). Anal. Calcd for $C_{15}H_{17}NOS$: C, 69.46; H, 6.61; N, 5.40; S, 12.36. Found: C, 69.07; H, 6.21; N, 5.18; S 12.63.

(1*S,2*S**,6*S**)-2-Methyl-6-[(*R*)-*p*-tolylsulfinyl]-3-cyclohexene-1-carbonitrile (*exo*-6A).** It was obtained from reaction of **1** with piperylene (**4**). Flash chromatography of the crude reaction (1:2 hexanes−ethyl acetate) afforded impure ***exo*-6A**, which could not be furtherly purified. ^{1}H NMR δ 7.61 and 7.37 (AA′BB′ system, 4H), 5.81 (dddd, 1H, J = 1.6, 2.8, 4.6, and 9.1), 5.63 (m, 1H), 2.97 (ddd, 1H, J = 3.2, 6.1 and 9.1), 2.78−2.53 (m, 3H), 2.49 (t, 1H, J = 3.6), 2.44 (s, 3H), 1.00 (d, 3H, J = 7.1).

(1*R,2*S**,6*R**)-2-Methyl-6-[(*R*)-*p*-tolylsulfinyl]-3-cyclohexene-1-carbonitrile (*endo*-6B).** It was obtained from reaction of **1** with piperylene (**4**). Chromatographic purification (1:2 hexanes−ethyl acetate) and crystallization from hexanes−ethyl acetate afforded ***endo*-6B** as a white solid (partially unpurified with ca. 4% of both ***endo*-6B** and ***exo*-6A**): mp 155−156 °C; ^{1}H NMR δ 7.59 and 7.35 (AA′BB′ system, 4H), 5.61 (ddt, 1H, J = 5.1, 9.9 and 2.6), 5.46 (m, 1H), 3.72 (dd, 1H, J = 3.0 and 5.1), 2.91 (ddd, 1H, J = 3.0, 5.7 and 11.9), 2.56 (m, 1H), 2.43 (s, 3H), 2.26 (m, 1H), 1.58 (m, 1H), 1.29 (d, 3H, J = 7.3); ^{13}C NMR δ 143.0, 137.9, 130.3, 130.2, 125.3, 123.9, 116.7, 63.3, 32.9, 32.6, 22.2, 21.5, 18.7; HRMS (FAB) 260.1109 $[M + H]^+$ ($C_{15}H_{18}NOS$ requires 260.1109). Anal. Calcd for $C_{15}H_{17}NOS$: C, 69.46; H, 6.61; N, 5.40; S, 12.36. Found: C, 68.84; H, 6.73; N, 5.13; S, 12.42.

Diels−Alder Cycloadditions of 1 with Dane's Diene 7. Method i: Thermal Conditions. A mixture of 48 mg (0.25 mmol) of **1** and 625 μL of 1 M benzene solution of **7**[16] (0.63

mmol) in CH_2Cl_2 was kept at 4 kbar for 7 days at room temperature. When the reaction was completed, the crude mixture was concentrated, and the residue was treated with 1:2 hexane-acetone, ***endo*-8A** remaining insoluble as a white solid. The mother liquors were evaporated and chromatographied (1:1 hexanes−ethyl acetate) to yield ***endo*-8A** and 3-sulfenylacrilamide (**9**).

Method ii: In the Presence of $ZnBr_2$. To a solution of $ZnBr_2$ (337.8 mg, 1.5 mmol) in THF (0.4 mL), under argon at room temperature, was added a solution of **1** (143.5 mg, 0.75 mmol) in CH_2Cl_2 (1 mL). The mixture was stirred for 1 h at room temperature, and then a 1 M solution of Dane's diene (**7**)[16] in benzene (1.5 mL, 1.5 mmol) was added. The reaction mixture was kept at 4 kbar for 3 days or stirred at atmospheric pressure for 7 days at room temperature. When the reaction was completed, it was poured into water (10 mL), and the aqueous layer was extracted with CH_2Cl_2 (3 × 8 mL). The combined organic layers were dried (Na_2SO_4) and concentrated. The residue was treated as described above.

(1*S*,2*S*,10a*S*)-1,2,3,9,10,10a-Hexahydro-7-methoxy-2-[(*R*)-*p*-tolylsulfinyl]phenanthrene-1-carbonitrile (*endo*-8A). It was obtained from reaction of **1** with Dane's diene. It was crystallized from hexane−CH_2Cl_2 (white solid): mp 176−177 °C; $[\alpha]^{20}_D = +138.4$ (*c* 1, $CHCl_3$); ^{1}H NMR δ 7.64 and 7.39 (AA′BB′ system, 4H), 7.53 (d, 1H, $J = 8.9$), 6.73 (dd, 1H, $J =$ 2.8 and 8.9), 6.57 (d, 1H, $J = 2.8$), 6.32 (m, 1H), 3.77 (s, 3H), 3.01−2.77 (m, 6H), 2.51 (m, 1H), 2.45 (s, 3H), 1.96−1.83 (m, 2H); ^{13}C NMR δ 159.0, 143.0, 138.0, 137.1, 132.1, 130.4, 125.2, 125.1, 125.0, 116.5, 115.1, 113.2, 113.1, 61.5, 55.2, 38.7, 32.5, 29.6, 27.6, 24.3, 21.5. Anal. Calcd for $C_{23}H_{23}NO_2S$: C, 73.18; H, 6.14; N, 3.71; S, 8.49. Found: C, 73.03; H, 6.12; N, 3.61; S, 8.44.

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Supporting Information Available: IR and MS data and copies of ^{1}H NMR spectra of adducts ***endo*-2B**, ***exo*-5A**, ***endo*-5B**, and ***endo*-6B**; X-ray diagrams for compounds ***endo*-2A**, ***endo*-5A**, and ***endo*-8A**; crystal data and structure refinement for compounds ***endo*-2A**, ***endo*-5A**, and ***endo*-8A** including atomic coordinates, isotropic and anisotropic displacement parameters, and a listing of bond angles and bond lengths. This material is available free of charge via the Internet at http://pubs.acs.org.

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