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SYNTHESIS AND DIELS–ALDER REACTIONS OF HOMOCHIRAL 2–SULFINYLMALEATES WITH CYCLOPENTADIENE

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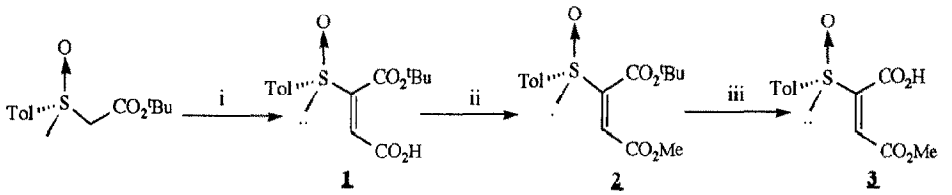
ABSTRACT: Enantiomerically pure 2-p-tolylsulfinylmaleates **1**, **2** and **3** have been readily prepared by Knoevenagel reaction between (S)-menthyl p-toluenesulfinate and glyoxylic acid. Their asymmetric Diels-Alder reactions with cyclopentadiene have been studied under a wide range of uncatalyzed and catalyzed conditions and the stereochemical results have been explained by assuming a steric control approach, in term of S-*cis* or S-*trans* favoured conformations. Uncatalyzed Diels-Alder reactions of **1** and some Lewis acid catalyzed Diels-Alder reactions of **2** show high facial and *endo* selectivities. The facial selectivity of dienophile **2** highly depends on the Lewis acid, whereas reactivity of **1** and **3** is very sensitive to the solvent. These sulfinylmaleates **1**, **2** and **3** act as synthetic equivalents of chiral acetylenedicarboxylates in Diels-Alder reactions after basic elimination of the sulfinylic moiety in the resulting adducts.

Since the pioneer study reported by Maignan[1] in 1983, homochiral vinylsulfoxides have been widely used as dienophiles in Diels Alder reactions due to the ability of the sulfinyl group to control the π-facial selectivity. The main problem of these substrates derives from their low reactivity as dienophiles.[2] Hence, the presence of an extra-activating group, directly bonded to the olefin, is necessary in order to improve the reactivity. Thus, most of the publications about vinylsulfoxides in Diels-Alder reactions deal with the use of sulfinylacrylates[3] and vinylketosulfoxides.[4] However, very little attention has been paid to the synthesis of 2-sulfinylmaleates[5] despite they would be even more reactive and could act as masked chiral synthetic equivalents of acetylenedicarboxylates, which are versatile dienophiles widely used for the preparation of natural products.[6]

In this paper, we describe in detail the synthesis of the sulfinylmaleates 1-3 and their reactions with cyclopentadiene in different conditions.[7] A plausible explanation of the stereochemical course of these reactions (which has been unequivocally established by chemical correlation and X-ray diffraction of the obtained adducts) is also reported.

RESULTS AND DISCUSSION

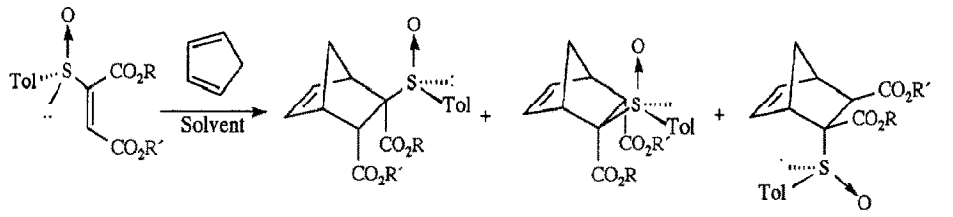
The sulfinylmaleates 1, 2 and 3 may be readily prepared following the sequence shown in Scheme 1. The reaction of t-butylacetate with (-)-(*S*)-menthyl *p*-toluenesulfinate in conditions previously reported[8] gives (*R*)-*t*-butyl *p*-toluenesulfinyl acetate, whose Knoevenagel condensation with glyoxylic acid (3 equiv.) in DMF, in the presence of Et_3N (3 equiv.) and pirrolidine (0.35 equiv.), stereoselectively afforded monoester 1 in 63% yield. The methylation of 1 with MeI/$NaHCO_3$ in DMF gave the mixed diester 2 (85% yield), whose optical purity was determined to be higher than 97% by using Yb(hfc)$_3$ as chiral shift reagent. When reactions i) and ii) (Scheme 1) were carried out without isolation of compound 1, the overall yield in the synthesis of 2 rose to 72%. Finally, selective hydrolysis of the CO_2Bu^t group in compound 2 (CF_3CO_2H in CH_2Cl_2, r.t.) afforded monoester 3 quantitatively. All dienophiles exhibit the (*E*)-configuration at the double bond. This could be deduced from the *cis* arrangement of both CO_2R groups in their adducts with cyclopentadiene (see below).



i) CHO-CO_2H / Et_3N / Pyrrolidine (DMF, rt), ii) $NaHCO_3$ / IMe (DMF, rt); iii) CF_3CO_2H (CH_2Cl_2, rt).

Scheme 1

The results obtained in reactions of cyclopentadiene with dienophiles 1-3 in different conditions (including the addition of Lewis acid as catalysts, the use of ultrasound[9] and activated silica-gel,[10] and the addition of $LiClO_4$[11]) are collected in table 1. In all cases the crude mixtures of two endo adducts and one (from 1 and 2) or two (from 3) exo adducts were evaluated by nmr. Excellent yields after chromatographic purification (eluent: CH_2Cl_2/Et_2O 30:1) were obtained for the mixture 5a, 5b and 5'a, from which the endo adducts (5a+5b, rf=0.16) could be easily separated of the exo one (5'a, rf=0.05). Unfortunately, decomposition of the adducts 4 and 6, both of them with free COOH groups, was observed during chromatography. Nevertheless, almost quantitative yields could be deduced from the nmr spectra of the crude adducts 4 and 6. The mixture of adducts 4, was transformed into their methyl esters 5 (IMe, $NaHCO_3$, DMF) and then purified by flash chromatography. The overall yields of this sequence range in the region 75-85%. This transformation allowed us to correlate 4a, 4b and 4'a with 5a, 5b and 5'a respectively. The stereochemistry of all adducts, except exo-adducts 6'a and 6'b, has been unequivocally established by chemical correlation (see below).



1: R=^{t}Bu, R'=H **4a** **4b** **4'a**
2: R=^{t}Bu, R'=Me **5a** **5b** **5'a**
3: R=H, R'=Me **6a** **6b** **6'a (+ 6'b)**

Table 1: Diels-Alder reactions of 2-sulfinylmaleates 1, 2 and 3 with cyclopentadiene.

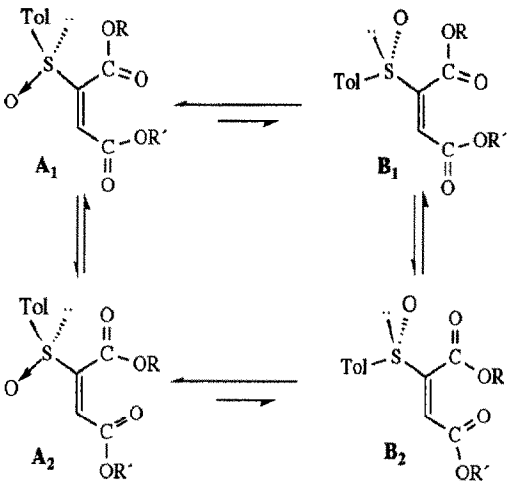
Entry	a)	b)	catalyst (1.2 eq)	T (°C)	t (h)	Products (%)[c] 4a	4b (d)	4'a (e)	1[f]	Yield (%)[g]
1	1(3)	A	-----	rt	1	89	6 (14.8)	5 (19)	--	--
2	1(3)	A	-----	0	3	88	7 (12.6)	5 (19)	--	--
3	1(10)	A	-----	-20	12	92	5 (18.4)	3 (32)	--	--
4	1(3)	B	-----	0	22	51	5 (10.2)	3 (19)	41	--
5	1(10)	C	-----	rt	28	30	47 (0.6)	---	23	--
6	1(3)	A[h]	-----	rt	2	86	8 (10.7)	6 (16)	--	--
7	1(6)	E	-----	rt	24	66	22 (3)	12 (7.3)	--	--
						6a	**6b (d)**	**6'a+6'b (e)**	**3[f]**	
8	3(3)	A	-----	0	3	67	11 (6.1)	22 (3.5)	--	--
9	3(3)	A	-----	-20	24	70	11 (6.4)	19 (4.3)	--	--
10	3(3)	B	-----	0	60	43	13 (3.3)	20 (2.8)	24	--
11	3(3)	D	-----	0	60	54	13 (4.1)	33 (2.0)	--	--
12	3(3)	C	-----	0	3	--	---	---	85	--
						5a	**5b (d)**	**5'a (e)**	**2[f]**	
13	2(10)	A	-----	rt	41	58	17 (3.4)	25 (3.0)	--	93
14	2(10)	E	-----	rt	48	52	24 (2.2)	24 (3.2)	--	90
15	2(6)	A	$BF_3 \cdot OEt_2$	-20	7	37	43 (0.9)	20 (4.0)	--	81
16	2(5)	A	$LiClO_4$[i]	rt	4	48	31 (1.5)	21 (3.8)	--	91
17	2(10)	A[j]	SiO_2	rt	2	45	33 (1.4)	22 (3.6)	--	90
18	2(6)	A	$MgBr_2 \cdot OEt_2$	0	2	10	78 (0.13)	12 (7.3)	--	96
19	2(6)	A	$ZnBr_2$	0	2	12	79 (0.15)	9 (10.0)	--	88
20	2(6)	A[k]	$ZnBr_2$	0	2	9	82 (0.11)	9 (10.0)	--	90
21	2(6)	A	$ZnBr_2$	-20	7	6	89 (0.07)	5 (19.0)	--	95
22	2(6)	A	$ZnBr_2$	-20	7	11	81 (0.14)	8 (11.5)	--	92
23	2(6)	A	$Eu(fod)_3$	rt	2	49	3 (16.3)	48 (1.1)	--	96
24	2(6)	A	$Eu(fod)_3$	-20	12	60	4 (15.0)	36 (1.7)	--	81
25	2(6)	A	$ClAlEt_2$	-20	16	-- complex mixture --			--	--

a) Dienophile (equivalents of diene in brackets). b) Solvent: A=CH_2Cl_2, B=Acetone, C=H_2O/$NaHCO_3$ (1.2 eq), D=i-PrOH, E=Acetone/H_2O (1:1). c) Proportions determined by ^{1}H-NMR. d) *endo* a/*endo* b ratio. e) *endo/exo* ratio. f) Starting product determined by ^{1}H-NMR. g) In pure adducts after chromatography. h) Concentration of 1: $2 \cdot 10^{-4}$ M. i) 5M solution in ether. j) Weight ratio SiO_2/2=10:1. k) Reaction carried out under sonication.

From table 1, it can be seen that the reactions of monoesters **1** and **3** are *endo*-selective (**endo/exo**>1) and they show a π-facial selectivity favouring the formation of the adducts **endo-a** (**endo-a/endo-b**>1, except in Entry 5) and **exo-a**. Both, *endo/exo* and π-facial selectivities, are more marked in the case of monoester 1, the best results being obtained at -20ºC in CH_2Cl_2 (**endo/exo**=32, **4a/4b**=18.4, entry 3). The reactivity and the selectivity decrease as the polarity solvent increases, the effect being maximum when the reactions were carried out in water containing $NaHCO_3$ (entries 5 and 12). These results contrast with the well-known increasing of the reactivity of other dienophiles in this solvent.[12] Changes in concentration also determine variations in the selectivity of the processes (entry 6). On the other hand, poor results (not shown in Table 1) were also obtained when the cycloadditions of 1 and 3 were carried out in the presence of some Lewis acids ($ZnBr_2$, SiO_2, BH_3.THF).

The reaction of diester **2** with cyclopentadiene in the absence of catalysts, is slower and less stereoselective than that of the monoesters **1** and **3** (compare entries 1, 8 and 13). In this case, an increase of the polarity of the solvent hardly modifies the reactivity and slighly decreases the π-facial selectivity observed in CH_2Cl_2 (compare entries 13 and 14). The addition of chelating agents and other Lewis acids substantially increases the reactivity of dienophile **2**, as expected. The *endo/exo* selectivity is progresively improved in the order Li<Mg<Zn, reaching optimum values with $ZnBr_2$ (**endo/exo**=19, entry 21), whereas the addition of $Eu(fod)_3$ strongly decreases this *endo/exo* selectivity (entry 23, **endo/exo**=1.1). The π-facial selectivity of the *endo*-approach of cyclopentadiene on diester **2**, depends on the catalyst. Thus, the use of $Eu(fod)_3$ favours the formation of **5a** (**5a/5b**=16.3, entry 23) whereas chelating agents, like $ZnBr_2$, increase the participation of **5b** (**5a/5b**=0.07, entry 21). On the contrary, in all cases a complete π-facial selectivity is observed in the *exo*-approach, favouring the formation of **5'a**. The use of different catalysts does not modify this fact, but only changes the *endo/exo* ratio obtained. Finally, the influence of $BF_3.OEt_2$, of SiO_2 (entries 15 and 17) and of the use of sonication (entry 16) on the selectivity are only moderate.

If we assume a steric control for the approach of diene and vinylsulfoxide in the Diels Alder reaction,[13] the stereochemical results indicated in table 1 would be explained on the basis of the conformational preferences of the dienophiles around the C-S bond. Thus, conformations **A** are those with the S-O and C=C bonds in *s-cis* arrangement, whereas this disposition is adopted by the Tol-S and C=C in the rotamers **B** (Scheme 2). The adducts "**a**" result in the *endo* or *exo* approach of cyclopentadiene from the less hindered face (the one containing the lone electron pair at sulfur) of conformations **A**. On the other hand, the adducts "**b**" would derive from the approach of the diene from the less hindered face of conformations **B**.

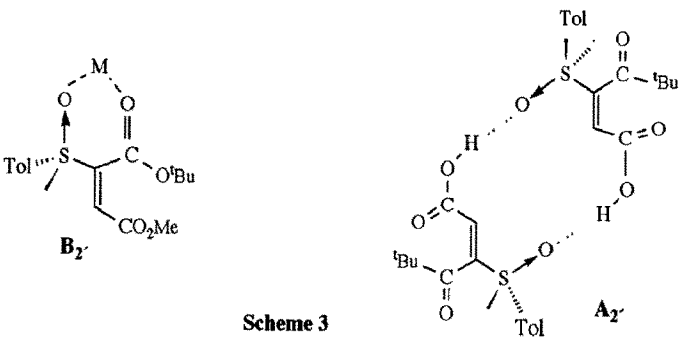


Scheme 2

The π-facial selectivity observed for *endo* and *exo* approaches on the dienophile 2 (it favours the adduct "a" in both cases) suggests that rotamers **A** must be favoured in this substrate. It can be explained taking into account that the *anti* relationship between the sulfinylic oxygen and any of the two oxygens of the CO_2Bu^t group minimizes their electrostatic repulsion. In the presence of a chelating agent, the equilibrium is shifted towards rotamers **B** (namely **B2'** in Scheme 3), which can explain the inversion of the π-facial selectivity observed for the *endo*-approach. The results obtained in reactions of cyclopentadiene with the optically active ethyl 2-*p*-tolylsulfinylacrilate[3c] [**endo-a/endo-b/exo-a/exo-b** = 64:11:23:2; which change to 2:77:2:19 in the presence of $ZnCl_2$] are quite similar to those observed for compound **2** (see entries 13 and 21 of table 1), except in the absence of the **exo-b** adduct[14] (**5'b**), in the mixture obtained from **2**.

The results obtained in reaction of **2** with cyclopentadiene in the presence of $Eu(fod)_3$ (entries 23 and 24), suggest that this catalyst does not act as chelating agent in conformations **B** (the π-facial selectivity for the *endo*-approach is the opposite to that observed with $ZnBr_2$), probably due to the large size of the catalyst. Thus, the association of Eu with the sulfinylic oxygen must yield more stable species from conformations **A**, because the steric interactions of the bulky $Eu(fod)_3$ must be lower, which determines that the reaction evolves mainly to the **5a** and **5'a** adducts. The **endo/exo** ratio obtained from **2** is also related to its conformational preferences, increasing when the **A** population become lower. Thus, the presence of $ZnBr_2$ (stabilizing rotamers **B**) increases, but that of $Eu(fod)_3$ (favouring rotamers **A**) decreases the **endo/exo** ratio, compared to that of the uncatalyzed reaction (entry 13). The fact that the *exo* approach with rotamers **B** is hindered (deduced from the absence of **5'b** in the adducts mixtures obtained from **2**) could explain this dependence.

The higher reactivity of acids **1** and **3** compared with diester **2** suggests that the inter and/or intramolecular hydrogen bonds, involving the sulfinylic and carboxylic groups, activate the double bond.[3d] According to this hypothesis the reactivity of **1** and **3** decreases in solvents able to affect the hydrogen bonds. On the other hand, the high π-facial selectivity exhibited by compound **1** in the *endo*-approach (**4a/4b**=18.4, entry 3) shows an important increase in the participation of type **A** conformations. Both facts could be explained by assuming the formation of a double intermolecular hydrogen bond involving the sulfinylic oxygen (the best acceptor in the molecule) and the CO_2H group, like that represented for **A2'** in Scheme 3. When the reaction of **1** is carried out in acetone:H_2O (entry 7), which breaks the hydrogen bonds precluding the formation of species like **A2'**, both π-facial and *endo/exo* selectivities strongly decrease. Dilution determines similar effects (entry 6). Both facts support the assumption of the intermolecular hydrogen bonds as responsible of the high observed selectivities for dienophile **1**. Other type of associations of the carboxylic group (intramolecular with the CO_2Bu^t group, or intermolecular with the CO_2H group of a second molecule) should not explain the increase in the participation of the **A** rotamers in the equilibrium. The use of aqueous solution of $NaHCO_3$ as solvent decreases even more the reactivity of **1** and inverts the π-facial selectivity (Entry 5). This behaviour must be related to the strong electrostatic repulsion between the CO_2^- group and the CO_2Bu^t one, which must change the conformational situation in the substrate. With respect to the *endo/exo* selectivity the behaviour of compound **1** is also remarkable. Thus, this dienophile shows very high value for the **endo-a/endo-b** ratio despite the large preference for conformations **A** (deduced from the high value of the **endo/exo** ratio, entry 3), which indicates that the *exo*-approach on the favoured conformation **A2'** must be hindered.



Scheme 3

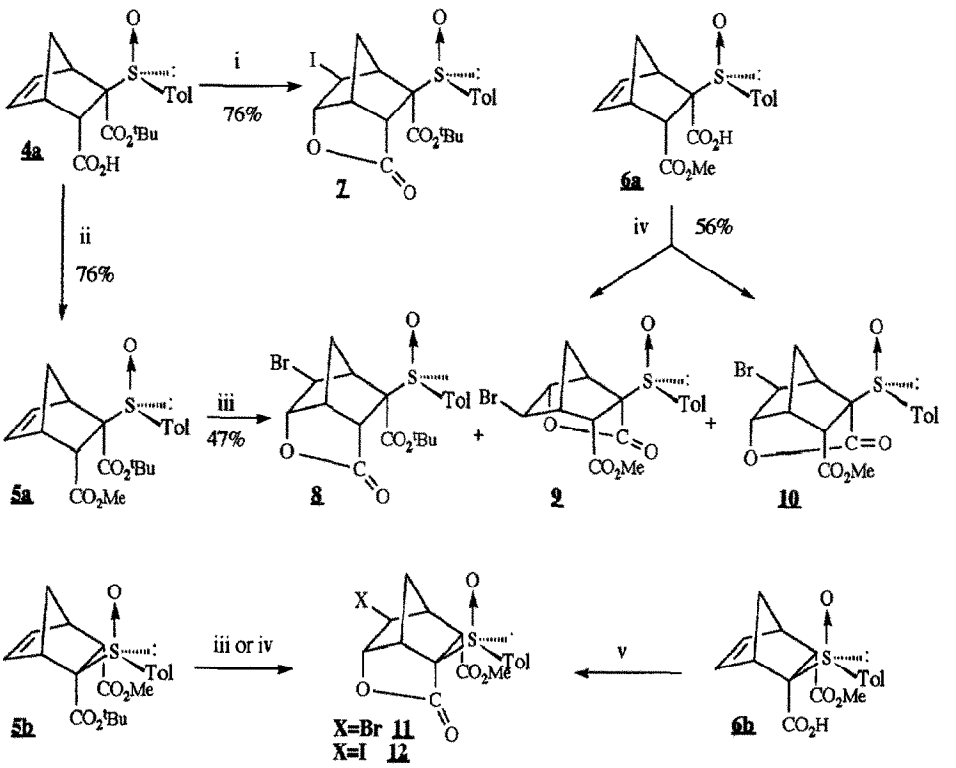
From Scheme 3, it can be seen that the common structural characteristic for conformations **B'2** and **A'2** (those where the *exo* approaches are hindered) is the *s-cis* arrangement of the OBu^t group with respect to the double bond, which is imposed by chelation and hydrogen bonding respectively. The strong steric repulsion between the bulky OBu^t and the cyclopentadiene in the *exo* approach (Scheme 3) could be responsible

of this behaviour.[15]

The stereoselectivity observed in reactions starting from **3** is lower than that observed starting from **1**, which decreases the synthetic interest of **3** as a dienophile. The position of the CO_2H group must favour the hydrogen bonds (inter and/or intramolecular) from spatial arrangements like to those of rotamers **A** and **B**. The most interesting finding of the reactions from this substrate is the formation of exo adduct **6b**, which could be a consequence of the absence of the bulky OBu^t group on this dienophile.

Stereochemical assignment of the adducts

Adducts **4** have been quantitatively correlated with adducts **5** by methylation of the carboxylic group with MeI/$NaHCO_3$ in DMF. The *endo* structure of the adducts **4a**, **4b**, **5a**, **5b**, **6a** and **6b** has been proved by straightforward intramolecular halolactonization reactions[16] as it is shown in Scheme 4.



i) I_2 (1.0 eq), KI (3.0 eq), $NaHCO_3$, H_2O, rt; ii) MeI (20 eq), $NaHCO_3$, DMF, rt; iii) Br_2 (1.2 eq), $CHCl_3$, rt; iii) Br_2 (1.2), $CHCl_3$, rt; iv) Br_2 (2.5 eq), $NaHCO_3$, MeOH, -20°.

Scheme 4

Compound **4a** readily afforded the iodolactone **7** in 76% yield after treatment with I_2/KI/$NaHCO_3$ and yielded **5a** in quantitative yield. On the other hand, the **endo** adducts **5a** and **6a** were transformed into the corresponding bromolactones. The bromolactonization of **5a** with Br_2 in chloroform yielded a mixture 2:2:3 of bromolactones **8**, **9** and **10** respectively, whereas bromolactonization of **6a** with Br_2/$NaHCO_3$ in methanol gave a mixture 1:10 of lactones **9** and **10** respectively. This shows that the three adducts **4a**, **5a** and **6a**, present identical relative configuration in all chiral centers. In the same way the adducts named "b" have been correlated with bromolactone **11** (**4b** → **5b** → **11** ← **6b**).

The absolute configuration of compound **11** has been established as $S_2S_3S_5$ by X-ray diffraction (see figure 1 and experimental part). This result unequivocally shows that the absolute configurations of all compounds depicted in Scheme 4 are correct.

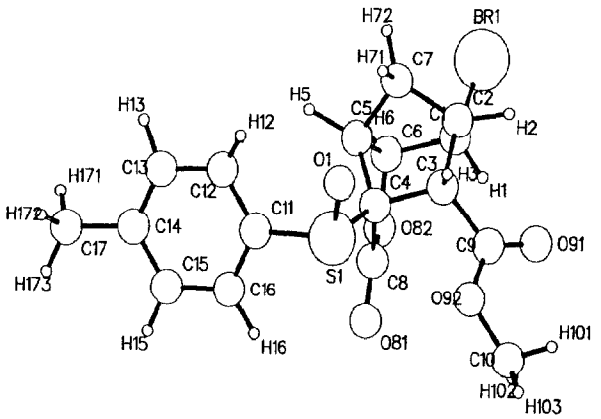
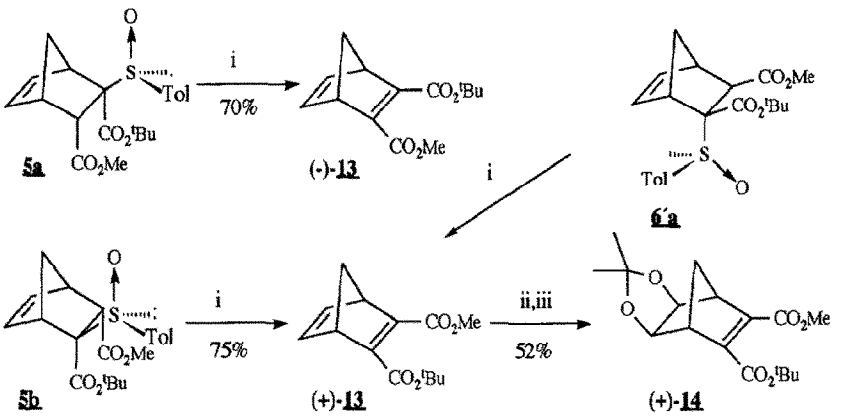


Fig. 1: X-ray diffraction of bromolactone **11**

In order to prove the usefulness of homochiral dienophiles **1** and **2** as synthetic equivalents of mixed dialkyl acetylenedicarboxylates in Diels-Alder reactions, we carried out the elimination of the sulfinyl group in the **endo** adducts **5**, by treatment with DBU in toluene (Scheme 5). At 50ºC, compound **5a** gave the norbornadiene (-)-**13** ([α] = -3.0, $CHCl_3$, c=1.16) in 48 h (70% yield), whereas **5b** afforded the corresponding enantiomer (+)-**13** ([α] = +3.0, $CHCl_3$, c=1.16) in 20 h (75% yield). Compound (+)-**12** has been readily transformed to acetonide **14**[17] ([α] =+22.0, $CHCl_3$, c=1.09); $[\alpha]^{lit}$=+24.5, $CHCl_3$) in two steps: stereoselective *cis*-hydroxylation of the double bond with OsO_4/$ONMe_3$ in *t*-BuOH and hydrolysis of *t*-butyl ester and ketalisation by reaction with acetone dimethylacetal and TsOH. Compound **14** has been reported in the literature[17] as a key intermediate in the synthesis of the carboxylic nucleosides neplanocin A and arysteromycin. In order to know the absolute configuration of the **exo** adduct **5'a**, it was treated with DBU in toluene. The elimination of the sulfinyl group on **5'a** was much slower. However after 4 days at 50ºC enantiomer (+)-**13** was isolated in 10% yield. Therefore its absolute configuration is that depicted in Scheme 5 (and hence that of **4'a**, whose methylation yielded **5'a**).



i) DBU (1 2 eq), 50°C, Touene; ii) OsO_4 (cat)/ $ONMe_3$ (1.2 eq), ^tBuOH, rt·
iii) $(MeO)_2CMe_2$ (2 eq), p-TsOH (0 1 eq), acetone, reflux.

Scheme 5

EXPERIMENTAL

Melting points were determined with a Gallenkamp apparatus in open capillaries and are uncorrected. ^1H-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 first order analysis of spin patterns. Mass spectra (MS) were recorded on a Hewlett-Packard 5985 spectrometer with electron impact (EI, 70eV) or at chemical ionization (CI, NH_3). Mass data are reported in mass units (m/z) and the values in brackets regard the relative intensity from base peak (as 100%). Infrared (IR) spectra were recorded on a Philips PU-9716 spectrometer. Elemental analysis were performed by the Universidad Autónoma de Madrid Microanalitycal Laboratory with a Perkin-Elmer 2400 CHN Elemental analyzer. Optical rotations were measured with a Perkin-Elmer 141 polarimeter.

All solvents were dried before use. Tetrahydrofuran and ether were distilled from sodium-benzophenone under argon. Dichloromethane and chloroform were distilled from P_2O_5. Dimethylformamide was distilled from molecular sieves (4Å). Diisopropylamine was distilled from sodium hydroxide. Cyclopentadiene was freshly distilled. Zinc bromide and zinc iodide were dried at 160°C for 12h with P_2O_5 under vacuo. $BF_3.OEt_2$ was freshly distilled. $EtAlCl_2$, Eu(fod)$_3$ and $MgBr_2.OEt_2$, pyrrolidine and iodomethane were purchased from Aldrich and used without further purification. SiO_2 and $LiClO_4$ were used as Lewis acids in Diels-Alder reactions according to the method previously reported[10,11]. Flash chromatography was performed by use of silica gel (MN-Kieselgel 60, 230-400 mesh).

(E)-(S)$_S$-3-*t*-butoxycarbonyl-3-*p*-tolylsulfinylpropenoic acid (1). To a solution of (+)-(R)-*t*-butyl *p*-tolylsulfinylacetate (1.31 g, 5.17 mmol, 1.0 eq) in DMF (13 ml) were added sequentially glyoxylic acid monohydrate (1.43 g, 15.51 mmol, 3 eq.), triethylamine (1.57 g, 15.51 mmol, 3 eq.) and pyrrolidine (0.13 g, 1.81 mmol, 0.35 eq.). The mixture was stirred at 25°C for 24h and 1% HCl was added to pH=1. The solution was extracted with ether (3x20 ml), the combined organic layers were dried ($MgSO_4$) and evaporated. The crude product was redissolved with 10% $NaHCO_3$ (5 ml) and washed with dichloromethane (2x1 ml) . The aqueous phase was acidified till pH=1 by addition of 10% HCl and extracted with ether (3x20 ml). The combined organic layers were washed with water (10 ml), dried ($MgSO_4$) and evaporated. The residue was recrystallized from ethyl acetate/hexane. Yield: 1.01 g of 1 (63%). m.p: 100-102°C (decom.). $[\alpha]_D^{20}$=+181 (c=0.76, $CHCl_3$). IR($CHCl_3$): 3100, 3030, 3000, 2960, 1740, 1725, 1380, 1220, 1160 and 740 cm^{-1}. ^1H-NMR($CDCl_3$) δ: 1.27(s, 9H,

*t*Bu), 2.41(s, 3H, CH_3Ar), 6.95(s, 1H, H_2), 7.31 and 7.56(AA'BB' system, 4H, arom) and 9.00(bs, 1H, CO_2H). ^{13}C-NMR($CDCl_3$) δ: 21.3, 27.3, 84.4, 126.2, 126.6(2C), 129.9(2C). 137.0, 143.3, 150.2, 160.3 and 166.3. MS(EI): 310(1.7,M^+), 254(13.6), 237(8.7), 189(17.7), 162(14.4), 161(11.1), 140(23.2), 139(100), 108(66.7), 91(27.6) and 57(68.1). Anal. Calcd. for $C_{15}H_{18}O_5S$: C, 58.05%,; H, 5.84%. Found: C, 57.45%; H, 5.69%.

(E)-(S)$_S$-3-*t*-butoxycarbonyl-3-*p*-tolylsulfinylpropenoic acid methyl ester (2). To a solution of (+)-(R)-*t*-butyl *p*-tolylsulfinylacetate (1.31 g, 5.17 mmol, 1.0 eq.) in DMF (13 ml) were added sequentially glyoxylic acid monohydrate (1.43 g, 15.51 mmol, 3 eq.), triethylamine (1.57 g, 15.51 mmol, 3 eq.) and pyrrolidine (0.13 g, 1.81 mmol, 0.35 eq.). The mixture was stirred at 25°C for 24h. Then, $NaHCO_3$ (1.30 g, 15.51 mmol, 3 eq.) and iodomethane (7.34 g, 51.7 mmol, 10 eq.) were added. The reaction was kept at r.t. for 6h. The mixture was treated with 20% NH_4Cl (15 ml) and extracted with ether (3x20 ml). The combined ether phases were washed with water (10 ml), dried ($MgSO_4$) and evaporated. The residue was purified by chromatography on silica gel (hexane-ether 5:2). Yield: 1.21 g of 2 (72%). m.p.: 46-48°C. $[\alpha]_D^{20}$=+179 (c=1, $CHCl_3$), ee>98% (by using Yb(hfc)$_3$ as chiral shift reagent). IR($CHCl_3$): 3030, 3000, 2980, 1730, 1645, 1610, 1350, 1270, 1150 and 1070 cm^{-1}. ^1H-NMR($CDCl_3$) δ: 1.28(s, 9H, *t*Bu), 2.41(s, 3H, CH_3Ar), 3.81(s, 3H, OMe), 6.89(s, 1H, H_3), 7.31 and 7.57(AA'BB' system, 4H, arom). ^{13}C-NMR($CDCl_3$) δ: 21.4, 27.5, 52.2, 84.1, 124.6, 126.4(2C), 129.9(2C). 137.7, 143.1, 152.1, 160.4 and 164.3. MS(EI): 324(3.1, M^+), 268(28.3), 237(10.9), 203(31.4), 161(35.3), 160(96.8), 139(100), 123(22.0), 108(25.0), 92(11.3), 91(22.0), 65(18.3) and 57(66.3). Anal. Calcd. for $C_{16}H_{20}O_5S$: C, 59.24%,; H, 6.21%. Found: C, 59.64%; H, 6.34%.

(E)-(S)$_S$-3-methoxycarbonyl-2-*p*-tolylsulfinylpropenoic acid (3). To a solution of **2** (2.04 g, 6.3 mmol, 1 eq.) in dichloromethane (25 ml) was added trifluoroacetic acid (13.3 ml, 189 mmol, 30 eq.). The mixture was stirred at r.t. for 1h, dichloromethane (20 ml) was added and the mixture was washed with water (20 ml). The organic phase was dried ($MgSO_4$) and evaporated to give 3 (1.76 g). Yield: 100%. m.p.: 86°C(decom.). $[\alpha]_D^{20}$=+178 (c=0.5, $CHCl_3$), IR($CHCl_3$): 3300-2500, 2940, 1725, 1625, 1440, 1350, 1275, 1210, 1165, 1080, 1055, 1010 and 970 cm^{-1}. ^1H-NMR($CDCl_3$) δ: 2.35(s, 3H, CH_3Ar), 3.97(s, 3H, OMe), 7,26(s, 1H, H_3), 7.27 and 7.61(AA'BB' system, 4H, arom). ^{13}C-NMR($CDCl_3$) δ: 21.1, 53.0, 126.1(2C),127.0, 129.9(2C). 136.3, 143.1, 150.1, 161.2 and 165.4. MS(EI): 268(60.2, M^+), 240(10), 139(10.2), 129(19.2), 71(38.6), 70(23.5), 69(47.6), 58(100), 57(63.3) and 55(53.9).

General procedure for uncatalyzed Diels-Alder reactions. To a 0.25M solution of dienophiles in the required solvent 3-10 eq. of cyclopentadiene were added. The mixture was kept at the temperature and reaction times showed in table 1. Then, the solvent was carefully evaporated in vacuo in a cold bath and the resulting mixture of adducts was studied by ^1H-NMR. Quantitative yields in crude products were obtained. The mixture of adducts could not be separated by chromatography.

2-*t*-butoxycarbonyl-2-*p*-tolylsulfinylbicycle[2.2.1]hept-5-ene-3-carboxylic acid (4) From dienophile **1**. Solvent: CH_2Cl_2. Reaction time: 12h. A mixture 92:5:3 of adducts **4a:4b:4'a** was obtained (entry 3 in table 1). IR ($CHCl_3$): 2990, 2915, 2880, 1710, 1375, 1305, 1265 and 1155. MS(CI): 396(8.0), 395(14.7), 394(57.7, M^++18), 378(3.7), 377(8.6), 376(0.6, M^+), 340 (1.2), 339(1.8), 338(8.9), 256(58.6), 255(15.3), 254(100), 237(13.2), 215(10.7), 200(32.2), 199(7.1) and 198(55.8). ^1H-NMR($CDCl_3$) data of the major isomer **4a** (R_1,R_2,S_3,S_4,S_8 configuration), δ: 1.17(s, 9H, *t*Bu),1.39 (bd, 1H, J=9.0 Hz, H_7), 2.06(bd, 1H, J=9.0 Hz, H_7), 2.40(s, 3H, CH_3Ar), 3.15(bs, 1H, H_4), 3.48(bs, 1H, H_1), 3.68(d, 1H, J=3.0Hz, H_3), 6.09(dd, 1H, J=3.0 and 5.4Hz, H_6), 6.62(dd, 1H, J=3.0 and 5.4 Hz, H_5), 7.27 and 7.63(AA'BB' system, 4H, arom) and 9.7 (bs, 1H, CO_2H). ^{13}C-NMR($CDCl_3$) δ: 21.5, 27.4(3C), 44.8, 46.1, 46.3, 53.9, 81.5, 83.8, 126.8(2C), 129.1(2C), 133.5, 137.1, 141.5, 142.5, 165.8 and 176.2. Significant ^1H-NMR($CDCl_3$) data for **4b** (S_1,S_2,R_3,R_4,S_8 configuration), δ: 6.2(dd, 1H), 6.55(dd,1H). Significant ^1H-NMR($CDCl_3$) data for **4'a**, δ: 6.36(dd, 1H, J=2.8 and 5.7Hz), 6.51(dd, 1H).

3-methoxycarbonyl-2-*p*-tolylsulfinylbicycle[2.2.1]hept-5-ene-2-carboxylic acid (6). From dienophile 3. Solvent: CH_2Cl_2. Reaction time: 24h . A mixture 70:11:19 of adducts **6a:6b:6'a+6'b** was obtained (entry 9 in table 1). IR ($CHCl_3$): 3020, 3005, 2980, 1740, 1600, 1490, 1440, 1330, 1250, 930 and 860 cm^{-1}. MS(EI): 195(16.6), 163(19.2), 139(85), 135 (26.4), 124(26.9), 119(18.1), 118(19.7), 105(18.7), 92(40.4), 91(100), 77(49.2), 66(54.9), and 65(46.6).

^{1}H-NMR($CDCl_3$) data of the major isomer **6a** (R_1,R_2,S_3,S_4,S_8 configuration), δ: 1.44(m, 1H, H_7), 2.13(m, 1H, H_7), 2.39(s, 3H, CH_3Ar), 3.23(m, 1H, H_1 or H_4), 3.33(m, 1H, H_1 or H_4), 3.40(s, 3H, OMe), 3.67(d, 1H, J=3.1Hz, H_3), 6.15(dd, 1H, J=3.1 and 5.6Hz, H_5 or H_6), 6.62(dd, 1H, J=2.9 and 5.4 Hz, H_5 or H_6), 7.26 and 7.55(AA'BB' system, 4H, arom). ^{13}C-NMR($CDCl_3$) δ: 21.4, 44.5, 45.2, 45.7, 51.3, 53.2, 80.0, 126.0(2C), 129.1(2C), 133.6, 141.7, 142.1, 168.6 and 172.4. Significative ^{1}H-NMR($CDCl_3$) data for **6b** (S_1,S_2,R_3,R_4,S_8 configuration), δ: 3.10(s, 3H, OMe), 6.14(dd, 1H, J=2.6 and 4.9Hz), 6.70(dd, 1H, J=2.9 and 5.4Hz). Significant ^{1}H-NMR($CDCl_3$) data for **6'a** and **6'b** (*exos*), δ: **6'a)** 3.75 (s, 3H, OMe); 6.43(dd, 1H, J=2.8 and 5.7Hz). **6'b)** 3.50(s, 3H, OMe). **6'a+6'b)**: 6.42-6.56(m, 3H).

Methylation of the carboxylic group in adducts 4. $NaHCO_3$ (54 mg, 0.64 mmol, 2.0 eq.) and iodomethane (910 mg, 6.4 mmol, 20 eq.) were added to a solution of crude adducts **4** (prepared from 100 mg of dienophile **1**) in DMF (1 ml). Stirring was continued for 3 days at r.t. Then, 20% NH_4Cl (10 ml) was added and the reaction mixture was extracted with ether (3x10 ml). The combined organic layers were dried ($MgSO_4$) and evaporated. The crude product was purified by flash chromatography (dichloromethane-ether 30:1) to give 95 mg of pure adducts **5**. Overall yield (Diels-Alder reaction and methylation): 76%.

Catalyzed Diels-Alder reaction of 2 with $MgBr_2.OEt_2$, $ZnBr_2$ or ZnI_2. A solution of dienophile **2** (200 mg, 0.62 mmol, 1.0 eq.) in 2 ml of dichloromethane was added, under argon atmosphere, to a suspension of the Lewis acid (0.74 mmol, 1.2 eq.) in 2 ml of dichloromethane (the temperature was indicated in table 1 for every case). The mixture was stirred for 10 min., and 5-10 eq. of cyclopentadiene were added. Stirring was continued for 2-7h with monitoring by t.l.c. Then, 10% $NaHCO_3$ (10 ml) was added. The organic layer was separated and the aqueous layer was extracted with dichloromethane (2x15 ml). The combined organic layers were dried ($MgSO_4$) and evaporated in vacuo. The mixture of adducts was analyzed by ^{1}H-NMR and purified by flash chromatography (dichloromethane-ether 30:1). The mixture of *endo* adducts (**5a+5b**, R_f:0.16) was readily separated of *exo* adduct (**5c**, R_f:0.05). Yield: 81-96% (see table 1).

Catalyzed Diels-Alder reaction of 2 with $BF_3.OEt_2$. The Lewis acid (0.74 mmol, 1.2 eq.) was added dropwise to a solution of dienophile **2** (200 mg, 0.62 mmol, 1.0 eq.) in 4 ml of dichloromethane at -20°C. The mixture was stirred for 10 min., and then 6 eq. of cyclopentadiene were added. Stirring was continued for 7h. Then 10% $NaHCO_3$ (10 ml) was added. The organic layer was separated and the aqueous layer was extracted with dichloromethane (2x15 ml). The combined organic layers were dried ($MgSO_4$) and evaporated. The mixture of adducts was analyzed by ^{1}H-NMR and separated by flash chromatography (dichloromethane-ether 30:1). Yield: 81%.

Catalyzed Diels-Alder reaction of 2 with $Eu(fod)_3$. A solution of dienophile **2** (200 mg, 0.62 mmol, 1.0 eq.) in 2 ml of dichloromethane was added to a suspension of $Eu(fod)_3$ (0.79 mmol, 1.2 eq.) in 2 ml of dichloromethane (the temperature is indicated in table 1 for every case). The mixture was stirred for 10 min., and then 6 eq. of cyclopentadiene were added. Stirring was continued for 2-12h (the reaction was monitored by t.l.c.) and 5% HCl (10 ml) was added. The organic layer was separated and the aqueous layer was extracted with dichloromethane (2x15 ml). The combined organic layers were dried ($MgSO_4$) and evaporated. The mixture of adducts was analyzed by ^{1}H-NMR and purified by flash chromatography (dichloromethane-ether 30:1). Yields: 81-96%.

(R_1,R_2,S_3,S_4,S_8)-2-*t*-butoxycarbonyl-3-methoxycarbonyl-2-*p*-tolylsulfinylbicycle[2.2.1]hept-5-ene (5a). Data corresponding to a mixture 92:5 of adducts **5a/5b** (entry 3 in table 1, after methylation). $[\alpha]_D^{20}$=-27.6°(c=0.88, $CHCl_3$). IR($CHCl_3$): 2990, 2930, 2850, 1730, 1370, 1255, 1155, 1085 and 1050 cm^{-1}. ^{1}H-NMR($CDCl_3$) δ: 1.30(s, 9H, *t*Bu), 1.32 (bd, 1H, J=9.0Hz, H_7), 2.16(bd, 1H, J=9.0Hz, H_7), 2.40(s, 3H, CH_3Ar), 3.10(bs, 1H, H_4), 3.27(s, 3H, OMe), 3.54(bs, 1H, H_1), 3.57(d, 1H, J=3.1Hz, H_3), 6.10(dd, 1H, J=3.0 and 5.5Hz, H_6), 6.73(dd, 1H, J=3.0 and 5.5Hz, H_5), 7.26 and 7.62(AA'BB' system, 4H, arom). ^{13}C-NMR($CDCl_3$) δ: 21.4, 27.8(3C), 44.3, 44.4, 45.6, 50.9, 54.9, 81.0, 83.3, 126.7(2C), 128.8(2C), 133.0, 138.2, 142.0, 142.4, 166.4 and 172.3. MS(CI): 410(10.9), 409(23.9), 408(100.0, M^++18), 392(7.8), 391(20.5, M^++1), 375(14.0), 352(15.4), 336(11.9), 296(18.1), 270(17.1), 251(10.6), 214(11.6), 212(10.6) and 174(15.4) Anal. Calcd. for $C_{21}H_{26}O_5S$: C, 64.59%,; H, 6.71%. Found: C, 63.89%; H, 6.40%.

(S_1,S_2,R_3,R_4,S_5)-2-*t*-butoxycarbonyl-3-methoxycarbonyl-2-*p*-tolylsulfinylbicycle[2.2.1]hept-5-ene (5b). Data corresponding to a mixture 6:89 of adducts **5a**:**5b** (entry 21 in table 1). $[\alpha]_D^{20}$=+68.2 (c=1.96, $CHCl_3$), IR($CHCl_3$): 2990, 2980, 1735, 1365, 1275, 1140, 1080 and 1050 cm^{-1}. ^{1}H-NMR($CDCl_3$) δ: 1.31(s, 9H, *t*Bu), 1.38 (dt, 1H, J=1.6 and 9.1Hz, H_7), 1.98(bd, 1H, J=9.1Hz, H_7), 2.42(s, 3H, CH_3Ar), 3.16(bs, 1H, H_4), 3.27(bs, 1H, H_1), 3.55(d, 1H,J=4.2Hz, H_3), 3.56(s, 3H, OMe), 6.13(dd, 1H, J=3.0 and 5.5Hz, H_6), 6.57(dd, 1H,J=3.0 and 5.5Hz, H_5), 7.31 and 7.64(AA'BB' system, 4H, arom). ^{13}C-NMR($CDCl_3$) δ: 21.1, 27.5(3C), 44.7, 46.4, 49.5, 49.8, 51.1, 81.0, 82.6, 125.8(2C), 128.9(2C), 134.1, 136.8, 140.1, 141.7, 165.7 and 171.5. MS(EI): 390(0.14, M^+), 375(0.07), 374(0.26), 352(0.13), 251(16), 195(100.0), 177(14), 163(15), 150(19), 149(17), 135(37) and 91(51.09).

(S_1,R_2,S_3,R_4,S_5)-2-*t*-butoxycarbonyl-3-methoxycarbonyl-2-*p*-tolylsulfinylbicycle[2.2.1]hept-5-ene (5c). $[\alpha]_D^{20}$=-7.9 (c=0.95, $CHCl_3$). IR($CHCl_3$): 2990, 2960, 2880, 1730, 1715, 1600, 1495, 1460, 1440, 1370, 1270, 1250, 1180, 1155, 1120, 1085, 1060 and 840 cm^{-1}. ^{1}H-NMR($CDCl_3$) δ: 1.13(s, 9H, *t*Bu), 1.72 (dd, 1H, J=1.9 and 9.3Hz, H_7), 2.18(d, 1H, J=9.3Hz, H_7), 2.41(s, 3H, CH_3Ar), 3.12(bs, 1H, H_1 or H_4), 3.22(d, 1H, J=2.2Hz, H_3), 3.35(bs, 1H, H_1 or H_4), 3.70(s, 3H, OMe), 6.41(m, 2H, H_5 and H_6), 7.28 and 7.58(AA'BB' system, 4H, arom). ^{13}C-NMR($CDCl_3$) δ: 21.4, 27.5(3C), 47.3, 47.5, 48.5, 49.4, 52.1, 81.5, 82.7, 125.8(2C), 129.3(2C), 135.6, 138.0, 139.0, 141.9, 165.7 and 173.7. MS(EI): 390(1.1, M^+), 251(8.7), 196(12.0), 195(100.0), 177(61.3), 163(39.3), 150(11.4), 149(94.3), 140(23.4), 139(32.3), 137(21.1), 135(46.6), 91(63.9), 85(39.4), 77(21.2), 65(27.2) and 57(73.2).

***t*-Butyl (S_2,S_3,S_6,S_9,S_5)-2-iodo-4-oxa-5-oxo-9-*p*-tolylsulfinyltricycle[4.2.1.$0^{3,7}$]nonane-9-carboxylate (7).** $NaHCO_3$ (30 mg, 0.36 mmol, 2.22 eq.) was added to a suspension of crude adducts **4** [prepared from 50 mg (0.16 mmol) of dienophile **1**] in water (0.3 ml). The mixture was stirred at r.t till complete disolution was observed. Then, a solution of 41 mg (0.16 mmol, 1.0 eq.) of iodine and 80 mg (0.48 mmol, 3 eq.) of KI in water (0.4 ml) was slowly added and stirring was continued for 1h at r.t. A yellow solid precipitated gradually and was filtered off and purified by flash chromatography (dichloromethane-ether 30:1) to give 61 mg of pure iodolactone **7**. Yield: 76%.m.p.: 58-60°C.$[\alpha]_D^{20}$=-63.1°(c=2.18, $CHCl_3$). IR($CHCl_3$): 1790, 1705, 1080, 1055 and 1010 cm^{-1}. ^{1}H-NMR($CDCl_3$) δ: 1.17(s, 9H, *t*Bu), 2.32 (d, 1H, J=12.5Hz, H_8), 2.41(s, 3H, CH_3Ar), 2.69(dd, 1H, J=2.9 and 12.9Hz, H_8), 3.33(bs, 2H, H_1 and H_7), 3.46(d, 1H,J=4.7Hz, H_6), 3.99(d, 1H,J=2.9Hz, Hz), 5.13(d, 1H, J=4.9Hz, H_3), 7.33 and 7.56(AA'BB' system, 4H, arom). ^{13}C-NMR($CDCl_3$) δ: 21.6, 25.2, 27.4(3C), 32.9, 38.5, 48.7, 55.5, 78.4, 85.3, 87.6, 126.7(2C), 129.9(2C). 137.3, 143.8, 164.7 and 174.2. MS(EI): 502(1.0, M^+), 446(12.9), 307(2.1), 263(11.6), 163(51.4), 139(91.3), 136(31.5), 128(2.5), 127(2.7) and 91(100).

General procedure for bromolactonization of adducts 5a and 5b. A solution of bromine (22.9 mg, 0.143 mmol, 1.1 eq.) in chloroform (0.2 ml) was added dropwise to an ice-cooled solution of **5b** (50 mg, 0.13 mmol, 1.0 eq.) in the same solvent (1 ml). The mixture was stirred at r.t. until the starting material was completely consumed (≈24h). Then, dichloromethane (15 ml) was added and the organic solution was succesively washed with 10% $NaHCO_3$ (5 ml) and water (5 ml), dried ($MgSO_4$) and evaporated. Flash chromatography of the residue (dichloromethane-ether 40:1) afforded 33.8 mg of lactone **11** (63%).
When adduct **5a** reacted with bromine under the same experimental conditions a mixture of lactones **8**, **9** and **10** was formed (Yield: **47%**, **8:9:10** ratio= 30:24:46, reaction time: 40h)

Procedure for bromolactonization of adducts 6. To a solution of 117 mg (0.35 mmol, 1.0 eq.) of adducts **6** (**6a:6b:6'a+6'b** = 70:11:19, entry 9 in table 1) in methanol (2.3 ml), at -20°C, were added sequentially 35 mg (0.42 mmol, 1.2 eq.) of $NaHCO_3$ and 1.2 ml (0.87 mmol, 2.5 eq.) of a solution 0.72M of bromine in chloroform. The solution was stirred for 3h, dichloromethane (15 ml) was added and the mixture was washed with water (2x10 ml). The organic layer was dried ($MgSO_4$) and evaporated. A mixture of lactones **9** and **10** was obtained (**9/10** ratio= 1/10). These lactones were separated by flash chromatography (hexane-ethyl acetate 3:1). Overall yield: 53% (Diels-Alder reaction and bromolactonization)

***t*-Butyl (S_2,S_3,S_6,S_9,S_5)-2-bromo-4-oxa-5-oxo-9-*p*-tolylsulfinyltricycle[4.2.1.$0^{3,7}$]nonane-9-carboxylate (8).** m.p.: 45-46°C.$[\alpha]_D^{20}$=-50.9 (c=1.25, $CHCl_3$). IR($CHCl_3$): 1795, 1710, 1370, 1340, 1295, 1160, 1150, 1085, 1055 and 1020 cm^{-1}. ^{1}H-NMR($CDCl_3$) δ: 1.61(s, 9H, *t*Bu), 2.28 (d, 1H, J=12.3Hz, H_8), 2.42(s, 3H, CH_3Ar), 2.61(dd, 1H, J=2.5 and 12.3Hz, H_8), 3.30(s, 1H, H_1),

3.36 (m, 1H, H_7), 3.48(d, 1H,J=4.5Hz, H_6), 3.93(d, 1H,J=2.5Hz, H_2), 4.94(d, 1H, J=5.0Hz, H_3), 7.33 and 7.56(AA'BB' system, 4H, arom). ^{13}C-NMR($CDCl_3$) δ: 21.6, 27.4(3C), 31.2, 38.8, 48.0, 50.0, 54.4, 85.4, 86.3, 126.7(2C), 129.9(2C), 137.3, 143.8, 164.5 and 174.2. MS(CI): 476(3.3), 475(9.5), 474(42.5), 473(9.4), 472(38.9, M^++18), 456(0.4), 454(0.2, M^+), 432(5.5), 430(5.2), 418(8.2), 416(8.4), 352(2.9), 350(9.1), 336(5.3), 334(6.2), 255(15.0), 254(100.0). Anal. Calcd. for $C_{20}H_{23}O_5SBr$: C, 52.75%; H, 5.09%. Found: C, 52.50%; H, 5.30%.

Methyl (R2,R3,R6,S9,S8)-2-bromo-4-oxa-5-oxo-6-*p*-tolylsulfinyltricycle[4.2.1.0^{3,7}]nonane-9-carboxylate (9). m.p.: 148-151°C.$[\alpha]_D^{20}$=+8.3 (c=1.18, $CHCl_3$). IR($CHCl_3$): 1775, 1730, 1150, 1050 and 1025 cm^{-1}. ^{1}H-NMR($CDCl_3$) δ: 1.99(ddd, 1H, J=1.4, 2.5 and 11.8Hz, H_8), 2.31 (dt, 1H, J=1.4 and 11.8Hz, H_8), 2.42(s, 3H, CH_3Ar), 2.86(m, 1H, H_1), 3.19(d, 1H, J=3.5Hz, H_9), 3.30 (s, 3H, OMe), 3.84(dd, 1H,J=1.4 and 5.3Hz, H_7), 4.30(d, 1H,J=2.5Hz, H_2), 5.09(d, 1H, J=5.3Hz, H_3), 7.33 and 7.83(AA'BB' system, 4H, arom). ^{13}C-NMR($CDCl_3$) δ: 21.4, 35.0, 48.2, 48.4, 48.6, 52.3, 53.1, 66.7, 86.4, 126.2(2C), 129.4(2C). 135.2, 142.4, 168.9 and 173.1. MS(EI): 414(10.4), 412(9.7, M^+), 165(12.0), 139(100.0), 91(35.0), 70(30.0) and 65(27.2). Anal. Calcd. for $C_{17}H_{17}O_5SBr$: C, 49.40%; H, 4.14%. Found: C, 49.10%; H, 4.27%.

Methyl (S2,S3,S6,S7,S8)-2-bromo-4-oxa-5-oxo-6-*p*-tolylsulfinyltricycle[4.3.0.0^{3,8}]nonane-7-carboxylate (10). m.p.: 104-107°C. $[\alpha]_D^{20}$=+94.5 (c=0.79, $CHCl_3$). IR($CHCl_3$): 1760, 1730, 1445, 1370, 1340, 1320 and 1045 cm^{-1}. ^{1}H-NMR($CDCl_3$) δ: 2.35(d, 1H, J=12.0Hz, H_9), 2.43(s, 3H, CH_3Ar), 2.88(ddd, 1H, J=1.5, 3.0 and 12.0Hz, H_9), 3.13(ddd, 1H, J=1.0, 3.0 and 10.0Hz, H_8), 3.14(s, 3H, OMe), 3.34(bs, 1H, H_1), 3.39(d, 1H, J=5.5Hz, H_7), 3.95(d, 1H, J=2.5Hz, H_2), 4.84(d, 1H, J=4.7Hz, H_3), 7.37 and 7.56(AA'BB' system, 4H, arom). ^{13}C-NMR($CDCl_3$) δ: 21.5, 35.8, 46.2, 49.5, 51.0, 52.6, 78.8, 89.2, 125.9(2C), 130.1(2C), 135.3, 143.4, 167.9 and 171.4. MS(EI): 414(4.6), 412(5.2, M^+), 241(25.2), 165(10.6), 151(11.9), 149(28.6), 139(36.8), 137(26.4), 125(21.9), 119(27.7), 111(39.8), 109(32.5), 97(63.8), 96(24.6), 95(52.0), 91(33.1), 85(50.8), 83(56.2), 82(23.1), 81(45.3), 79(21.6), 71(71.4), 69(82.7), 57(100.0) and 55(74.2).

Methyl (S2,S3,S6,R9,S8)-2-bromo-4-oxa-5-oxo-6-*p*-tolylsulfinyltricycle[4.2.1.0^{3,7}]nonane-9-carboxylate (11). m.p.: 187-189°C. $[\alpha]_D^{20}$=+194.9 (c=0.85, $CHCl_3$). IR($CHCl_3$): 1780, 1735, 1080, 1040 and 1015 cm^{-1}. ^{1}H-NMR($CDCl_3$) δ: 2.03(dd, 1H, J=1.8 and 11.7Hz, H_8), 2.25 (dt, 1H, J=1.5 and 11.7Hz, H_8), 2.43(s, 3H, CH_3Ar), 3.03-3.07(m, 2H, H_1 and H_7), 3.83 (s, 3H, OMe), 4.03(d, 1H,J=3.5Hz, H_9), 4.60(d, 1H,J=2.3Hz, H_2), 4.80(d, 1H, J=6.2Hz, H_3), 7.36 and 7.60(AA'BB' system, 4H, arom). MS(EI): 414(17.1), 412(18.9, M^+), 333(0.3), 273(1.3), 165(10.8), 139(100.0), 123(13.9), 91(24.5), 79(9.3), 78(10.0), 77(22.3), 65(21.0) and 59(11.2).

Experimental data and estructure solution and refinement procedures. *Crystal data*: *Formula*: $C_{17}H_{17}O_5SBr$. *Crystal habit*: prismatic. *Crystal size (mm)*: 0.15 x 0.10 x 0.12. *Symmmetry*: monoclinic, P21. *Unit cell determination*: least-squares fit from 41 reflexions (0<52). *Unit cell dimensions*: 17.243 (1), 6.841 (1), 7.198 (1), 90, 91.23 (2), 90. *Packing*: V(A), Z: 848.88; Dc (g.cm), M, F(000): 1.6169, 413.282, 420; u(cm): 46.683. *Experimental data*: *Technique*: four circle diffractometer: Philips 1100, bisecting geometry; graphite oriented monochromator: Cu K; w/2θ scans, scan width: 1.6; detector apertures 1.1, up 0max. 65; 1.0 min./reflex.. *Number of reflexions*: measured: 3379; independent: 2886; observed: 2883 (2 (I) criterion). *Range of hkl*: -20 20, -8 8, -8 8, (sin θ/λ) mx. 0.59. *Value of Rint.*: 0.006. *Standard reflexions*: 2 reflexions every 90 minutes; variation: no. *Max-min transmission factors*: 1.797, 0.769. *Solution and refinement*: *Solution*: heavy atom method. *Refinement*: L.S. on Fobs, with 1 block. *H atoms*: difference Fourier synthesis. *Final F peaks*: 3.0 eA-3. *Final R and Rw*: 0.053, 0.071. *Computer and programs*: VAX 750, XRAY76System, PARST, CONFAB. *Scattering factors*: Int. Tables for X-Ray Crystallography. *Anomalous dispersion*: Int. Tables for X-Ray Crystallography.

Methyl (S2,S3,S6,R9,S8)-2-iodo-4-oxa-5-oxo-6-*p*-tolylsulfinyltricycle[4.2.1.0^{3,7}]nonane-9-carboxylate (12). A mixture of adducts 5 (50 mg, **5a/5b**=0.07, 0.13 mmol, 1.0 eq.) was dissolved in formic acid (0.4 ml). Stirring was continued for 3h at r.t. Then, water (10 ml) was added and the product was extracted with ether (3x10 ml), dried ($MgSO_4$) and evaporated. The residue was suspended in water (0.3 ml) and $NaHCO_3$ (24 mg, 0.29 mmol, 2.22 eq.) was added. The mixture was stirred till complete disolution was observed. Then, a solution of iodine (33 mg, 0.13 mmol, 1.0 eq.) and KI (65 mg, 0.39 mmol, 3.0 eq.) in water (0.4 ml) was added and stirring was continued for 4h. The product was extracted with ether (3x20 ml) and washed sequentially with 10% $Na_2S_2O_3$ (1x5 ml) and water (1x5 ml), dried ($MgSO_4$) and evaporated. The crude product was purified by flash

chromatography (hexane-ethyl acetate 7:1) to give 22.4 mg of pure iodolactone **12** (Yield: 38%). m.p.: 175-178°C. $[\alpha]_D^{20}$=+152.6 (c=1.49, $CHCl_3$). IR($CHCl_3$): 1770, 1730, 1070, 1040, 1030 and 995 cm^{-1}. ^{1}H-NMR($CDCl_3$) δ: 2.12(ddd, 1H, J=2.0, 2.5 and 11.7Hz, H_8), 2.29 (dt, 1H, J=1.4 and 11.7Hz, H_8), 2.43(s, 3H, CH_3Ar), 3.01(ddd, 1H, J=1.3, 2.8 and 5.3Hz, H_7), 3.08(m, 1H, H_1), 3.83 (s, 3H, OMe), 3.96(d, 1H,J=3.4Hz, H_9), 4.64(d, 1H,J=2.5Hz, H_2), 4.97(d, 1H, J=5.3Hz, H_3), 7.35 and 7.59(AA'BB' system, 4H, arom). ^{13}C-NMR($CDCl_3$) δ: 21.5, 23.7, 36.8, 50.1, 52.8, 68.7, 87.7, 88.1, 89.5, 125.6(2C), 130.2(2C). 135.7, 143.0, 169.5 and 172.0. MS(EI): 462(1.6), 461(2.4), 460(14.6, M^+), 167(11.7), 166(12.5), 139(100.0), 123(15.4), 105(13.8), 91(55.5), 77(59.2) and 65(61.9). Anal. Calcd. for $C_{17}H_{17}O_5SI$: C, 44.36%; H, 3.72%. Found: C, 44.73%; H, 3.74%.

(+)-(1S,4R)-2-*t*-butoxycarbonyl-3-methoxycarbonylbicycle[2.2.1]hepta-2.5-diene (+)-(13). To a solution of 232 mg (0,59 mmol, 1.0 eq.) of adduct **5b** (**5a/5b**=0.07) in dry toluene (2 ml) were slowly added 108.5 mg (0.71 mmol, 1.2 eq.) of DBU. The solution was stirred at r.t. for 20h and then, 20% NH_4Cl (15 ml) was added. The organic layer was separated and the aqueous layer was extracted with dichloromethane (2x15 ml). The combined organic layers were dried ($MgSO_4$) and evaporated. The residue was purified by flash chromatography (hexane-ethyl acetate 20:1) to give 111 mg of pure **(+)-13.** Yield: 75%. $[\alpha]_D^{20}$=+3.0 (c=1.16, $CHCl_3$), e.e=87% [by using Yb(hfc)$_3$ as chiral shift reagent]. IR($CHCl_3$): 3010, 2970, 1730, 1705, 1635, 1445, 1380, 1305, 1160 and 1115 cm^{-1}. ^{1}H-NMR($CDCl_3$) δ: 1.49(s, 9H, *t*Bu), 2.06(dt, 1H, J=1.5 and 6.7Hz, H_7), 2.26 (dt, 1H, J=1.5 and 6.7Hz, H_7), 3.77(s, 3H, OMe), 3.89(m, 2H, H_1 and H_4), 6.91(m, 2H, H_5 and H_6). ^{13}C-NMR($CDCl_3$) δ: 27.9(3C), 51.6, 53.1(2C), 72.5, 81.5, 142.1, 142.3, 150.0, 153.6, 164.3 and 165.6. MS(EI): 252(28.2), 195(100.0), 194(49.4), 193(15.4), 179(26.9), 177(64.7), 176(34.0), 163(66.0), 162(44.2), 161(35.3), 149(64.7), 135(39.7), 118(39.7), 91(52.6) and 57(78.8).

Enantiomer (-)-13. This compound was obtained from adduct **5a** (**5a/5b** ratio= 18.4) following the same experimental procedure described for **(+)-13.** Reaction time= 48h. Yield= 70%. $[\alpha]_D^{20}$=-3.0 (c=1.17, $CHCl_3$).

(+)-(3aR,4R,7S,7aS)-3a,4,7,7a-tetrahydro-2,2-dimethyl-6-methoxycarbonyl-4,7-methano-1,3-benzodioxole-5-carboxylic acid (+)-(14). To a solution of 50 mg (0.2 mmol, 1.0 eq.) of **(+)-13** (ee=78%) in *t*BuOH (0.6 ml) were added 27 mg (0.24 mmol, 1.2 eq.) of $Me_3NO.2H_2O$ and 10μl of a 4% solution of OsO_4 in water. Stirring was continued for 24h at r.t. A solution of 20 mg of $Na_2S_2O_4$ in 0.5 ml of water was added. After this, 10% HCl was added dropwise to pH≈2. The mixture was extracted with dichloromethane (2x10 ml), the combined organic layers were washed with water (5 ml), dried ($MgSO_4$) and evaporated to give a crude mixture of the dihydroxylated derivative (92% yield). This product was employed without further purification.

To a solution of 43 mg (0.15 mmol, 1.0 eq.) of the dihydroxylated derivative in acetone (1 ml) were added 31 mg (0.3 mmol, 2 eq.) of $(MeO)_2CMe_2$ and 2 mg (0.01 mmol, 0,07 eq.) of *p*-toluenesulphonic acid. The mixture was refluxed for 17h. The solvent was removed and 10% $NaHCO_3$ (5 ml) was added. This aqueous phase was washed with dichloromethane (5 ml) and acidified to pH=1 by addition of 10% HCl, then the solution was extracted with dichloromethane (3x10 ml), the combined organic layers were dried (Na_2SO_4) and evaporated to give 22 mg of pure **(+)-14** (yield: 57%).$[\alpha]_D^{20}$=+22 (c=1.09, $CHCl_3$). ee: 77%. [lit[17]: $[\alpha]_D^{20}$=-29.5 (c=1.2, $CHCl_3$), ee>98%]. ^{1}H-NMR($CDCl_3$) δ: 1.35(s, 3H, Me), 1.51(s, 3H, Me), 1.89(dt, 1H, J=1.6 and 9.9Hz), 2.07(dt, 1H, J=1.4 and 9.9Hz), 3.37(m, 1H), 3.53(m, 1H), 3.94(s, 3H, OMe), 4.39(d, 2H, J=1.3Hz).

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14.- Similar anomalous situations involving a stereoselective reaction for the *exo*-approach but not for the *endo*-approach, have been observed in 3-sulfinyl acrylates (ref. 3b).

15.- The fact that **5'b** was not obtained from **2** under any conditions (even in the absence of chelating agent) could be explained by assuming that B_2 rotamer, which exhibits the same *s-cis* arrangement between the C-OBu^t and C=C bonds, is more stable than B_1 rotamer. A donor-aceptor interaction between the unshared electron pair on the carbonyl and the empty d orbital on sulfinyl sulfur, when both groups adopt a spatial arrangement like that of B_2, was proposed to explain the conformational behaviour of 2-phenylsulfinylcyclohexanone (M.C. Carreño et *al. J. Org. Chem.*, **1990**, *55*, 2120). A similar interaction could be invoked to justify the larger stability of B_2 with respect to B_1.

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