Synthesis and Dienophilic Behavior of Enantiomerically Pure (*Z*)-3-*p*-Tolylsulfinylacrylonitriles

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The syntheses of enantiomerically pure (*Z*)-3-*p*-tolylsulfinylacrylonitrile (**1b**) and its 2-*n*-butyl (**1a**), 2-*tert*-butyl (**1c**), and 2-benzyl (**1d**) derivatives, by stereoselective hydrocyanation with Et_2AlCN of their corresponding alkynylsulfoxides, are described. Asymmetric Diels−Alder reactions of these dienophiles with cyclopentadiene are also reported, the most significant finding being their total π-facial diastereoselectivity, controlled by the sulfur configuration, which can be readily inverted by using BF_3 as a catalyst. The endo selectivity is very high for **1b** under thermal and catalytic ($ZnBr_2$) conditions and complete in the presence of BF_3, whereas **1a** and **1d** only exhibit a complete endo selectivity in the presence of BF_3.

Introduction

The use of activated vinyl sulfoxides as dienophiles in asymmetric Diels−Alder reactions has gained wide attention in recent years[1] due to the ability of the sulfinyl group to control the π-facial selectivity. The presence of additional activating groups at vinyl sulfoxides is necessary in order to increase their reactivity (unsubstituted vinyl sulfoxides are very poor dienophiles) and restrict the conformational mobility around the C−S bond. In this sense, several groups have been added to sulfinyl ethylenes, such as carbonyl,[2] nitro,[3] sulfonyl,[4] and sulfinyl.[1g,5] Nevertheless, the most widely studied one is doubtlessly the ester group,[1b] the contribution of Koizumi in this field clearly being the most significant.[6] One of the problems limiting the scope of these dienophiles is the lack of efficient methods for their syntheses. In the case of 3-sulfinylacrylates (which are the most used sulfinyl dienophiles in the synthesis of natural products), it is due to the formation of mixtures of aryl vinyl sulfoxide epimers at sulfur (when asymmetric oxidation of chiral vinyl sulfides is required[7]) and/or (*E*)- and (*Z*)-isomers (always observed from methods using Emmons−Horner reactions[8]), the separation of which was required previous to their use as dienophiles. The second problem associated with the use of these dienophiles derives from their moderate or low reactivity. To increase it, the most usually adopted solution has been the use of sulfoxides bearing aryl groups with higher electron-withdrawing power than that of *p*-tolylsulfinyl (usually pyridyl derivatives) and/or Lewis acids as catalysts (not always compatible with dienes or adducts), which, in their turn, are essential to achieve an efficient control of the π-facial selectivity in many cases.[6] The control of the endo/exo selectivity is more difficult. It is moderate with 2-sulfinylacrylates[9] and even lower with *trans*-3-sulfinylacrylates,[8a,10] which should be inferred from the endo-director character of both groups (SOAr and CO_2R). The best results were obtained from *cis*-3-sulfinylacrylates, which afforded endo adducts in a highly stereoselective manner only when reactions with cyclopentadiene were catalyzed by Et_2AlCl.[11]

Since acrylonitriles are among the most widely used dienophiles, it was surprising that the cyano group had never been used as an activating moiety of vinyl sulfox-

(1) (a) Carreño, M. C. *Chem. Rev.* **1995**, *95*, 1717. (b) Carretero, J. C.; García Ruano, J. L.; Martín Cabrejas, L. M. *Tetrahedron: Asymmetry* **1997**, *8*, 2215 (and references cited). (c) Carreño, M. C.; García Ruano, J. L.; Urbano, A.; López-Solera, M. I. *J. Org. Chem.* **1997**, *62*, 976 (and references cited). (d) Yamakoshi, Y. N.; Ge, W.-Y.; Sugita, J.; Okayama, K.; Takahashi, T.; Koizumi T. *Heterocycles* **1996**, *42*, 129 (and references cited). (e) Cecchet, E.; Di Furia, F.; Licini, G.; Modena, G. *Tetrahedron: Asymmetry* **1996**, *7*, 369. (f) Hayes, P.; Dujardin, G.; Maignan, C. *Tetrahedron Lett.* **1996**, *21*, 3687 (and references cited). (g) Aggarwal, V. K.; Drabowicz, J.; Grainger, R. S.; Gültekin, Z.; Lightowler, M.; Spargo, P. L. *J. Org. Chem.* **1995**, *60*, 4962 (and references cited).

(2) (a) Alcudia, F.; Llera, J. M.; Ordoñez, M. *Tetrahedron Lett.* **1995**, *36*, 4889. (b) Guessous, A.; Rouessac, F.; Maignan, C. *Bull Soc. Chim. Fr.* **1986**, 837. (c) De Lucchi, O.; Lucchini, V.; Marchioro, C.; Valle, G.; Modena, G. *J. Org. Chem.* **1986**, *51*, 1457. (d) Brimble, M. A.; Davis, B. R. *Tetrahedron* **1985**, *41*, 4965.

(3) Fuji, K.; Tanaka, K.; Abe, H.; Matsumoto, K.; Harayama, T.; Ikeda, A.; Taga, T.; Miwa, Y.; Node, M. *J. Org. Chem.* **1994**, *59*, 2221.

(4) López, R.; Carretero, J. C. *Tetrahedron: Asymmetry* **1991**, *2*, 93.

(5) (a) Arai, Y.; Kuwayama, S.; Takeuchi, Y.; Koizumi, T. *Synth. Commun.* **1986**, *16*, 233. (b) De Lucchi, O.; Fabbri, D.; Lucchini, V. *Synlett* **1991**, 565. (c) Aggarwal, V. N.; Lightowler, M.; Lindell, S. D. *Synlett* **1992**, 730. (d) Katagiri, N.; Ise, S.; Watanabe, N.; Kaneko, C. *Chem. Pharm. Bull.* **1990**, *38*, 3242. (e) Carretero, J. C.; García Ruano, J. L.; Martín Cabrejas, L. M. *Tetrahedron: Asymmetry* **1997**, *8*, 409.

(6) See Arai, Y.; Koizumi, T. *Sulfur Rep.* **1993**, *15*, 41 (and references cited).

(7) Takayama, H.; Iyobe, A.; Koizumi, T. *J. Chem. Soc., Chem. Commun.* **1986**, 771. The use of sulfoxides bearing bornyl and isobornyl moieties joined to the sulfur atom, which control the asymmetric oxidation of thioethers into sulfoxides, allowed solution of this problem (De Lucchi, O.; Lucchini, V.; Marchioro, C.; Valle, G.; Modena, G. *J. Org. Chem.* **1986**, *51*, 1457), but these sulfoxides have never been used in the synthesis of natural products.

(8) (a) Koizumi, T.; Hakamada, I.; Yoshii, E. *Tetrahedron Lett.* **1984**, *25*, 87. (b) Maignan, C.; Guessoues, A.; Rouessac, F. *Tetrahedron Lett.* **1984**, *25*, 1727.

(9) Arai, Y.; Kuwayama, S.; Takeuchi, Y.; Koizumi, T. *Tetrahedron Lett.* **1984**, *25*, 6205.

(10) Proust, S. M.; Ridley, D. D. *Aust. J. Chem.* **1984**, *37*, 1677.

(11) Arai, Y.; Hayashi, M.; Yamamoto, M.; Takayama, H.; Koizumi, T. *Chem. Lett.* **1987**, 185.

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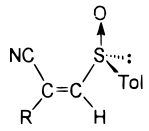
Scheme 1



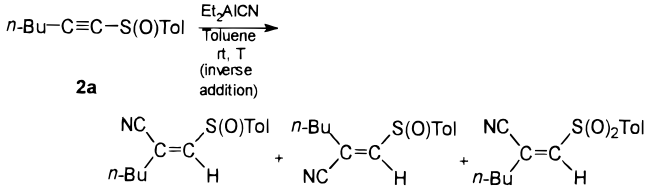
R = *n*-Bu (**1a**), H (**1b**)
t-Bu (**1c**), Bn (**1d**)

ides in asymmetric Diels−Alder reactions.[12] Taking into account that CN and CO_2R groups are synthetic equivalents and the synthesis of nitriles can be achieved by methods different to those of esters, we decided to set up the search of efficient methods to prepare optically pure 3-sulfinylacrylonitriles and the study of their behavior as asymmetric dienophiles. In this sense, the linear structure of the cyano group, as compared with the trigonal structure of the CO_2R group, suggested significant differences in both π-facial and mainly endo/exo selectivities (the steric interactions of these groups with the sulfinyl one must be quite different) for the evolution of sulfinylacrylates and sulfinylnitriles. Finally, despite that the reactivity of both types of dienophiles must be predictably similar, the influence of different Lewis acids as catalysts could be different and must also be investigated. In this paper we report the highly stereocontrolled hydrocyanation of alkynyl sulfoxides with Et_2AlCN to afford (*R*,*Z*)-3-*p*-tolylsulfinylacrylonitriles **1a**−**d** (Scheme 1), as well as the behavior of these compounds as dienophiles, which present clear advantages with respect to sulfinyl esters, mainly due to their ability to invert the π-facial selectivity, depending on the Lewis acid used as the catalyst, and the interesting behavior of the resulting sulfinylnitriles under acidic hydrolysis conditions.

Results and Disccussion

Synthesis of sulfinylacrylonitriles. To achieve the synthesis of the starting (*Z*)-sulfinyldienophiles **1a**−**d**, we have investigated the reaction of 1-alkynyl sulfoxides **2a**−**d**[13] with Et_2AlCN (Tables 1 and 2). In previous papers,[14] we had demonstrated that the addition of this hydrocyanating reagent to the carbonyl group of α-sulfinyl ketones takes place with very high stereoselectivity, presumably due to the association of the sulfinyl oxygen with the metal as a previous step to the intramolecular cyanide transfer. On the basis of this assumption, we reasoned that a similar highly stereoselective addition could take place on alkynyl sulfoxides, provided that the species resulting from their association with Et_2AlCN were able to evolve through an intramolecular conjugated addition.

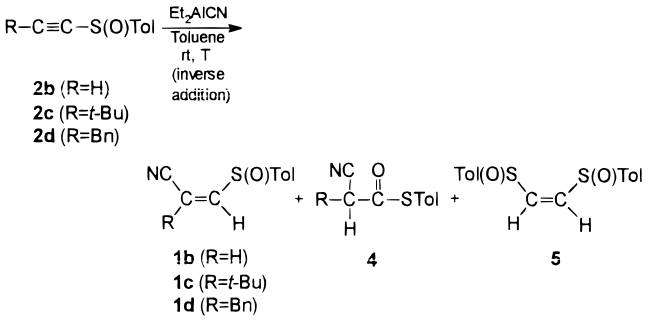
Table 1. Composition of Reaction Mixtures Obtained by Treatment of 2a with Et_2AlCN (2 equiv) in Toluene



entry	*T* (°C)[a]	*t* (h)	**2a**	**1a**	**1e**	**3**
1	−78	0.5	86	14		
2	−78	2	74	26		
3	−78	24	40	40		20
4	−20	0.5	24	75	1	
5	−20	2		95	5	
6	−20	14		56	5	39
7	20	0.5		80	20	
8	20	2		76	24	
9	20	24		61	24	15

[a] At 60 °C the formation of side products can be detected.

Table 2. Composition of the Reaction Mixtures Obtained by Treatment of 2d and 2c with Et_2AlCN (2 equiv) in Toluene



entry	substrate	*T* (°C)	*t* (h)	**1d**	**1c**	**1b**	others
1	**2d**	−20	2	100(90)[a]			
2	**2c**	−20	2		41(30)[a]		59 (55)[a,b]
3	**2c**	+20	1		25		75[b]
4	**2c**	−78	2		24		76[c]
5	**2c**	−78	24		66(60)[a]		34[c]
6	**2b**	−20	2		complex mixture		
7	**2b**	−20	3[e]			(55)[a]	9[d]

[a] In parentheses are the isolated yields after chromatography of the crude reaction. [b] Compound **4**. [c] Starting **2c**. [d] Compound **5**. [e] In minutes.

The results obtained in reactions of alkynyl sulfoxide **2a** with Et_2AlCN in toluene are collected in Table 1. As we can see, an increase in the reaction time provokes the oxidation of **1a** into sulfone **3**.[15] As the temperature became higher, the formation of (*E*)-sulfinyl derivative **1e** could be detected and its proportion increased with the temperature. Further experiences varying the amount of reagent demonstrated that the use of 4, 6, or 8 equiv of Et_2AlCN gave the same results. Much lower reactivity and selectivity were observed when the amount of reagent was smaller than 2 equiv.

The best conditions found in the above experiences (Table 1, entry 5) were successfully used to synthesize 1-alkynyl sulfoxide **1d** (Table 2), which was obtained from

(12) Ono, T.; Tamaoka, T.; Yuasa, Y.; Matsuda, T.; Nokami, J.; Wakabayashi, S. *J. Am. Chem. Soc.* **1984**, *106*, 7890. Trost, B. M.; Mallarts, S. *Tetrahedron Lett.* **1993**, *34*, 8025. Hiroi, K.; Umemura, M. *Tetrahedron* **1993**, *49*, 1831.

(13) The synthesis of optically pure 1-alkynyl *p*-tolyl sulfoxides **2a-d** was accomplished following the previously described procedure (Kosugi, H.; Kitaoka, M.; Tagami, K.; Takahashi, A.; Uda, H. *J. Org. Chem.* **1987**, *52*, 1078) consisting in the reaction of *l*-menthyl (*S*)-*p*-toluenesulfinate (Mioskowsky, C.; Solladié, G. *Tetrahedron* **1980**, *36*, 227. Solladié, G. *Synthesis* **1981**, 185) and the corresponding 1-alkynylmagnesium bromide in toluene. In our hands, the reaction temperature had to be increased from −20 °C, as described, to 20 °C in order to get good yields.

(14) (a) García Ruano, J. L.; Martín Castro, A. M.; Rodríguez, J. H. *Tetrahedron Lett.* **1991**, *32*, 3195. (b) García Ruano, J. L.; Martín Castro, A. M.; Rodríguez, J. H. *J. Org. Chem.* **1992**, *57*, 7235. (c) Escribano, A.; García Ruano, J. L.; Martín Castro, A. M.; Rodríguez, J. H. *Tetrahedron* **1994**, *50*, 7567.

(15) We had observed the oxidation of sulfoxides into sulfones during hydrocyanation of β-sulfinylimines with Et_2AlCN (unpublished results) in those cases requiring long reaction times. The course of these reactions is not clear.

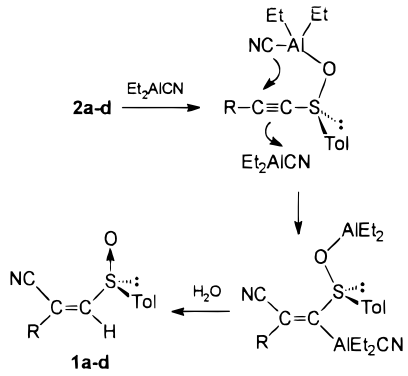
2d and Et_2AlCN (2 equiv) as the sole reaction product in 90% yield. When compound **2c** reacted under identical conditions (−20 °C, 2 h), **1c** was obtained in moderate yield (entry 2). The major product of this reaction was (±)-*S*-*p*-tolyl 3,3-dimethyl-2-cyanobutanethioate (**4**),[16] the proportion of which increased up to 75% when the reaction was conducted at room temperature (entry 3). Nevertheless, it was not detected when the reaction was carried out at −78 °C (entries 4 and 5). Under these conditions, compound **1c** was the sole reaction product (60% yield after 24 h).[17] The formation of the sulfone derived from **2c** was not detected even after 5 days of reaction.

The synthesis of (*Z*)-3-[(*R*)-*p*-tolylsulfinyl]propenenitrile **1b** was accomplished by reaction of (*R*)-ethynyl *p*-tolyl sulfoxide (**2b**) with Et_2AlCN. When the reaction was conducted at −20 °C for 2 h, a complex mixture of compounds containing **1b** in very low proportion (<5%) was obtained. Better results were achieved at −20 °C at shorter times (3 min), **1b** being the major product (55% isolated yield).[18]

Reactions with TMSCN/18-crown-6 ether/KCN[19] were also studied, but the results obtained with the different substrates were less satisfactory.[20]

The formation of (*Z*)-3-*p*-tolylsulfinylacrylonitriles as the major hydrocyanation products could be rationalized as indicated in Scheme 2, by assuming an intramolecular cyanide transfer from the species resulting from association of the sulfinyl oxygen with the reagent.

Scheme 2



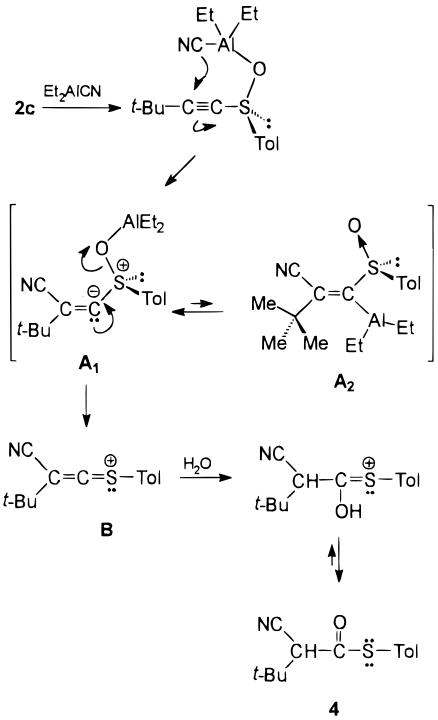
This mechanistic proposal was supported by treatment of the 1:1 complex **2b**−MAD [methylbis(di-2,6-*tert*-butyl-4-methylphenoxy)aluminum] with Et_2AlCN. Under these conditions, the association of the aluminum of the hydrocyanating reagent with the sulfinylic oxygen was prevented, and the unaltered starting material **2b** was recovered.

Reactions with Cyclopentadiene. Reactions of dienophiles **1a** and **1d** with cyclopentadiene in refluxing CH_2Cl_2 for several hours afforded mixtures of *endo*-**6** and *exo*-**6** cycloadducts (Table 3, entries 1 and 4). Unaltered **1c** could be recovered after 120 h under these conditions (entry 3), whereas **1b** only required 1 h to be completely transformed into a major adduct, *endo*-**6b** (entry 2). Addition of $ZnBr_2$ improved the reactivity (**1c** remains unaltered after 120 h, but at room temperature **1a**, **1b**, and **1d** required reaction times identical to those at reflux in the absence of a catalyst), but it had scarce effect on the π-facial selectivity (it remains complete with all the dienophiles) and on the endo/exo selectivity (which remains low with **1a** and **1d** and high with **1b**) (entries 5, 6, and 8).

The endo or exo stereochemistry of the obtained adducts could be established from the value of the coupling constants $J_{3,4}$ (3.2 Hz for the endo adducts and ca. 0 Hz for the exo ones) and $J_{3,7}$ (2.3 Hz for the exo adducts, as a consequence of the W planar arrangement between H-3 and H-7; see the reaction shown in Table 3). The absolute configuration of substrates *endo*-**6a** and *exo*-**6a** could be unequivocally determined by X-ray studies (Supporting Information).

To explain the complete π-facial diastereoselectivity observed for these reactions, it is necessary to assume that the conformational equilibrium of dienophiles **1** is completely shifted toward rotamer **B** depicted in Scheme 3, with the sulfinyl oxygen in an *s*-trans arrangement. This preference must be a consequence of the strong dipolar repulsion between the CN and SO groupings.[21] The attack of the diene, governed by a steric approach

(16) To explain the formation of racemic thioester **4**, we assume the process is an additive Pummerer reaction (see de Lucchi O.; Miotti U.; Modena G. In *Organic Reactions*; Paquette, L., et al., Eds.; John Wiley & Sons: New York, 1991; Vol. 40, p 157). The equilibrium between ylide $\mathbf{A_1}$ and α-methalated species $\mathbf{A_2}$ must be shifted toward $\mathbf{A_1}$ due to unstabilizing steric interactions between one of the substituents of the aluminum and the *tert*-butyl group. From $\mathbf{A_1}$ we postulate the formation of **B**, the hydrolysis of which and further deprotonation explain the formation of **5c**.



(17) At low temperature (−78 °C), thioester **5c** was detected only after long reaction times.

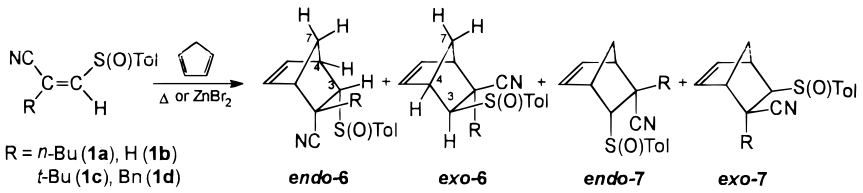
(18) A decrease in the reaction temperature hinders the transformation of substrate **2b** and favors the predominance of undesired products.

(19) Kunz, H.; Sager, W.; Pfrengle, W.; Schanzenbach, D. *Tetrahedron Lett.* **1988**, *29*, 4397.

(20) Lower reactivity and sluggish reactions containing so far unidentified decomposition products were the general characteristics of these reactions. Under the best conditions, compound **2a** yielded **1a** (60% estimated yield) at 0 °C after 72 h, whereas **1b** was obtained from **2b** (−78 °C, 46 h, 42% estimated yield by NMR), and **1c** from **2c** (0 °C, 21 h, 62% estimated yield).

(21) To check this assumption, we carried out the cycloaddition of **1a** in solvents of higher polarity, thus favoring the most polar *s*-cis conformations. The obtained results indicate the formation of a mixture containing four adducts, the proportion of the two new adducts being higher with the increase in the solvent polarity (Table 3, entries 9 and 10).

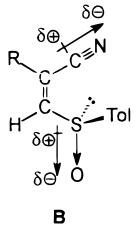
Table 3. Diels-Alder Reactions of Dienophiles 1a-1d with Cyclopentadiene under Thermal Conditions or in the Presence of $ZnBr_2$



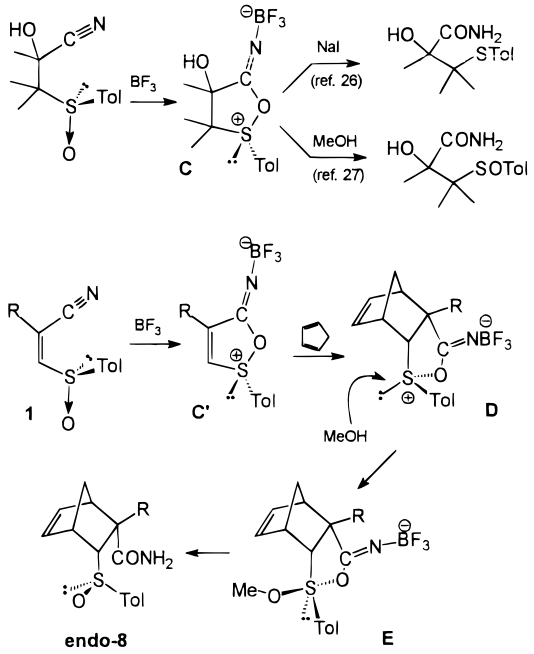
		cycloaddition conditions					
entry	dienophile	cat. (2 equiv)	solvent	*T* (°C)	*t* (h)	*endo*-**6**/*exo*-**6**/ *endo*-7/*exo*-7[a]	yield (%)
1	**1a**		CH_2Cl_2	50	72	48/52/0/0	89
2	**1b**		CH_2Cl_2	50	1	>90/<10/0/0	78
3	**1c**		CH_2Cl_2	50	120		
4	**1d**		CH_2Cl_2	50	20	45/55/0/0	91
5	**1a**	$ZnBr_2$	CH_2Cl_2	20	70	45/55/0/0	82
6	**1b**	$ZnBr_2$	CH_2Cl_2	20	1	>90/<10/0/0	75
7	**1c**	$ZnBr_2$	CH_2Cl_2	20	120		
8	**1d**	$ZnBr_2$	CH_2Cl_2	20	20	58/42/0/0	81
9	**1a**		MeOH	50	48	42/48/6/4	71
10	**1a**		1:1 MeOH− H_2O	50	36	36/45/13/6	72

[a] Isomeric ratio as determined by ^1H NMR analysis of the crude mixtures.

Scheme 3



Scheme 4



control, must take place from the less hindered diastereotopic face of the dienophile (back face in Scheme 3) adopting such a conformation.

The comparison of the results obtained from our sulfinylnitriles with those from (*Z*)-3-*p*-tolylsulfinylacrylates[8,22,23] suggests that the first ones are slightly more reactive. Otherwise, the π-facial selectivity of reactions of **1** is also higher than that of their corresponding esters, but this does not mean a significant improvement because de are usually higher than 90% starting from acrylates. Concerning the endo/exo selectivity, the behavior of nitriles and esters is quite similar. It is very high for **1b**, but substantially decreases for **1a** and **1d**. The observed influence of the $ZnBr_2$ as a catalyst of cycloadditions of **1** (it increases the reactivity, slightly modifies the endo/exo selectivity, but does not affect the π-facial selectivity) suggests that it can associate with nitrogen, oxygen, or both, but this association must not modify the conformational preferences of the dienophiles. A similar behavior was observed for reactions of (*Z*)-3-sulfinylacrylates catalyzed by other Lewis acids.[10] Therefore, despite the wide use of these substrates as dienophiles in the asymmetric synthesis of many natural products,[7,24] there is not any known catalyst able to reverse the sense of the π-facial selectivity of their cycloadditions.

At this point we decided to study the influence of the BF_3 on the π-facial diastereoselectivity of our sulfinylnitriles.[25] This idea derived from the finding by our research group that the hydrolysis of β-sulfinylnitriles with BF_3/NaI into β-sulfenylcarboxyamides[26] or BF_3/MeOH into β-sulfinylcarboxyamides[27] took place under very mild conditions, presumably due to the formation of a cyclic oxosulfonium intermediate (**C**, Scheme 4). On the basis of this assumption we reasoned that compounds **1** could evolve into intermediates **C′** in the presence of

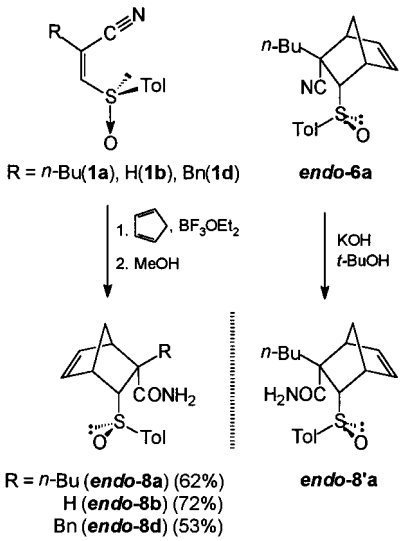
(22) Guessous, A.; Rouessac, F.; Maignan, C. *Bull. Soc. Chim. Fr.* **1986**, 837.

(23) Brimble, M. A.; Davis, B. R. *Tetrahedron* **1985**, *41*, 4965.

(24) (a) Arai, Y.; Hyashi, Y.; Matatoshi, Y.; Takayama, H.; Koizumi, T. *Chem. Lett.* **1987**, 185. (b) Arai, Y.; Hayashi, Y.; Matatoshi, Y.; Takayama, H.; Koizumi, T. *J. Chem. Soc., Perkin Trans. 1* **1988**, 3133. (c) Takayama, H.; Iyobe, A.; Koizumi, T. *Chem. Pharm. Bull.* **1987**, *35*, 433. (d) Takahashi, T.; Iyobe, A.; Arai, Y.; Koizumi, T. *Synthesis* **1989**, 189. (e) Takahashi, T.; Katsubo, H.; Iyobe, A.; Namiki, T.; Koizumi, T. *J. Chem. Soc., Perkin Trans. 1* **1990**, 3065. (f) Takayama, H.; Hayashi, K.; Takeuchi, Y.; Koizumi, T. *Heterocycles* **1986**, *24*, 2137. (g) Takayama, H.; Hayashi, K.; Koizumi, T. *Tetrahedron Lett.* **1986**, *27*, 5509.

(25) It had been unsuccessfully used with sulfinylacrylates (ref 10).

Scheme 5



BF_3. The evolution of **C′** would exhibit the π-facial selectivity opposite to that observed under thermal conditions [compare the spatial arrangement of the substituents around the sulfur for conformation **B** (see Scheme 3) and species **C′**].

Diels−Alder reactions of compounds **1**, catalyzed by $BF_3{\cdot}OEt_2$, were studied at −20 °C, because higher temperatures determine the fast polymerization of the diene (Scheme 5). Under these conditions, reactions of **1a** and **1d** were very slow and required long reaction times (15 days) to afford *endo*-**8a** (62%) and *endo*-**8d** (53%), respectively, as sole adducts, after quenching the reaction mixtures with methanol. Compound *endo*-**8b** was obtained as a sole adduct (72% yield) by treatment of **1b** with BF_3 in CH_2Cl_2 at reflux for 1 h, further reaction with cyclopentadiene for 3 h at −20 °C, and final addition of methanol.[28]

The spectroscopic study of compounds *endo*-**8** revealed that they are adducts containing *p*-tolylsulfinyl and carboxamide groups (the latter presumably resulting from hydrolysis of the cyano group), both in an endo arrangement. The absolute configuration of these adducts has been established as follows: basic hydrolysis (KOH/*t*-BuOH at reflux[29]) of nitrile *endo*-**6a**, the configuration of which had been unequivocally established by X-ray diffraction (see above), led to the amide *endo*-**8′a**, which turned out to be an enantiomer of *endo*-**8a**.[30] This result allowed us to assign to the latter, and therefore to all *endo*-**8** adducts, the configuration depicted in Scheme 5.

The formation of *endo*-**8** as the only adducts from reactions of cyclopentadiene and **1** catalyzed by BF_3 can be explained as indicated in Scheme 4. The reaction of intermediate **C′** with the diene must take place in a completely endo- and π-facial-selective manner, yielding species **D**, which would be attacked by the nucleophile (methanol) added during the workup of the reaction, affording an intermediate sulfurane **E,** which evolves into *endo*-**8** adducts by further reaction with a second molecule of MeOH. To our knowledge, this is the first report on a complete inversion of the configuration of sulfoxides in acidic medium.[31]

Conclusion

We have demonstrated that hydrocyanation of alkynyl sulfoxides with Et_2AlCN is highly stereoselective, thus allowing the first synthesis of optically pure (*Z*)-3-*p*-tolylsulfinylacrylonitrile (**1b**) as well as its 2-*n*-butyl (**1a**), 2-*tert*-butyl (**1c**), and 2-benzyl (**1d**) derivatives. The dienophilic reactivity of these acrylonitriles is similar or slightly higher than that of their corresponding acrylates. The π-facial selectivity of their reactions with cyclopentadiene is complete under thermal and catalytic $ZnBr_2$ conditions, and it can be totally reversed in the presence of BF_3. The endo-selectivity is scarce for 2-substituted derivatives, but very high for compound **1b**. All the reactions are completely endo-selective, when conducted under BF_3 catalysis, and yield sulfinyl carboxamides (instead of the expected nitriles), due to the hydrolysis of the cyano group, which takes place with concomitant inversion of the configuration at sulfur.

Experimental Section

General Methods. All moisture sensitive reactions were performed in flame-dried glassware equipped with rubber septa under positive pressure of argon. Solvents were dried according to literature procedures.[32] Et_2AlCN was used as a commercially available 1.0 M solution in toluene. The cyclopentadiene used in Diels−Alder cycloadditions was obtained following the procedure described in the literature.[33] $ZnBr_2$ was flame-dried in the reaction flask before use. Flash chromatography was carried out with silica gel 60 (230−400 mesh ASTM), and silica gel F254 plates were used for preparative TLC. NMR spectra (Tables 4 and 5) were determined in $CDCl_3$ solutions at 200.1 and 50.3 MHz for ^1H and ^{13}C NMR, respectively.

1-Alkynyl *p*-tolyl sulfoxides **2a**−**d** were prepared following the described procedure, with slight modification.[13]

(+)-(*S*)-1-Hexinyl *p*-tolyl sulfoxide (2a):[13] $[\alpha]^{20}_D$ +89.7 (*c* 1.0, acetone); ^1H NMR δ 7.68 and 7.35 (AA′BB′ system, 4H), 2.41 (s, 3H), 2.40 (t, 2H, J = 7.0), 1.70−1.10 (m, 4H), 0.90 (t, 3H, J = 7.0); ^{13}C NMR δ 141.4, 140.6, 129.3 (2C), 124.2 (2C), 104.9, 77.7, 28.8, 21.1, 20.6, 18.6, 12.7.

(+)-(*R*)-Ethynyl *p*-tolyl sulfoxide (2b):[13] $[\alpha]^{20}_D$ +220.1 (*c* 1.0, $CHCl_3$); ^1H NMR δ 7.71 and 7.36 (AA′BB′ system, 4H), 3.71 (s, 1H), 2.43 (s, 3H); ^{13}C NMR δ 142.7, 140.6, 130.1 (2C), 125.0 (2C), 90.2, 81.6, 21.3.

(+)-(*S*)-3,3-Dimethyl-1-butynyl *p*-Tolyl Sulfoxide (2c). Compound **2c** (white solid) was obtained in 81% yield from the reaction of 3,3-dimethyl-1-butynylmagnesium bromide and *l*-menthyl (*S*)-*p*-toluenesulfinate. Reaction time 3.5 h. It was crystallized from hexane: mp 71−72 °C; $[\alpha]^{20}_D$ +84.8 (*c* 0.23,

(26) García Ruano, J. L.; Martín Castro, A. M.; Rodríguez Ramos, J. H. *Tetrahedron Lett.* **1996**, *37*, 4569.

(27) García Ruano, J. L.; Martín Castro, A. M.; Rodríguez, J. H. Rubio Flamarique, A. C. *Tetrahedron: Asymmetry* **1997**, *8*, 3503.

(28) These conditions were not successful for **1a** and **1d**, which yielded mixtures containing **8a** and **8d** in minor proportion. The structure of the major compounds obtained in these reactions is currently under investigation.

(29) Hall, J. H.; Gisler, M. *J. Org. Chem.* **1976**, *41*, 3769. Under these conditions, sulfur configuration should not be affected.

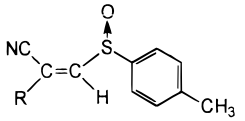
(30) In this reaction compound **11** was also recovered (see Experimental Section). It results from epimerization at C-α of the sulfinyl group under basic reaction conditions.

(31) We are currently investigating the mechanistic proposal depicted in Scheme 4 to explain the inversion of the herein described configuration, studying the scope of these hydrolysis reactions for other β-sulfinyl nitriles and related substrates, and searching the proper experimental conditions to get the complete inversion of the sulfoxides in acidic medium. The results of this study will be published in due course.

(32) Perrin, D. D.; Armarego, W. L. F.; Perrin, D. R. *Purification of Laboratory Chemical*, 2nd ed.; Pergamon Press: New York, 1980.

(33) Vogel A. I. *Practical Organic Chemistry*, 5th ed., Longman Scientific and Technical: London, 1989; p 1122.

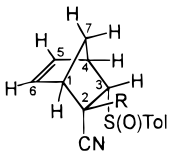
Table 4. ^{1}H NMR Data of Compounds 1a−e



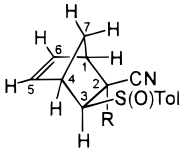
compd	δ (multiplicity, *J* in hertz)			
	C_6H_4[b]	CH_3Ar	=CH	R
1a (R = *n*-Bu)	7.59 and 7.35	2.43 (s)	6.76 (s)	2.32 (t, 2H, 7.0), 1.70−1.20 (m, 4H), 0.89 (t, 3H, 7.0)
1b (R = H)	7.59 and 7.35	2.41 (s)	7.10 (d, 10.2)	5.89 (d, 10.2)
1c (R = *t*-Bu)	7.58 and 7.35	2.42 (s)	6.73 (s)	1.18 (s, 9H)
1d (R = Bn)	7.57 and 7.35	2.42 (s)	6.76 (s)	7.40−7.25 (m, 3H), 7.20−7.05 (m, 2H), 3.60 (s, 2H)
1e[a] (R = *n*-Bu)	7.52 and 7.37	2.43 (s)	6.86 (s)	2.85−2.50 (m, 2H), 1.80−1.30 (m, 4H), 0.97 (t, 3H, 7.0)

[a] *E* isomer. [b] All are an AA′BB′ system.

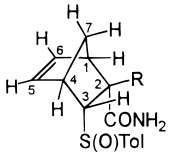
Table 5. ^{1}H NMR Data of Adducts 6 and 8



endo-**6**



exo-**6**



endo-**8**

compd	δ (multiplicity, *J* in hertz)								
	C_6H_4[b]	CH_3Ar	H-1	H-3	H-4	H-5	H-6	H-7a and H-7b	R
endo-**6a** (R = *n*-Bu)	7.80, 7.33	2.41 (s)	3.20−3.00 (m)	3.12 (d, 3.2)	3.70−3.50 (m)	6.73 (dd, 3.2 & 5.4)	6.55 (dd, 3.2 & 5.4)	1.85−1.65 (m), 1.65−1.50 (m)	1.60−0.85 (m, 6H), 0.67 (t, 3H, 7.0)
endo-**6b** (R = H)	7.79, 7.32	2.41 (s)	3.50−3.30 (m)	2.90 (dd, 3.2 & 8.6)	3.70−3.55 (m)	6.71 (dd, 2.7 & 5.9)	6.52 (dd, 2.7 & 5.9)	1.85−1.65 (m), 1.45−1.25 (m)	3.62 (dd, 1H, 3.2 & 8.6)
endo-**6d** (R = Bn)	7.77, 7.31	2.40 (s)	3.20−3.00 (m)	3.23 (d, 3.2)	3.70−3.50 (m)	6.69 (dd, 2.7 & 5.4)	6.38 (dd, 3.2 & 5.4)	1.85−1.65 (m, 2H)	7.35−7.15 (m, 3H), 7.10−6.90 (m, 2H), 2.59 & 2.30 (AB system, 2H, 13.7)
exo-**6a** (R = *n*-Bu)	7.78, 7.34	2.41 (s)	3.40−3.20 (m)	2.34 (d, 3.2)	3.70−3.50 (m)	6.32 (dd, 3.2 & 5.4)	6.11 (dd, 3.2 & 5.4)	2.32−2.20 (m), 1.90−1.70 (m)	1.20−1.00 (m, 6H), 0.73 (t, 3H, 7.0)
exo-**6d** (R = Bn)	7.65, 7.30	2.38 (s)	3.20−3.00 (m)	2.40 (d, 2.1)	3.65−3.45 (m)	6.39 (dd, 3.1 & 5.5)	6.27 (dd, 3.1 & 5.5)	2.25−2.20 (m), 1.76−1,71 (m)	7.40−7.15 (m, 3H), 7.10−6.90 (m, 2H), 2.41 & 1.93 (AB system, 2H, 13.3)
endo-**8a** (R = *n*-Bu)	7.77, 7.25	2.37 (s)	2.90−2.70 (m)	3.13 (d, 3.2)	3.60−3.40 (m)	6.68 (dd, 2.7 & 5.9)	6.33 (dd, 2.7 & 5.4)	1.90−1.40 (m, 2H)	5.66 (bs, 1H), 5.30 (bs, 1H), 1.90−1.40 (m, 4H), 1.05 (m, 2H, 7.0), 0.63 (t, 3H, 7.0)
endo-**8b** (R = H)[a]	7.52, 7.18	2.25 (s)	2.20−3.00 (m)	2.98 (dd, 3.3 & 8.7)	3.40−3.30 (m)	6.38 (dd, 2.9 & 5.4)	6.12 (dd, 3.0 & 5.9)	1.60−1.45 (m), 1.45−1.30 (m)	3.67 (dd, 1H, 3.3 & 8.7)
endo-**8d** (R = Bn)	7.49, 7.33	2.48 (s)	3.20−3.00 (m)	3.24(d, 2.7)	3.40−3.20 (m)	6.76 (dd, 2.7 & 5.4)	6.31 (dd, 2.7 & 5.4)	1.95−1.75 (m), 1.75−1.60 (m)	7.50−7.15 (m, 5H), 6.20 (bs, 1H), 5.40 (bs, 1H), 3.68 & 2.78 (AB system, 2H, 13.4)

[a] Methanol-d_4 as solvent. [b] All are an AA′BB′ system.

$CHCl_3$); ^{1}H NMR δ 7.68 and 7.34 (AA′BB′ system, 4H), 2.43 (s, 3H), 1.27 (s, 9H); ^{13}C NMR δ 142.2, 141.5, 130.2 (2C), 125.3 (2C), 112.8, 78.0, 30.0 (3C), 28.6, 21.5. Anal. Calcd for $C_{13}H_{16}$SO: C, 70.87; H, 7.32; S, 14.55. Found: C, 70.74; H, 7.02; S, 14.78.

(+)-(*S*)-3-Phenyl-1-propynyl *p*-Tolyl Sulfoxide (2d). Compound **2d** (white solid) was obtained in 40% yield from the reaction of 3-phenyl-1-propynylmagnesium bromide and *l*-menthyl (*S*)-*p*-toluenesulfinate.[34] Reaction time 3 h. It was crystallized from hexane: mp 86−87 °C; $[\alpha]^{20}_D$ +43.5 (*c* 0.7, $CHCl_3$); ^{1}H NMR δ 7.73 and 7.35 (AA′BB′ system, 4H), 7.40−7,10 (m, 5H,), 3.83 (s, 2H), 2.44 (s, 3H); ^{13}C NMR δ 142.2, 140.9, 133.8, 130.0 (2C), 128.6 (2C), 127.8 (2C), 127.0, 125.0 (2C), 112.4, 80.1, 25.8, 21.3. Anal. Calcd for $C_{16}H_{14}$SO: C, 75.56; H, 5.55; S, 12.60. Found: C, 75.06; H, 5.36; S, 12.44.

Hydrocyanation of 1-Alkynyl Sulfoxides into β-Sulfinylacrylonitriles. (i) With Et_2AlCN.[14] A solution of 1-alkynyl *p*-tolyl sulfoxide in 4 mL of toluene was added into a solution of 2 mmol of Et_2AlCN in 3 mL of toluene, and the mixture was stirred under argon; reaction times and temperatures are indicated in each case. The reaction mixture was quenched with 5 mL of a saturated aqueous solution of potassium sodium tartrate. The organic layer was diluted with 5 mL of CH_2Cl_2 and the mixture was stirred until there was clean layer separation. The aqueous solution was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried over Na_2SO_4 and the solvent was evaporated. The crude mixture was purified by flash chromatography using the eluent indicated in each case.

(ii) With TMSCN/18-Crown-6 Ether/KCN.[19] A solution of 1 mmol of 1-alkynyl *p*-tolyl sulfoxide in 10.2 mL of CH_2Cl_2 was added into a solution of 26.8 mg (0.1 mmol) of 18-crown-6 ether and 7.8 mg (0.12 mmol) of KCN in 4 mL of CH_2Cl_2. The

(34) In this reaction the following products were also isolated: (−)-(*R*)-[(*E*)-2-bromo-3-phenyl-1-propenyl] *p*-tolyl sulfoxide (**9**), (−)-(*R*)-[(*Z*)-2-benzyl-5-phenyl-1-penten-3-ynyl] *p*-tolyl sulfoxide (**10**) (14%), and the starting (−)-(*S*)-*p*-toluenesulfinate (13%). Compound **9** (white solid) was crystallised from diethyl ether: mp 103−104 °C; $[\alpha]^{20}_D$ −196.8 (*c* 0.51, $CHCl_3$); ^{1}H NMR δ 7.61 and 7.33 (AA′BB′ system, 4H), 7.40−7.25 (m, 3H), 7.25−7.10 (m, 2H), 6.60 (s, 1H), 3.84 (s, 2H), 2.43 (s, 3H); ^{13}C NMR δ 141.7, 140.7, 138.4, 135.6, 135.2, 130.1 (2C), 129.1 (2C), 128.7 (2C), 127.5, 124.1 (2C), 48.0, 21.4. Anal. Calcd for $C_{16}H_{15}$BrSO: C, 57.32; H, 4.51; S, 9.56. Found: C, 57.05; H, 4.32; S, 9.80. Compound **10** (white solid) was crystallized from hexane−EtOAc (1: 1): mp 66−67 °C; $[\alpha]^{20}_D$ −528.7 (*c* 0.51, $CHCl_3$); ^{1}H NMR δ 7.54 and 7.32 (AA′BB′ system, 4H), 7.50−7.15 (m, 8H), 7.30−7.10 (m, 2H), 6.39 (s, 1H), 3.82 (s, 2H), 3.57 (s, 2H), 2.43 (s, 3H); ^{13}C NMR δ 141.7, 141.5, 141.1, 136.2, 135.4, 133.4, 129.9 (2C), 129.1 (2C), 128.6 (4C), 127.8 (2C), 127.0, 126.7, 123.9 (2C), 99.3, 78.9, 43.7, 25.9, 21.3. Anal. Calcd for $C_{25}H_{22}$SO: C, 81.04; H, 5.98; S, 8.51. Found: C, 80.51; H, 5.75; S, 8.47.

mixture was cooled at the temperature indicated in each case and 248 mg (2.5 mmol) of TMSCN was added. The solution was stirred at this temperature for the corresponding time. After hydrolysis with 10 mL of water, the crude product was extracted with CH_2Cl_2 (3 × 10 mL), dried over Na_2SO_4, and concentrated. The reaction mixture was purified by flash chromatography; the eluent is indicated in each case.

(−)-(*R,Z*)-2-*n*-Butyl-3-(*p*-tolylsulfinyl)propenenitrile (1a). Compound **1a** was prepared by hydrocyanation of **2a** with Et_2-AlCN (2 h, −20 °C, 85% yield) or with TMSCN/18-crown-6 ether/KCN (72 h, 0 °C, 60% yield). In both cases, chromatography of the reaction mixtures (1:3 EtOAc−hexane) afforded pure **1a** as a yellow oil: $[\alpha]^{20}_D$ −340.0 (*c* 1.0, $CHCl_3$); ^{1}H NMR δ 7.59 and 7.35 (AA′BB′ system, 4H), 6.76 (s, 1H), 2.43 (s, 3H), 2.32 (t, 2H, J = 7.0), 1.70−1.20 (m, 4H), 0.89 (t, 3H, J = 7.0); ^{13}C NMR δ 150.4, 142.4, 139.4, 130.3 (2C), 123.9 (2C), 122.3, 114.7, 34.5, 29.0, 21.4, 21.3, 13.3. HRMS exact mass calcd for $C_{14}H_{17}NOS$ (M^+) 247.1031, found 247.1031.

(−)-(*R,Z*)-3-(*p*-Tolylsulfinyl)propenenitrile (1b). Compound **1b** was prepared by hydrocyanation of **2b** with Et_2AlCN (3 min, −20 °C, 55% yield) or with TMSCN/18-crown-6 ether/KCN (46 h, −78 °C, 30% yield). In both cases, chromatography of the reaction mixtures (3:2 EtOAc−hexane) afforded pure **1b** as a white solid. It was crystallized from hexane−EtOAc (2:1): mp 112−113 °C; $[\alpha]^{20}_D$ −441.8 (*c* 0.69, $CHCl_3$); ^{1}H NMR δ 7.59 and 7.35 (AA′BB′ system, 4H), 7.10 (d, 1H, J = 10.2), 5.89 (d, 1H, J = 10.2), 2.41 (s, 3H); ^{13}C NMR δ 157.7, 142.9, 138.4, 130.4 (2C), 124.1 (2C), 113.1, 104.1, 21.3. Anal. Calcd for $C_{10}H_9NOS$: C, 62.80; H, 4.74; N, 7.32; S, 16.76. Found: C, 62.64; H, 4.64; N, 7.17; S, 17.03.

(−)-(*R,Z*)-2-*t*-Butyl-3-(*p*-tolylsulfinyl)propenenitrile (1c). Compound **1c** was prepared by hydrocyanation of **2c** with Et_2-AlCN (48 h, −78 °C, 60% yield) and ii) with TMSCN/18-crown-6 ether/KCN (21 h, 0 °C, 62% yield). In both cases, chromatography of the reaction mixtures (1:1 EtOAc−hexane) afforded pure **1c** as a white solid. It was crystallized from hexane−EtOAc (6:1): mp 131−132 °C; $[\alpha]^{20}_D$ −234.6 (*c* 0.41, $CHCl_3$); ^{1}H NMR δ 7.58 and 7.35 (AA′BB′ system, 4H), 6.73 (s, 1H), 2.42 (s, 3H), 1.18 (s, 9H); ^{13}C NMR δ 147.7, 142.4, 139.4, 132.5, 130.4 (2C), 123.9 (2C), 114.1, 36.8, 27.9 (3C), 21.4. Anal. Calcd for $C_{14}H_{17}NOS$: C, 67.98; H, 6.93; N, 5.66; S, 12.96. Found: C, 67.94; H, 6.51; N, 5.88; S, 13.03.

(−)-(*R,Z*)-2-Benzyl-3-(*p*-tolylsulfinyl)propenenitrile (1d). Compound **1d** was prepared by hydrocyanation of **2d** with Et_2-AlCN (2 h, −20 °C, 90% yield). Chromatography of the reaction mixture (1:4 EtOAc−hexane) afforded pure **1d** as a white solid. It was crystallized from EtOAc−hexane (1:6): mp 88−89 °C; $[\alpha]^{20}_D$ −336.9 (*c* 0.80, $CHCl_3$); ^{1}H NMR δ 7.57 and 7.35 (AA′BB′ system, 4H), 7.40−7.25 (m, 3H), 7.20−7.05 (m, 2H), 6.76 (s, 1H), 3.60 (s, 2H), 2.42 (s, 3H); ^{13}C NMR δ 151.5, 142.6, 139.3, 133.5, 130.4 (2C), 129.1 (2C), 129.0 (2C), 127.9, 124.1 (2C), 121.3, 114.7, 40.8, 21.4. Anal. Calcd for $C_{17}H_{15}$-NOS: C, 72.57; H, 5.37; N, 4.98; S, 11.39. Found: C, 72.10; H, 5.20; N, 5.08; S, 11.32.

(−)-(*R,E*)-2-*n*-Butyl-3-(*p*-tolylsulfinyl)propenenitrile (1e). Compound **1e** was obtained as a white solid by hydrocyanation of **2a** with Et_2AlCN. When the reaction was carried out at room temperature, after 2 h **1e** (16% yield) and **1a** (70% yield) were isolated after flash chromatography (1:3 EtOAc−hexane) of the reaction mixture. Compound **1e** was crystallized from hexane−diethyl ether (1:1): mp 59−60 °C; $[\alpha]^{20}_D$ −67.0 (*c* 0.64, $CHCl_3$); ^{1}H NMR δ 7.52 and 7.37 (AA′BB′ system, 4H), 6.86 (s, 1H), 2.85−2.50 (m, 2H), 2.43 (s, 3H), 1.80−1.30 (m, 4H), 0.97 (t, 3H, J = 7.0); ^{13}C NMR δ 149.9, 142.3, 138.7, 130.1 (2C), 123.9 (2C), 123.0, 115.9, 29.9, 29.5, 21.4, 21.0, 13.2. Anal. Calcd for $C_{14}H_{17}NOS$: C, 67.98; H, 6.93; N, 5.66; S, 12.96. Found: C, 67.83; H, 6.71; N, 5.79; S, 12.98.

(±)-*p*-Tolyl 3,3-dimethyl-2-cyanobutanethioate (4). Compound **4** was obtained as a white solid in the hydrocyanation of **2c** with Et_2AlCN. When the reaction was carried out at −20 °C for 2 h, **4** (55% yield) and **1c** (30% yield) were isolated after flash chromatography (1:1 EtOAc−hexane) of the reaction mixture. Compound **4** was crystallized from hexane: mp 59−60 °C; ^{1}H NMR δ 7.35 and 7.15 (m, 4H), 3.48 (s, 1H), 2.37 (s, 3H), 1.20 (s, 9H); ^{13}C NMR δ 189.3, 140.5, 134.1 (2C), 130.1 (2C), 122.6, 115.6, 55.2, 35.7, 27.7 (3C), 21.2. Anal. Calcd for $C_{14}H_{17}NOS$: C, 67.98; H, 6.93; N, 5.66; S, 12.96. Found: C, 67.97; H, 6.36; N, 5.58; S, 13.43.

(−)-(*R,R,Z*)-1,2-Bis(*p*-tolylsulfinyl)ethene (5). Compound **5** was obtained as a byproduct of hydrocyanation of **2b** with Et_2AlCN or with TMSCN/18-crown-6 ether/KCN. When the reaction was carried out with Et_2AlCN at −78 °C for 24 h, **5** (27% yield) and **1b** (26% yield) were isolated after flash chromatography (3:2 EtOAc−hexane) of the reaction mixture. Compound **5** was crystallized from hexane−EtOAc (2:3): mp 86−87 °C; $[\alpha]^{20}_D$ −904.8 (*c* 0.56, $CHCl_3$); ^{1}H NMR δ 7.64 and 7.30 (AA′BB′ system, 8H), 6.73 (s, 2H), 2.42 (s, 3H); ^{13}C NMR δ 144.1 (2C), 142.3 (2C), 139.7 (2C), 130.4 (4C), 124.8 (4C), 21.4 (2C). Anal. Calcd for $C_{16}H_{16}O_2S_2$: C, 63.13; H, 5.30; S, 21.06. Found: C, 62.99; H, 5.00; S, 20.85.

Diels−Alder Cycloadditions of *β*-Sulfinylacrylonitriles with Cyclopentadiene. Method i: Thermal Conditions. To a stirred solution of *β*-sulfinylacrylonitrile (1 mmol) in CH_2-Cl_2 (3.75 mL), in the presence of some hydroquinone crystals, freshly distilled cyclopentadiene (675 μL, 8 mmol) was added at room temperature. When the addition was completed, the reaction mixture was heated at reflux for the time indicated in each case. The crude mixture was concentrated and purified by flash chromatography (the eluent is indicated in each case).

Method ii: In the Presence of $ZnBr_2$. To a solution of $ZnBr_2$ (450.4 mg, 2 mmol) in THF (0.5 mL), under argon at room temperature, was added a solution of *β*-sulfinylacrylonitrile (1 mmol) in CH_2Cl_2 (3.7 mL). The mixture was stirred for 1 h and then freshly distilled cyclopentadiene (675.4 μL, 8 mmol) was added. The reaction mixture was stirred at room temperature for the time indicated in each case, poured into water (4 mL), and extracted with CH_2Cl_2 (3 × 4 mL). The organic layer was dried over Na_2SO_4 and concentrated. The crude product was purified by flash chromatography with the eluent indicated in each case.

Method iii: In the Presence of $BF_3{\cdot}OEt_2$. Method iii.A. $BF_3{\cdot}OEt_2$ (148 μL, 1.2 mmol) was added, under argon at room temperature, to a solution of *β*-sulfinylacrylonitrile (1 mmol) in CH_2Cl_2 (10 mL), and the mixture was stirred for 2.5 h. Then it was cooled at −20 °C and freshly distilled cyclopentadiene (675.4 μL, 8 mmol) was added. The reaction mixture was stirred at −20 °C for the time indicated in each case and then decomposed by treatment with methanol (10 mL) for 1.5 h at room temperature. The resulting mixture was poured into water (5 mL) and extracted with CH_2Cl_2 (3 × 15 mL). The organic layer was dried over Na_2SO_4 and concentrated. The crude product was purified by flash chromatography with the eluent indicated in each case.

Method iii.B. The experimental procedure was identical to that reported in method A except that in this case the mixture of *β*-sulfinylacrylonitrile and $BF_3{\cdot}OEt_2$ was heated at reflux of CH_2Cl_2 for 1 h before addition of cyclopentadiene.

(+)-(1*S*,2*S*,3*S*,4*R*,(*S*)*R*)-2-*n*-Butyl-3-(*p*-tolylsulfinyl)-bicyclo[2.2.1]hept-5-ene-2-carbonitrile (*endo*-6a). Compound *endo*-**6a** was obtained as a white solid from **1a** by following method i [Table 3, entry 1, 42% isolated yield after chromatographic purification (1:5 EtOAc−CH_2Cl_2)] or method ii [Table 3, entry 5, 40% isolated yield after chromatographic purification (1:5 EtOAc−CH_2Cl_2)]. It was crystallized from EtOAc−hexane (1:2): mp 115−116 °C; $[\alpha]^{20}_D$ +34.9 (*c* 0.91, $CHCl_3$); ^{1}H NMR δ 7.80 and 7.33 (AA′BB′ system, 4H), 6.73 (dd, 1H, J = 3.2 and 5.4), 6.55 (dd, 1H, J = 3.2 and 5.4), 3.70−3.50 (m, 1H), 3.12 (d, 1H, J = 3.2), 3.20−3.00 (m, 1H), 2.41 (s, 3H), 1.85−1.65 (m, 1H), 1.65−1.50 (m, 1H), 1.60−0.85 (m, 6H), 0.67 (t, 3H, J = 7.0); ^{13}C NMR δ 142.9, 140.1, 138.0, 136.9, 130.0 (2C), 126.5 (2C), 120.8, 76.5, 51.7, 46.2, 44.9, 44.6, 38.4, 27.1, 22.4, 21.1, 13.6. Anal. Calcd for $C_{19}H_{23}NOS$: C, 72.80; H, 7.40; N, 4.47; S, 10.23. Found: C, 72.72; H, 7.25; N, 4.38; S, 10.80.

(−)-(1*R*,2*S*,3*S*,4*S*,(S)*R*)-2-*n*-Butyl-3-(*p*-tolylsulfinyl)-bicyclo[2.2.1]hept-5-ene-2-carbonitrile (*exo*-6a). Compound ***exo*-6a** was obtained as a white solid starting from **1a** by following method i [Table 3, entry 1, 47% isolated yield after chromatographic purification (1:5 EtOAc−CH_2Cl_2)] or method ii [Table 3, entry 5, 42% isolated yield after chromatographic

purification (1:5 EtOAc−CH_2Cl_2)]. It was crystallized from EtOAc−hexane (1:2): mp 154−155 °C; $[\alpha]^{20}_D$ −54.3 (*c* 0.90, $CHCl_3$); ^{1}H NMR δ 7.78 and 7.34 (AA′BB′ system, 4H), 6.32 (dd, 1H, *J* = 3.2 and 5.4), 6.11 (dd, 1H, *J* = 3.2 and 5.4), 3.70−3.50 (m, 1H), 3.40−3.20 (m, 1H), 2.41 (s, 3H), 2.34 (d, 1H, *J* = 3.2), 2.32−2.20 (m, 1H), 1.90−1.70 (m, 1H) 1.20−1.00 (m, 6H), 0.73 (t, 3H, *J* = 7.0); ^{13}C NMR δ 142.7, 140.1, 138.3, 134.5, 130.0 (2C), 126.2 (2C), 122.2, 73.8, 52.8, 46.6, 45.3, 44.4, 37.3, 27.4, 22.3, 21.5, 13.6. Anal. Calcd for $C_{19}H_{23}NOS$: C, 72.80; H, 7.40; N, 4.47; S, 10.23. Found: C, 72.59; H, 7.16; N, 4.52; S, 10.72.

(1*R*,2*R*,3*R*,4*S*,(S)*R*) and (1*S*,2*R*,3*R*,4*R*,(S)*R*)-2-*n*-Butyl-3-(*p*-tolylsulfinyl)bicyclo[2.2.1]hept-5-ene-2-carbonitrile (*endo*-7a + *exo*-7a). A mixture of diastereomers *endo*-**7a** + *exo*-**7a** was obtained as a white solid starting from **1a** under thermal conditions (method i) as a result of a change in the reaction solvent: (a) by using MeOH (Table 3, entry 9), from 95 mg (0.385 mmol) of **1a** were obtained 48.2 mg (0.154 mmol) of a mixture of adducts *exo*-**6a**, *endo*-**7a**, and *exo*-**7a**, (83:10:7) and 37.4 mg (0.119 mmol) of *endo*-**6a** after chromatographic purification (1:20 acetone-CH_2Cl_2); (b) by using MeOH + H_2O (1:1) (Table 3, entry 10), from 100 mg (0.405 mmol) of **1a** were obtained 10 mg (0.032 mmol) of a mixture of adducts *endo*-**7a** and *exo*-**7a** (51:49), 44 mg (0.140 mmol) of *exo*-**6a**, and 38 mg (0.121 mmol) of *endo*-**6a** after chromatographic purification (2:3 EtOAc−hexane). Data corresponding to a 74:26 mixture of *endo*-**7a**/*exo*-**7a**: $[\alpha]^{20}_D$ +263.8 (*c* 0.09, $CHCl_3$); ^{1}H NMR δ 7.65 and 7.37 (AA′BB′ system, 8H), 6.54 (dd, 1H, *J* = 3.2 and 5.9), 6.28 (dd, 1H, *J* = 2.7 and 5.4), 6.20−6.00 (m, 2H) 3.45−3.30 (m, 1H), 3.30−3.10 (m, 1H), 2.95 (d, 1H, *J* = 3.2), 2.44 (m, 7H), 2.40−2.25 (m, 2H), 2.28 (d, 1H, *J* = 3.2), 2.20−2.10 (m, 16H), 0.96 (t, 6H, *J* = 7.0); ^{13}C NMR δ 142.6, 142.7, 140.2 (2C), 138.1, 137.7, 135.1, 134.5, 130.1 (4C), 125.8 (2C), 125.3 (2C), 122.0, 120.7, 79.4, 75.8, 52.5, 51.3, 47.9, 47.5, 47.3, 46.2, 46.1, 45.5, 39.9, 38.7, 28.0, 27.7, 22.6, 22.5, 21.5 (2C), 13.8 (2C).

(+)-(1*S*,2*S*,3*S*,4*R*,(S)*R*)-3-(*p*-Tolylsulfinyl)bicyclo[2.2.1]-hept-5-ene-2-carbonitrile (*endo*-6b). Compound *endo*-**6b** was obtained from **1b** as a white solid after chromatographic purification (EtOAc) following method i (Table 3, entry 2, 78% isolated yield), method ii (Table 3, entry 6, 75% isolated yield), or method iii.A (reaction time 1 h, 80% isolated yield). It was crystallized from EtOAc−hexane (1:2): mp 140−141 °C; $[\alpha]^{20}_D$ +6.2 (*c* 0.32, $CHCl_3$); ^{1}H NMR δ 7.79 and 7.32 (AA′BB′ system, 4H), 6.71 (dd, 1H, *J* = 2.7 and 5.9), 6.52 (dd, 1H, *J* = 2.7 and 5.9), 3.55−3.70 (m, 1H), 3.62 (dd, 1H, *J* = 3.2 and 8.6), 3.50−3.30 (m, 1H), 2.90 (dd, 1H, *J* = 3.2 and 8.6), 2.41 (s, 3H), 1.85−1.65 (m, 1H), 1.45−1.25 (m, 1H); ^{13}C NMR δ 142.4, 139.3, 136.1 (2C), 129.7 (2C), 125.9 (2C), 118.4, 67.9, 47.3, 47.0, 45.5, 29.7, 21.2. Anal. Calcd for $C_{15}H_{15}NOS$: C, 70.01; H, 5.87; N, 5.44; S, 12.46. Found: C, 69.93; H, 5.55; N, 5.28; S, 12.54.

(−)-(1*S*,2*S*,3*S*,4*R*,(S)*R*)-2-Benzyl-3-(*p*-tolylsulfinyl)-bicyclo[2.2.1]hept-5-ene-2-carbonitrile (*endo*-6d). Compound *endo*-***6d*** was obtained as a white solid from **1d** by following method i [Table 3, entry 4, 39% isolated yield after chromatographic purification (1:2 EtOAc−hexane)] or method ii [Table 3, entry 8, 53% isolated yield after chromatographic purification (1:1 EtOAc−hexane)]. It was crystallized from EtOAc−hexane (1:2): mp 140−141 °C; $[\alpha]^{20}_D$ −122.5 (*c* 0.70, $CHCl_3$); ^{1}H NMR δ 7.77 and 7.31 (AA′BB′ system), 7.35−7.15 (m, 3H), 7.10−6.90 (m, 2H), 6.69 (dd, 1H, *J* = 2.7 and 5.4), 6.38 (dd, 1H, *J* = 3.2 and 5.4), 3.70−3.50 (m, 1H), 3.23 (d, 1H), 3.20−3.00 (m, 1H), 2.59 and 2.30 (AB system, 2H, *J* = 13.7), 2.40 (s, 3H), 1.85−1.65 (m, 1H); ^{13}C NMR δ 142.7, 140.2, 137.8, 137.2, 134.1, 130.0 (2C), 128.4 (4C), 127.5, 126.2 (2C), 120.4, 76.3, 50.2, 46.1, 45.7, 44.6, 43.7, 21.4. Anal. Calcd for $C_{22}H_{21}$-NOS: C, 76.05; H, 6.09; N, 4.03; S, 9.23. Found: C, 76.14; H, 5.63; N, 3.92; S, 9.64.

(−)-(1*R*,2*S*,3*S*,4*S*,(*S*)*R*)-2-Benzyl-3-(*p*-tolylsulfinyl)-bicyclo[2.2.1]hept-5-ene-2-carbonitrile (*exo*-6d). Compound *exo*-**6d** was obtained as a white solid from **1d** by following method i [Table 3, entry 4, 42% isolated yield after chromatographic purification (1:2 EtOAc−hexane)] or method ii [Table 3, entry 8, 38% isolated yield after chromatographic purification (1:1 EtOAc−hexane)]. It was crystallized from EtOAc−hexane (1:2): mp 120−121 °C; $[\alpha]^{20}_D$ −208.4° (*c* 0.59, $CHCl_3$); ^{1}H NMR δ 7.65 and 7.30 (AA′BB′ system, 4H), 7.40−7.15 (m, 3H), 7.10−6.90 (m, 2H), 6.39 (dd, 1H, *J* = 3.1 and 5.5), 6.27 (dd, 1H, *J* = 3.1 and 5.5), 3.65−3.45 (m, 1H), 3.20−3.00 (m, 1H), 2.41 and 1.93 (AB system, 2H, *J* = 13.3), 2.38 (s, 3H), 2.40 (d, 1H, *J* = 2.1), 2.23 (m, 1H), 1.74 (m, 1H); ^{13}C NMR δ 142.4, 140.1, 138.7, 134.9, 134.8, 130.0 (2C), 129.6 (2C), 128.5 (2C), 127.4, 125.6 (2C), 121.7, 72.9, 52.4, 47.0, 46.9, 43.9, 42.6, 21.4. Anal. Calcd for $C_{22}H_{21}NOS$: C, 76.05; H, 6.09; N, 4.03; S, 9.23. Found: C, 76.22; H, 5.98; N, 4.07; S, 9.66.

(−)-(1*R*,2*R*,3*R*,4*S*,(S)*S*)-2-*n*-Butyl-3-(*p*-tolylsulfinyl)-bicyclo[2.2.1]hept-5-ene-2-carboxamide (*endo*-8a). Adduct *endo*-**8a** was obtained as a white solid starting from **1a** in the presence of BF_3·OEt_2 by following method iii.A [reaction time 360 h; 62% isolated yield after chromatographic purification (6:1 CH_2Cl_2−MeOH)]. It was crystallized from CH_2Cl_2: mp 205−206 °C; $[\alpha]^{20}_D$ -28.9 (*c* 0.27, $CHCl_3$);^{1}H NMR δ 7.77 and 7.25 (AA′BB′ system, 4H), 6.68 (dd, 1H, *J* = 2.7 and 5.9), 6.33 (dd, 1H, *J* = 2.7 and 5.4), 5.66 (bs, 1H), 5.30 (bs, 1H), 3.60−3.40 (m, 1H), 3.13 (d, 1H, *J* = 3.2), 2.90−2.70 (m, 1H), 2.37 (s, 3H), 1.90−1.40 (m, 6H), 1.05 (m, 2H), 0.63 (t, 3H, *J* = 7.0); ^{13}C NMR δ 175.3, 143.8, 140.8, 136.7 (2C), 129.1 (2C), 126.5 (2C), 79.5, 60.9, 54.2, 46.3, 46.2, 41.5, 29.6, 27.2, 21.3, 13.7. Anal. Calcd for $C_{19}H_{25}NO_2S$: C, 68.85; H, 7.60; N, 4.23; S, 9.67. Found: C, 68.63; H, 7.13; N, 4.15; S, 9.69.

(−)-(1*R*,2*R*,3*R*,4*S*,(S)*S*)-3-(*p*-Tolylsulfinyl]bicyclo[2.2.1]-hept-5-ene-2-carboxamide (*endo*-8b). Adduct *endo*-**8b** was obtained as a white solid from **1b** in the presence of $BF_3.OEt_2$ by following method iii.B [reaction time 3 h; 72% isolated yield after chromatographic purification (12:1 CH_2Cl_2-MeOH)]. It was crystallized from CH_2Cl_2-MeOH (20:1): mp 226−227 °C; $[\alpha]^{20}_D$ -20.6 (*c* 0.12, $CHCl_3$); ^{1}H NMR δ 7.52 and 7.18 (AA′BB′ system, 4H), 6.38 (dd, 1H, *J* = 2.9 and 5.4), 6.12 (dd, 1H, *J* = 3.0 and 5.9), 3.67 (dd, 1H, *J* = 3.3 and 8.7), 3.40−3.30 (m, 1H), 3.20−3.00 (m, 1H), 2.98 (dd, 1H, *J* = 3,3 and 8.7), 2.25 (s, 3H), 1.60−1.45 (m, 1H), 1.45−1.30 (m, 1H); ^{13}C NMR δ 175.4, 143.6, 141.6, 138.0, 135.1, 130.8 (2C), 128.2 (2C), 72.1, 50.3, 50.1, 49.4, 48.2, 21.3. Anal. Calcd for $C_{15}H_{17}NO_2S$: C, 65.43; H, 6.22; N, 5.09; S, 11.64. Found: C, 64.91; H, 5.93; N, 4.91; S, 11.53.

(+)-(1*R*,2*R*,3*R*,4*S*,(S)*S*)-2-Benzyl-3-(*p*-tolylsulfinyl)-bicyclo[2.2.1]hept-5-ene-2-carboxamide (*endo*-8d). Adduct *endo*-**8d** was obtained as a white solid starting from **1d** in the presence of BF_3·OEt_2 by following method iii.A [reaction time 360 h; 53% isolated yield after chromatographic purification (20:1 CH_2Cl_2−MeOH)]. It was crystallized from CH_2Cl_2: mp 209−210 °C; $[\alpha]^{20}_D$ +15.0 (*c* 0.10, $CHCl_3$); ^{1}H NMR δ 7.49 and 7.33 (AA′BB′ system, 4H), 7.50−7.15 (m, 5H), 6.76 (dd, 1H, *J* = 2.7 and 5.4), 6.31 (dd, 1H, *J* = 2.7 and 5.4), 6.20 (bs, 1H), 5.40 (bs, 1H), 3.68 and 2.78 (AB system, 2H, *J* = 13.4), 3.40−3.20 (m, 1H), 3.24 (d, 1H, *J* = 2.7), 3.20−3.00 (m, 1H), 2.48 (s, 3H), 1.95−1.75 (m, 1H), 1.75−1.60 (m, 1H); ^{13}C NMR δ 175.0, 141.8, 140.9, 137.5, 137.2, 135.6, 130.2 (2C), 129.5 (2C), 128.5 (2C), 127.1, 125.2 (2C), 77.2, 61.7, 52.1, 46.7, 46.2, 45.0, 21.4.

Hydrolysis of Carbonitrile *endo*-6a into Carboxamide.[29] To a stirred solution of 60 mg (0.192 mmol) of adduct *endo*-**6a** in 1 mL of *t*-BuOH was added 200 mg of finely powdered KOH. The reaction mixture was stirred at reflux for 16 h, cooled at room temperature, and poured into 2 mL of aqueous NaCl solution. The mixture was extracted with CH_2Cl_2 (3 × 2 mL). The organic layer was dried over Na_2SO_4 and $CaCl_2$ and then concentrated. The crude product was purified by flash chromatography (12:1 CH_2Cl_2−MeOH) to give 20 mg (0.060 mmol, 32%) of (+)-(1*S*,2*S*,3*S*,4*R*,(S)*R*)-2-*n*-butyl-3-(*p*-tolylsulfinyl)bicyclo[2.2.1]hept-5-ene-2-carboxamide (*endo*-**8′a**) [spectroscopic data are coincident with those of *endo*-**8a**: $[\alpha]^{20}_D$ +30.4 (*c* 0.27, $CHCl_3$)] and 27.6 mg (0.083 mmol, 44%) of (+)-(1*S*,2*S*,3*R*,4*R*,(S)*R*)-2-*n*-butyl-3-(*p*-tolylsulfinyl)bicyclo[2.2.1]-hept-5-ene-2-carboxamide (**11**) which was crystallized from hexane: mp 203−205 °C; $[\alpha]^{20}_D$ +149.4 (*c* 0.20, $CHCl_3$); ^{1}H NMR 7.66 and 7.37 (AA′BB′ system, 4H), 7.42 (bs, 1H), 6.42 (dd, *J* = 3.0 and 5.5), 5.87 (dd, *J* = 3.2 and 5.5), 5.21 (bs, 1H), 3.25−3.23 (m, 1H), 2.87 (d, 1H, *J* = 2.0), 2.77−2.62 (m, 1H), 2.46 (s, 3H), 2.20−2.10 (m, 1H), 2.15−1.90 (m, 1H), 1.85−1.79 (m, 1H), 1.70−1.10 (m, 5H), 0.96 (t, 3H, *J* = 7.0); ^{13}C NMR

176.9, 142.9, 140.6, 139.0, 134.9, 130.1 (2C), 125.6 (2C), 77.0, 59.1, 47.1, 44.6, 44.0, 33.1, 27.5, 23.1, 21.4, 13.9. Anal. Calcd for $C_{19}H_{25}NO_2S$: C, 68.85; H, 7.60; N, 4.23; S, 9.67. Found: C, 68.35; H, 7.46; N, 4.12; S, 9.50.

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Supporting Information Available: IR and MS data of compounds **1, 2,** and **4**−**11**. X-ray diagram and data of compounds *endo*-**6a** and *exo*-**6a** (6 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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