Pergamon

Tetrahedron, Vol. 53, No. 41, pp. 14115-14126, 1997
© 1997 Elsevier Science Ltd
All rights reserved. Printed in Great Britain
0040-4020/97 $17.00 + 0.00

PII: S0040-4020(97)00913-7

Dienophilic Behavior of (S)-2-*p*-Tolylsulfinyl Butenolide*

Juan Carlos Carretero,* Jose Luis García Ruano,* Luisa M. Martín Cabrejas

Departamento de Química Orgánica, Universidad Autónoma de Madrid, Cantoblanco, 28049-Madrid, Spain

Abstract: The study of the reactions of (S)-2-p-tolylsulfinyl butenolide (**2**) with cyclic and acyclic dienes is reported. The reactivity and stereoselectivity of this dienophile is compared with those of (S)-2-*p*-tolylsulfinyl cyclopentenone (**3**) in order to obtain information about the stereochemical models so far proposed. © 1997 Elsevier Science Ltd.

The use of butenolides in asymmetric Diels-Alder reactions has been restricted to their 5-substituted compounds (mainly the 5-alkoxy derivatives).[1] In these substrates the configuration at C-5 efficiently controls the π-facial selectivity of the cycloadditions. In contrast with the high number of papers dealing with the use of sulfinylacrylates as dienophiles,[2] only one concerns the study of their cyclic analogues.[3] In this paper, the reactions of optically pure 5-ethoxy-3-*p*-tolylsulfinyl butenolides (**1**) with cyclopentadiene were studied to evaluate the influence of the sulfinyl group on both, the dienophilic reactivity of the butenolides (which was slightly improved) and the stereoselectivity of their cycloadditions. Concerning the last point, the results showed that both the configuration at C-5 and at sulfur were important, prevailing the control of C-5 in the uncatalysed reactions and the control by the sulfoxide in the catalysed reactions by $ZnBr_2$. These results suggested that 2-*p*-tolylsulfinyl butenolides (**2**) could evolve with very high π-facial selectivity. Otherwise, the reactions of (S)-2-*p*-tolylsulfinyl-2-cyclopentenone (**3**) with cyclopentadiene[4] and Dane's diene[5] had proved to be highly stereoselective. All these facts prompted us to investigate the behavior of the (S)-2-*p*-tolylsulfinyl butenolide **2** as dienophile[6] (figure 1).

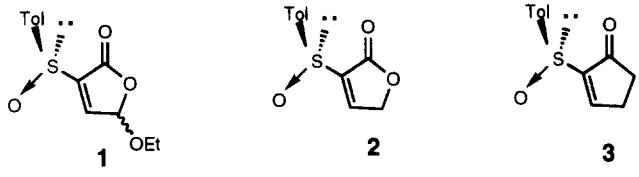
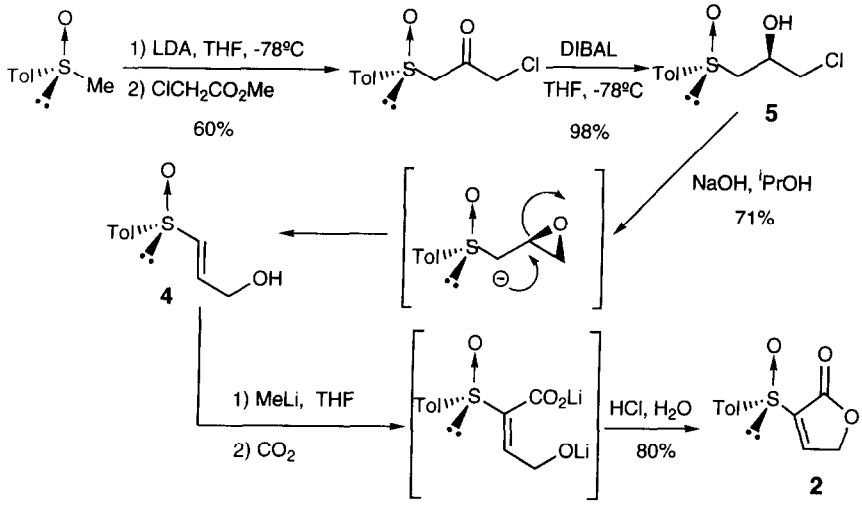


Figure 1

Two previous synthesis of compound **2** had been reported by the groups of Posner[7] and Holton,[8] respectively, both based on the α-carboxylation of enantiopure 3-*p*-tolylsulfinyl-2-propenol (**4**) or derivatives. Nevertheless, due to its experimental simplicity we used the method described by Hamdouchi and Solladié[9] for

* In memorian Prof. Felix Serratosa

the preparation of **4**. Deprotonation of (R)-methyl *p*-tolyl sulfoxide with LDA (THF, -78°C) and subsequent acylation with methyl chloroacetate, followed by stereoselective DIBAL reduction of the resulting β-keto sulfoxide yielded the hydroxy sulfoxide **5** (59% overall yield), which was transformed into the alcohol **4** by treatment with NaOH/i-PrOH.[10] Compound **4** was lithiated and carboxylated according to Posner's procedure,[7] but further lactonization was carried out without isolating the intermediate hydroxy acid (by addition of 10% HCl). In these conditions, butenolide **2** was isolated in 80% yield from **4** (scheme 1).[11]



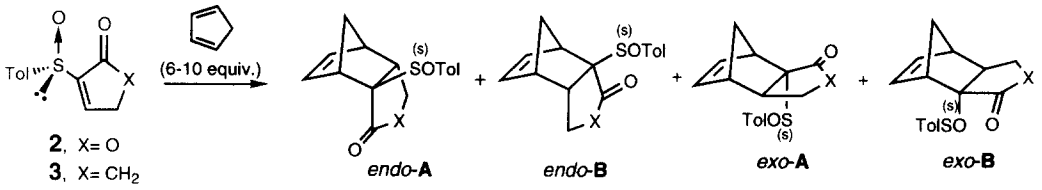
Scheme 1

The main results obtained in the reaction of compound **2** with cyclopentadiene are depicted in table 1. As we can see, its dienophilic reactivity is very poor. In the absence of catalyst, the conversion is 20% after 4 days at rt (entry 1), and in the presence of $Eu(fod)_3$ a similar conversion was achieved after 5 days at 0°C (entry 3). On the other hand, when the reaction were conducted in toluene at 110°C or catalyzed by $TiCl_4$ decomposition of dienophile was observed. A better result was obtained in the reaction catalysed by $EtAlCl_2$ (52% yield, entry 4), although the best yield (81%) was obtained under high pressures (13 Kbar, entry 2).

The comparison of these results with those obtained from 2-*p*-tolylsulfinyl cyclopentenone **3**[4] (it required 1h in the presence of $EtAlCl_2$, entry 5) and 5-ethoxy-3-(2-*p*-tolylsulfinyl)butenolide **1**[3] (complete evolution of the uncatalysed reaction in 3 days at rt) evidences the lower reactivity of **2**, which is not unexpected taking into account the higher electron withdrawing character of the carbonyl group in **3** (with respect to the ester function in **2**) and the inductive effect of the ethoxy group in **1**.

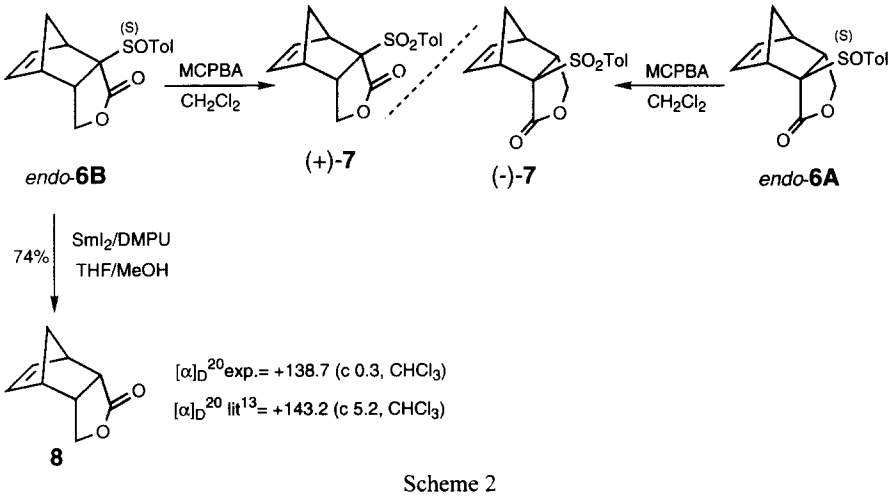
The *endo* and *exo* stereochemistry of the adducts was established from their NMR parameters and mainly by NOESY experiments.[12] Unequivocal configurational assignment of *endo*-**6A** and *endo*-**6B** adducts was established by their oxidation to enantiomeric sulfones *endo*-**7** and by conversion of *endo*-**6B** into the known lactone **8**[13], used in the enantioselective synthesis of prostaglandins (scheme 2).

Table 1. Results obtained in reactions of compounds **2** and **3** with cyclopentadiene.



Entry	Dienophile	Catalyst	Reaction conditions	Yield (%)[a]	Isomer ratio[b]			
					endo **A**	*endo* **B**	*exo* **A**	*exo* **B**
1	**2**	---	CH_2Cl_2, 4d, rt	20[b]	40	40	---[c]	---[c]
2	**2**	---	CH_2Cl_2, 24h, 13 Kbar	81	30	42	11	17
3	**2**	$Eu(fod)_3$[d]	CH_2Cl_2, 5d, 0°C	20[b]	40	40	---[c]	---[c]
4	**2**	$EtAlCl_2$[d]	Toluene, 10h., rt	52	40	---	60	---
5	**3**[e]	$EtAlCl_2$[d]	Toluene, 1h., rt	92	40	---	60	---

[a]After chromatographic purification. [b]Evaluated by ^{1}H-NMR on the crude mixtures. [c]The *exo* **A**/*exo* **B** ratio could not be evaluated. [d]1.2 equiv. [e]Data taken from reference 4.



Scheme 2

Concerning the stereoselectivity, the results for compounds **2** and **3** in the presence of $EtAlCl_2$ are identical (entries 4 and 5, table 1). The complete π-facial selectivity (both for the *endo* and *exo* approaches) can be explained by assuming the formation of a chelated species **A** (figure 2) with the two diastereotopic faces sterically quite differentiated. A similar explanation was proposed to explain the evolution of sulfinyl cycloalkenone **3**[4,6], as well as the results obtained from sulfinyl acrylates in their reactions with cyclopentadiene catalysed by chelating agents like ZnX_2.[14] The low *endo/exo* selectivity (de = 20%) must be the result of the competence between the ester and sulfinyl groups (both exhibiting an *endo* orientating character), and the influence of the alkyl residue in **2** and **3**.

In the absence of catalyst, a mixture of the four possible adducts **6** was obtained, all of them in significant amounts (entries 1 and 2). The fact that the *endo* adducts were now predominant (entries 1 and 2) contrasts with the results obtained under $EtAlCl_2$ catalysis (the *exo* adduct is the major one, entry 4), suggesting that the *endo* orientating character of the ester group is higher than that of the sulfinyl one in conditions of entries 1-3, whereas this situation is inverted in the presence of $EtAlCl_2$. Taking into account the enhancement of the *endo* orientating character of the functional groups by association with the Lewis acids, this behavior is consistent with the higher ability of the sulfinyl to associate with the catalyst. Otherwise, the quite low π-facial selectivity suggests that conformational restrictions around the C-S bond must be negligible in the absence of catalyst, and thus the attack of diene to the less hindered face of the dienophile in conformations **B** and **C**[15] must be taken into account (figure 2). These considerations are based on the assumption that the influence of the high pressures on the *endo/exo* and π-facial selectivities is scarce as it has been deduced from the results obtained using other sulfinyl esters as dienophiles.[16]

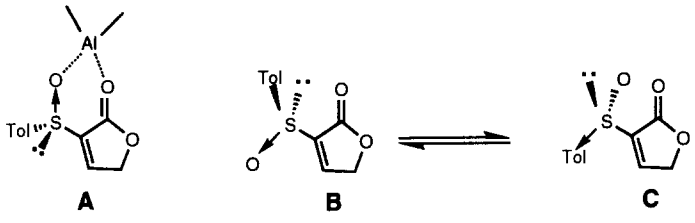
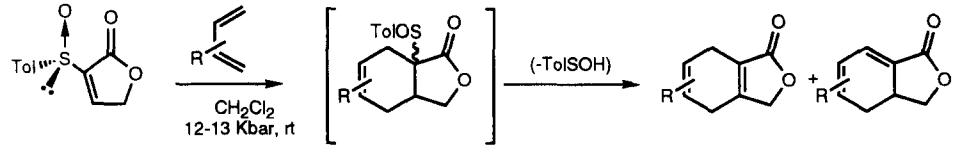


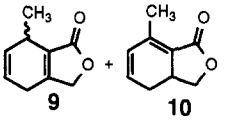
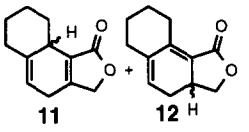
Figure 2

The reactions of **2** with piperylene and 1-vinylcyclohexene were carried out under high pressures (table 2), yielding mixtures of desulfinylated compounds (resulting from the *syn*-pyrolytic elimination of the sulfoxide), easily separated by column chromatography. All attempts conducted at normal pressure under thermal or catalysed conditions ($TiCl_4$, $EtAlCl_2$, $Eu(fod)_3$, $BF_3.OEt_2$) were unsuccessful. From the results of table 2 it can be concluded that the regioselectivity of the cycloadditions is complete, although the desulfinylation afforded a mixture of the conjugated and non-conjugated polycyclic cyclohexadienes with low selectivity. Despite the fast desulfinylation precluded obtaining direct information about the *endo/exo* and π-facial selectivities of these cycloadditions, the optical purity of compounds isolated in conditions of entry 2 (ee=45%) indicates that at least one of them must be only moderate. On the other hand, the fact that acyclic dienes evolve with much higher *endo* selectivity than cyclopentadiene in reactions other sulfinyl maleates[17] suggests that only *endo*-adducts were formed in these cycloadditions, and thus a poor π-facial selectivity would be responsible of the low optical purity of compounds **9** and **10**. The evolution of rotamers **B** and **C** (figure 2), both largely populated for uncatalysed reactions, would explain the poor π-facial selectivity.

Much more interesting were the results obtained in the reactions of **2** with the Dane's diene (table 3), which on the other hand support the above mentioned assumptions. The reactions were carried out under high

Table 2. Results obtained in reactions of compound **2** with pyperilene and 1-vinylcyclohexene.



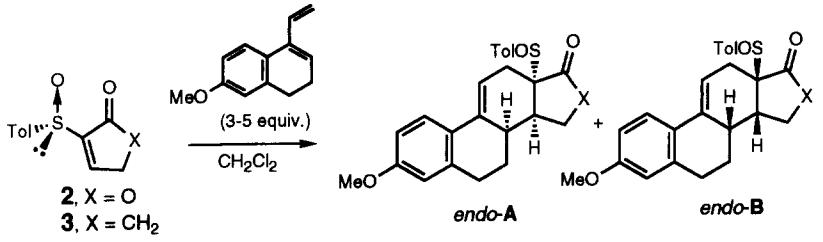
Entry	Diene[a]	Cat.	P (Kbar)	t (h)	Products	ratio[b]	Yield (%)[c]
1		--	12.5	48	 **9** **10**	**9/10** = 72/28	88[d]
2	"	$ZnBr_2$[e]	13	48	**9** (44%ee) + **10** (46%ee)	**9/10** = 53/47	68
3		--	13	144	 **11** **12**	**11/12** = 58/42	53
4	"	$ZnBr_2$[e]	13	46	**11** + **12**	**11/12** = 43/57	66

[a]3-4 equiv. [b]Determined by ^{1}H-NMR on the crude mixtures. [c]In isolated product after chromatographic purification. [d]In converted product. [e]1.5 equiv.

pressure (13 Kbar, entry 1) or in the presence of $EtAlCl_2$ (entries 2 and 4), affording in both cases mixtures of the two *endo*-adducts, **13A** and **13B**. These results shown the complete *endo* selectivity of the reactions with acyclic dienes, which agrees with those observed for sulfinylmaleates.[17] The regioselectivity of the cycloaddition is also complete and it is controlled by the aromatic substituent at C-2 in the diene.

In table 3 we have also included the results obtained in the reactions of compound **3** with the Dane's diene under $EtAlCl_2$ catalysis (entries 3 and 5)[5], which are very similar to those obtained from dienophile **2**. The first significant fact is the opposite π-facial selectivity observed depending on the use of 1 or 2 equiv. of catalyst (compare entries 2 with 4 and 3 with 5). In the case of cyclopentenone **3**, this behavior was explained[5] by assuming the formation of chelated species **A** (in the presence of just one equivalent of catalyst), or **B** (when two equivalents of $EtAlCl_2$ are used), both exhibiting opposite less hindered faces (figure 3). A similar explanation can be used to justify the results observed in reactions from butenolide **2**. The lower reactivity and π-facial selectivity of **2** with respect to **3** in the presence of 1 equivalent of catalyst (compare entries 2 and 3) could be a consequence of the larger ability of the enone to become chelated.

Table 3. Results obtained in reaction of **2** (and **3**) with the Dane's diene.



Entry	Dienophile	Catalyst	Reaction conditions	*endo*-**A**/*endo*-**B**[a]	Yield (%)[b]
1	**2**	---	13 Kbar, 46h, rt	[c]	53
2	**2**	$EtAlCl_2$ (1.2 equiv.)	-25°C, 12h	73/27	33[d]
3	**3**[e]	$EtAlCl_2$ (1.0 equiv.)	-25°C, 4h	>98/<2	93
4	**2**	$EtAlCl_2$ (2.0 equiv.)	rt, 15h	16/84	72
5	**3**[e]	$EtAlCl_2$ (2.0 equiv.)	-25°C, 1h	27/73	90

[a]Determined by ^{1}H-NMR on the crude mixtures. [b]After chromatographic purification. [c]*endo*-**A**>*endo*-**B**, however a more precised data could not be obtained due to the polimerization of the diene. [d]In converted product. [e]Data taken from ref. 5.

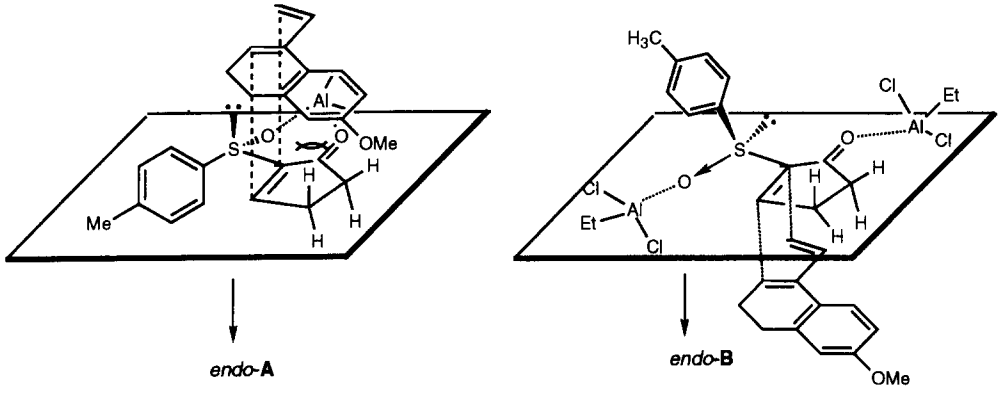


Figure 3

In conclusion, we have described the synthesis and dienophilic behavior of the (S)-2-*p*-tolylsulfinyl butenolide. Its reactivity is quite low requiring the use of high pressure or catalyst to reach high yields. The π-facial selectivity of its reactions with cyclopentadiene is very high in the presence of $EtAlCl_2$, but the *endo/exo* selectivity is only moderate. An opposite situation is observed in the reaction with acyclic dienes, which reacts with total *endo* but moderate π-facial selectivity.

EXPERIMENTAL

Melting points were determined with a Gallenkamp apparatus in open capillaries and are uncorrected. ^{1}H-NMR spectra and ^{13}C-NMR spectra were recorded in the FT mode on a Bruker WP-200-SY instrument coupled to an ASPECT 2000 computer, transforming 16K data points. Both chemical shifts (ppm downfield

from internal tetramethylsilane) and coupling constants (Hz) were obtained by the first order analysis of spin patterns. Mass data are reported on a Hewlett-Packard 5985 spectrometer with electron impact (EI, 70 eV). Mass data are reported in mass units (m/z) and the values in brackets regard to the relative intensity from the base peack (as 100%). High-resolution mass spectra were determined at an ionizing voltage of 70 eV. Infrared (IR) spectra were recorded on a Philips PU-9716 spectrometer. Optical rotations were measured with a Perkin-Elmer 241 polarimeter. High pressure reactions were performed in a Unipress Equipment 101LV 30/16 in polyethylene vials. Analytical thin-layer chromatography was performed on DC-Alufolien 0.2 mm silica gel 60-F plates (MERCK). Visualization was accomplished with UV light and phosphomolybdic acid solution followed by heating. Flash chromatography was performed by using of silica gel (MN-Kieselgel 60, 230-400 mesh).

All solvents were dried before use. THF was distilled from sodium-benzophenone under argon. Dichloromethane and chloroform were distilled from P_2O_5. Diisopropylamine was distilled from sodium hydroxyde. Cyclopentadiene was distilled before use. Zinc Bromide was dried at 160°C for 12h with P_2O_5 under vacuo. $Eu(fod)_3$, $EtAlCl_2$ and *trans*-1,3-pentadiene were purchased from Aldrich and used without further purification. Vinylcyclohexene and Dane's diene were prepared according to described procedures.[18]

(R2,RS)-1-Chloro-3-(p-Tolylsulfinyl)-2-propanol **(5).**

To a freshly prepared solution of LDA (57.2 mmol) in THF (27 ml) was added at -40°C a solution of (R) methyl *p*-tolyl sulfoxide (4 g, 25.9 mmol) in THF (16 ml) under argon atmosphere. The mixture was stirred at -40°C for 30 min. Then the reaction was cooled at -78°C and a solution of methyl chloroacetate (2.7 ml, 31.2 mmol) in 15 ml of THF was slowly added. After being stirred at -78°C for 1h, 5% H_2SO_4 was added until reaching acid pH. The mixture was extracted with diethyl ether (3 x 30 ml), the combined of organic layers was dried ($MgSO_4$) and evaporated. The residue was purified by flash chromatography (Et_2O/CH_2Cl_2 1:3) to give 3.6 g (60%) of (R)-1-chloro-3-(*p*-tolylsulfinyl)-2-propanone.

DIBAL 1M solution in hexane (31.2 ml, 31.2 mmol) was slowly added at -78°C to a solution of 3.6 g (15.6 mmol) of (R)-1-chloro-3-(*p*-tolylsulfinyl)-2-propanone in THF (60 ml) under argon atmosphere. The reaction was stirred at -78°C for 1h. Then the mixture was successively treated with methanol (30 ml), ethyl acetate (50 ml) and saturated sodium tartrate (50 ml). The organic layer was separated and the aqueous phase was extracted with ethyl acetate (2 x 50 ml). The combined of organic layers was washed with saturated NaCl (50 ml), dried (Na_2SO_4) and evaporated to afford 3.56 g (98%) of **5**. $[\alpha]_D^{20}$= +260 (c=2, acetone). ^{1}H-NMR δ: 2.43 (s, 3H), 2.83 (dd, 1H, J= 13.8 and 2.1 Hz), 3.14 (dd, 1H, J= 13.8 and 9.5 Hz), 3.57 (m, 2H), 4.40 (m, 1H), 7.39 and 7.55 (AA'BB' system, 4H, J= 8.0 Hz).

(2E,RS)-3-(p-Tolylsulfiny)l-2-propen-1-ol **(4).**

To a solution of **5** (920 mg, 4.0 mmol) in ^{i}PrOH (25 ml) was added 20% NaOH (20ml) and the mixture was stirred at rt for 20 min. The reaction mixture was extracted with diethyl ether (2x50 ml), the combined of organic layers was washed (50 ml of sat NaCl), dried ($MgSO_4$), and concentrated. The residue was purified by flash chromatography (hexane: EtOAc 1:9) to give 560 mg of **4** (71%).$[\alpha]_D^{20}$= +233 (c=1, $CHCl_3$), ^{1}H-NMR δ: 2.40 (s, 3H), 3.30 (m, 1H), 4.35 (m, 2H), 6.50 (dt, 1H, J= 15.0 and 1.5 Hz), 6.68 (dt, 1H, J= 15.0 and 1.5 Hz), 7.30 and 7.50 (AA'BB' system, 4H, J=8.0 Hz).

(S) 2-(p-Tolylsulfinyl)-2-butenolide **(2)**.

To a solution of the hydroxysulfoxide **4** (550 mg, 2.80 mmol) in THF (24 ml) were slowly added 5.2 ml of MeLi 1.5 M in ether (7.8 mmol) at -78°C under argon atmosphere. The reaction mixture was stirred at -78°C for 30 min and then a flow of anhydrous CO_2 was introduced for 5-10 min. Stirring was continued for 2h at-20°C. 10% HCl (30 ml) was added and the mixture was extracted with ethyl acetate (3 x 20 ml). The combined of organic layers was dried (Na_2SO_4) and concentrated. The residue was purified by precipitation with ether, to give 495 mg (80%). m.p.: 121-125°C. $[\alpha]_D^{20}$= +244 (c= 1.3, $CHCl_3$), ^{1}H-NMR δ: 2.42 (s, 3H), 4.92 (dd, 1H, J= 18.3 and 1.7 Hz), 5.06 (dd, 1H, J=18.3 and 1.7 Hz), 7.32 and 7.71 (AA'BB' system, 4H, J= 8.3 Hz) and 8.07 (t, 1H, J= 1.7 Hz).

General Procedure for the Diels-Alder Reaction of **2** *under High Pressure.*

In a high pressure reaction tube was placed a solution of 60 mg (0.27 mmol) of **2** and the corresponding diene (3-8 equiv.) in CH_2Cl_2 (1 ml). The reaction was pressured at 13 Kbar at rt for the time indicated in tables 1-3. Then, the reaction was allowed to reach atmospheric pressure and the solvent was evaporated. The residue was analyzed by ^{1}H-NMR and purified by flash chromatography.

General Procedure for the Diels-Alder Reactions of **2** *under High Pressure and Catalyzed by* $ZnBr_2$.

In a high pressure reaction tube were placed 60 mg (0.27 mmol) of **2**, 91 mg (0.40 mmol) of $ZnBr_2$ and the corresponding diene (1-vinylcyclohexene or piperylene, 3-4 equiv.) in CH_2Cl_2 (1 ml). The mixture was pressured at 13 Kbar at rt for the reaction times indicated in table 2. The reaction was allowed to reach atmospheric pressure and 10% $NaHCO_3$ (5 ml) was added. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (2 x 5 ml). The combined of organic layers was washed with water (5 ml), dried ($MgSO_4$), and concentrated. The residue was analyzed by ^{1}H-NMR and purified by flash chromatography.

General Procedure for the Diels-Alder Reaction of **2** *Catalyzed by* $EtAlCl_2$.

The required amount of a 1.8 M toluene solution of $EtAlCl_2$ (1.2 or 2.0 equiv. with respect to **2**) was added dropwise, under argon atmosphere, to a solution of dienophile **2** (60 mg, 0.27 mmol) in toluene (1 ml) at

the temperature indicated in tables 1 and 3. The mixture was stirred for 10 min., followed by addition of an excess of the diene (3-6 equiv of cyclopentadiene or Dane's diene). Stirring was continued at the temperature and for the time indicated in tables 1 and 3. Then, 10% $NaHCO_3$ (4 ml) was added and the mixture was extracted with CH_2Cl_2 (2 x 25 ml). The combined of organic layers was washed with water (10 ml), dried ($MgSO_4$), and concentrated. The mixture was analyzed by ^{1}H-NMR and purified by flash chromatography (the eluent was indicated below for each case). The yields are shown in tables 1 and 3.

Lactone of (R1,R2,S3,S4,SS)-3-(hydroxymethyl)-2-(p-tolylsulfinyl)bicyclo[2.2.1]hept-5-ene-2-carboxylic acid **(*endo*-6B)**.

Diene: cyclopentadiene. Eluent: hexane-ethyl acetate 2:1. m.p.: 100-102°C. $[\alpha]_D^{20}$=+ 97.17 (c= 2.3, $CHCl_3$). IR ($CHCl_3$): 2960, 1745, 1380 and 1045 cm^{-1}. ^{1}H-NMR δ: 1.65(dt, 1H, J= 1.6 and 8.9 Hz), 2.28 (bd, 1H, J= 8.9 Hz), 2.41 (s, 3H), 3.12 (m, 1H), 3.19 (ABX system, AB part, 2H, J= 8.5 Hz), 3.29 (m, X part, 1H), 3.60 (m, 1H), 6.42(m, 2H), 7.32 and 7.57 (AA'BB' system, 4H, J= 8.2Hz). ^{13}C-NMR δ: 21.5, 40.6, 45.6, 49.2, 50.7, 70.5, 80.4, 124.8, 129.9, 137.5, 138.2, 138.5, 142.7 and 173.2. MS (EI): 290 (4.4, M^++2), 289 (12.7, M^++1), 288 (58.8, M^+), 222 (25.3), 206 (12.2), 149 (69.1), 124 (99.0), 91 (100.0), 77 (92.6) and 65 (76.5). Anal. Calcd. for $C_{16}H_{16}O_3S$: C, 66.65; H, 5.60; S, 11.10. Found: C, 65.95; H, 5.43; S, 10.84.

Lactone of (S1,S2,R3,R4,SS)-3-(hydroxymethy)l-2-(p-tolylsulfinyl)bicyclo[2.2.1]hept-5-ene-2-carboxylic acid **(*endo*-6A)**.

Diene: cyclopentadiene. Eluent: hexane-ethyl acetate 2:1. IR ($CHCl_3$): 2960, 1760, 1375, 1175, 1085 and 1050 cm^{-1}. ^{1}H-NMR δ: 1.75(dt, 1H, J= 1.2 and 9.5 Hz), 2.40 (s, 3H), 3.12 (m, 1H), 3.21 (m, 1H), 3.59 (m, 1H), 3.65 (AB system, 2H, J= 8.1 Hz), 6.37 (m, 2H), 7.32 and 7.70 (AA'BB' system, 4H, J= 8.2 Hz). MS (EI): 290 (2.0, M^++2), 289 (6.4, M^++1), 288 (36.2, M^+), 222 (13.6), 206 (12.4), 149 (89.0), 124 (72.9), 91 (100.0), 77 (87.7) and 65 (70.6).

Lactone of (R1,S2,R3,S4,SS)-3-(hydroxymethy)l-2-(p-tolylsulfinyl)bicyclo[2.2.1]hept-5-ene-2-carboxylic acid **(*exo*-6A)**.

^{1}H-NMR δ: 1.60 (bd, 1H, J= 9.1 Hz), 1.84 (dt, 1H, J= 1.6 and 9.1 Hz), 2.41 (s, 3H), 3.05 (m, 1H), 3.52 (m, 1H), 3.61 (m, 1H), 3.72 (bs, 1H), 3.82 (dd, 1H, J= 9.0 and 1.6 Hz), 6.43 (dd, 1H, J= 2.7 and 6.0 Hz), 6.63 (dd, 1H, J= 2.7 and 6.0 HZ), 7.37 and 7.65 (AA'BB' system, 4H, J= 8.1 Hz).

Lactone of 2-(hydroxymethyl)-6-methyl-1,4-cyclohexadiene-1-carboxylic acid **(9)**.

Diene: piperylene. Eluent: hexane-ethyl acetate 6:1. IR ($CHCl_3$): 2900, 1745, and 1010 cm^{-1}. ^{1}H-NMR δ: 1.27 (d, 3H, J= 6.9 Hz), 3.00 (m, 2H), 3.11 (m, 1H), 4.73 (m, 2H), and 5.76 (m, 2H). ^{13}C-NMR δ: 19.4, 21.4, 25.3,

71.3, 130.5, 157.0, and 173.1. MS (EI): 152 (1.6, M^++2), 151 (8.1, M^++1), 150 (10.6, M^+), 137 (54.1), 135 (15.6), 91 (100.0), and 77 (39.7).

Lactone of 6-(hydroxymethyl)-2-methyl-1,3-cyclohexadiene-1-carboxylic acid **(10).**

Diene: piperylene. Eluent: hexane-ethyl acetate 6:1. IR ($CHCl_3$): 2890, 1730, and 1030 cm^{-1}. ^{1}H-NMR δ: 2.25 (d, 3H, J= 3.0 Hz), 2.60-1.90 (m, 2H), 3.05 (m, 1H), 3.85 (t, 1H, J= 8.6 Hz), 4.62 (t, 1H, J= 8.7 Hz) and 6.10 (m, 2H). MS (EI): 151 (11.5, M^++1), 150 (17.6, M^+), 149 (25.5), 137 (83.1), 124 (53.1), and 67 (40.1).

Lactone of 2-(hydroxymethyl)-3,5,6,7,8,8a-hexahydronaphthalene-1-carboxylic acid **(11).**

Diene: 1-vinylcyclohexene.[18] Eluent: hexane-ethyl acetate 6:1. IR ($CHCl_3$): 2920, 1750, 1100 and 1020 cm^{-1}. ^{1}H-NMR δ: 0.90-2.10 (m, 6H), 2.30 (m, 1H), 2.45 (m, 1H), 2.82 (m, 1H), 2.92 (m, 2H), 4.65 (bs, 2H) and 5.38 (m, 1H). ^{13}C-NMR: 25.5, 26.1, 28.3, 29.7, 32.5, 35.2, 35.4, 71.3, 112.5, 129.5, 140.0, 157.6 and 168.0. MS (EI): 192 (M^++2, 1.6), 191 (M^++1, 15.7), 190 (M+, 100.0), 175 (6.7), 145 (59.9), 91 (78.5) and 77.0 (40.7).

Lactone of 2-(hydroxymethyl)-2,3,5,6,7,8-hexahydronaphthalene-1-carboxylic acid **(12).**

Diene: 1-vinylcyclohexene. Eluent: hexane-ethyl acetate 6:1. ^{1}H-NMR δ: 1.3-2.6 (m, 8H), 3.0 (m, 1H), 3.65 (bd, 2H, J= 16.5 Hz), 3.75 (t, 1H, J= 8.8 Hz), 4.50 (t, 1H, J= 8.8 Hz), 5.75 (m, 1H).

(R_8,S_{13},S_{14},S_S)-6,7,8,12,13,14,15-Heptahydro-3-methoxy-13-(p-tolylsulfinyl)-16-oxa-17-oxocyclopenta[a]phenanthrene **(13A).**

Diene: Dane's diene.[18] Eluent: hexane-ethyl acetate 4:1. $[\alpha]_D^{20}$=+95.3 (c= 1.1, $CHCl_3$). IR ($CHCl_3$): 2990, 1750, 1600 and 1050 cm^{-1}. ^{1}H-NMR δ: 2.10 (m, 1H), 2.38 (m, 1H), 2.42 (s, 3H), 2.57 (m, 3H), 2.98 (dt, 1H, J=2.8 and 14.5 Hz), 3.23 (dd, 1H, J= 7.2 and 14.8 Hz), 3.38 (m, 1H), 3.50 (t, 1H, J= 9.1 Hz), 3.61 (dd, 1H, J= 6.3 Hz), 3.78 (s, 3H), 6.27 (m, 1H), 6.62 (d, 1H, J= 2.7 Hz), 6.73 (dd, 1H, J= 2.7 and 8.7 Hz), 7.33 (half of an AA'BB' system, 2H, J= 8.3 Hz), 7.43 (d, 1H, J= 8.7 Hz) and 7.57 (half of an AA'BB' system, 2H, J= 8.3 Hz). ^{13}C-NMR δ: 22.7, 25.7, 29.2, 29.8, 36.5, 37.1, 55.2, 69.4, 112.9, 114.9, 124.7, 125.3, 129.8, 138.1, 139.0, 142.8, 159.0 and 174.9. MS (FAB^+): 409 (M^++1, 100).

(S_8,R_{13},R_{14},S_S)-6,7,8,12,13,14,15-Heptahydro-3-methoxy-13-(p-tolylsulfinyl)-16-oxa-17-oxocyclopenta[a]phenanthrene **(13B).**

Diene: Dane's diene. Eluent: hexane-ethyl acetate 4:1. ^{1}H-NMR (significant signals) δ: 2.58 (dt, 1H, J= 2.8 and 14.5 Hz), 2.78 (dd, 1H, J= 8.0 and 15.0 Hz), 3.55 (m, 1H), 3.55 (m, 1H), 3.79 (s, 3H), 4.29 (t, 1H, J= 8.5 Hz), 6.15 (m, 1H), 6.60 (d, 1H, J= 2.7 and 8.7 Hz), 6.75 (dd, 1H, J= 8.7 and 2.7 Hz), 7.39 (half of an AA'BB' system, 2H, J= 8.3 Hz), 7.45 (d, 1H, J= 8.7 Hz) and 7.67 (half of an AA'BB' system, 2H, J= 8.3 Hz).

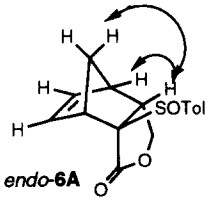
Lactone of (R1,R2,S3,S4)-3-(hydroxymethy)l-2-(p-tolylsulfonyl)bicyclo[2.2.1]-5-heptene-2-carboxylic acid **(+)-7**.

To a solution of *endo*-**6B** (100 mg, 0.35 mmol.) in CH_2Cl_2 (2 ml), cooled at 0°C, was added a solution of MCPBA (0.70 mmol, 2.0 equiv.) in CH_2Cl_2 (1 ml). The mixture was stirred at 0°C for 1h. Then, 10% $Na_2S_2O_3$ (5 ml) was added, the organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (2 x 25 ml). The combined of organic layers was washed with 10% $NaHCO_3$ (10 ml), dried ($MgSO_4$), and concentrated, to give 97 mg (92%) of **(+)-7** as a white solid. m.p.: 107-109°C. $[\alpha]_D^{20}$=+ 44.0 (c= 0.5, $CHCl_3$). IR ($CHCl_3$): 2900, 1750, 1720, 1310, 1240-1180, 1140, 1080 and 1030 cm^{-1}. ^{1}H-NMR δ: 1.70 (dt, 1H, J= 9.2 and 1.5 Hz), 2.42 (bd, 1H, J= 9.2 Hz), 2.47 (s, 3H), 3.27 (m, 1H), 3.64 (m, 1H), 3.84 (dd, 1H, J= 2.5 and 8.9 Hz), 4.28 (t, 1H, J= 8.1 Hz), 6.15 (dd, 1H, J= 3.0 and 5.6 Hz), 6.35 (dd, 1H, J= 3.0 and 5.6 Hz), 7.35 and 7.78 (AA'BB' system, 2H, J= 9.2 Hz).

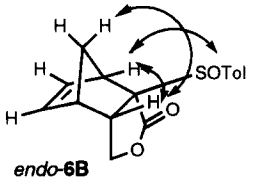
Acknowledgments: We thank *Dirección General de Investigación Científica y Técnica* (DGICYT) for financial support (Grants PB93-244 and PB95-210).

REFERENCES AND NOTES

1. a) de Jong, J. C.; van Bolhuis, F.; Feringa, B. L. *Tetrahedron: Asymmetry*, **1991**, *2*, 1247 (and references cited therein). b) Casas, R.; Parella, T.; Branchadell, V.; Oliva, A.; Ortuño, R. M.; Guingant, A. *Tetrahedron* **1992**, *48*, 2659 (and references cired therein). c) Branchadell, V.; Sodupe, M.; Ortuño, R. M.; Oliva, A.; Gómez-Pardo, D.; Guingant, A.; d'Angelo, J. *J. Org. Chem.* **1991**, *56*, 4135.
2. See Arai, Y.; Koizumi, T. *Sulfur Reports* **1993**, Vol. 15, pp 41-65 and references cited therein.
3. Carretero, J. C.; García Ruano, J. L.; Lorente, A.; Yuste, F. *Tetrahedron: Asymmetry* **1993**, *4*, 177. For the Diels Alder reactions of enantiomerically pure sulfinyl maleimides, see: Arai, Y.; Matsui, M.; Koizumi, T.; Shiro, M. *J. Org. Chem.* **1991**, *56*, 1983.
4. Alonso, I.; Carretero, J. C.; García Ruano, J. L. *Tetrahedron Lett.* **1989**, *30*, 3853.
5. Alonso, I.; Carretero J. C. ; García Ruano, J. L.; Martín Cabrejas, L. M.; López Solera, I.; Raithby, P. R. *Tetrahedron Lett.* **1994**, *35*, 9461.
6. For the use of **2** and **3** as Michael acceptors, see: Posner, G. H. *Acc. Chem. Res.* **1987**, *20*, 72.
7. Posner, G. H.; Frye, L. L.; Hulce, M. *Tetrahedron* **1984**, *40*, 1401.
8. Holton R. A.; Kim, H.-B. *Tetrahedron Lett.* **1986**, *27*, 2191.
9. Hamdouchi, C.; Ph. D. Thesis, E.H.I.C.S., Estrasbourg, 1991.
10. The use of bases or solvents different to those indicated (NaOH and i-PrOH) determines a substantial decrease of the yields.
11. If the hydroxyacid intermediate is isolated, as described in ref. 7, the yield in the preparation of **2** is much lower (46% from **4**).
12. Significant NOE's of *endo*-**6A** and *endo*-**6B**.



endo-**6A**



endo-**6B**

13. Jones, G.; Raphael, R. A.; Wright, S. *J. Chem. Soc. Perkin Trans. 1,* **1974**, 1676.
14. a) Carretero, J. C.; García Ruano, J. L.; Martín Cabrejas, L. M. *Tetrahedron: Asymmetry* **1997**, *8*, 0000. b) Arai, Y.; Kuwayama, S.-I.; Takeuchi, Y.; Koizumi, T. *Tetrahedron Lett.* **1985**, *26*, 6205. See also: c) Arai, Y.; Takayama, H.; Koizumi, T. *Tetrahedron Lett.* **1987**, *28*, 3689.
15. Rotamer **B** exhibits the lowest electrostatic repulsion between the sulfinyl and alkoxycarbonyl oxygens, while **C** could be stabilized by $n^2 \rightarrow d^0$ donor-acceptor interaction between the lone electron pair at oxygen and the empty d orbitals of the sulfur atom. A similar situation was found in the case of 2-*p*-tolylsulfinyl quinones (see Carreño, M. C., García Ruano, J. L.; Urbano, A. *J. Org. Chem.* **1992**, *57*, 6870 and Carreño, M. C., García Ruano, J. L. Toledo, M. A.; Urbano, A.; Remor, C. Z.; Stefani, W. *J. Org. Chem.* **1996**, *61*, 503).

    The low π-facial selectivity of the cycloadditions of compound **2** in the absence of catalysts contrasts with that observed in reactions of alkyl 2-*p*-tolylsulfinyl acrylates (see ref. 14a and referenced cited therein), which exhibit an important steric discrimination of its diastereotopic faces. Although this difference could be partially attributed to the forced conditions required to achieve the complete evolution of **2** (high pressure), it reveals that the conformational preferences around the C-S bond must be different in cyclic and acyclic esters, which in turn must be related with the conformational mobility around the C-CO_2R bond in the latter. For acyclic sulfinylesters, rotamers with the single C-O bond in s-*trans* arrangement with respect to the C=C bond could be the major ones in the conformational equilibrium around the C-CO_2R bond. A lower $n^2 \rightarrow d^0$ donor-acceptor interaction, as well as a higher (less likely) electrostatic repulsion between the oxygens in these rotamers could be invoked to explain the larger population of the rotamers like **B** in acyclic esters and consequently the higher π-facial selectivity of their cycloadditions.
16. Carretero, J. C.; García Ruano, J. L.; Martín Cabrejas, L. M. *Tetrahedron* **1995**, *51*, 8323.
17. a) Alonso, I.; Carretero, J. C.; García Ruano, J. L. *J. Org. Chem.* **1993**, *58*, 3231. b) Alonso, I.; Carretero, J. C.; García Ruano, J. L. *J. Org. Chem.* **1994**, *59*, 1499.
18. a) Junning, L.; Snyder, J. S. *J. Org. Chem.* **1990**, *55*, 4995. b) Symmes, C.; Quin, L.D. *J. Org. Chem.* **1979**, *44*, 1048. c) Hajos, Z. H.; Parrish, D. R.; Goldberg, M. W. *J. Org. Chem.* **1965**, 1213. d) Robins, P. A.; Walker, J. *J. Chem. Soc.* **1956**, 3249.

(*Received in UK* 30 *June* 1997; *revised* 4 *August* 1997; *accepted* 7 *August* 1997)