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# Remote stereocontrol by the sulfinyl group. Diels—Alder reaction of cyclopentadiene with substituted (S)-[2-(p-tolylsulfinyl)styrenes and (S)-[2-(p-tolylsulfinyl)phenyl] vinyl ketones

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#### ABSTRACT

The ability of a homochiral sulfinyl group at the dienophile to act as a remote stereocontrol inductor in the Diels–Alder reaction with cyclopentadiene has been evaluated. High pressure conditions were required for the reactions of (*S*)-2-(*p*-tolylsulfinyl)styrenes **3–5** (*E*-1,2-disubstituted double bond) and **6–8** (1,1-disubstituted double bond). A good facial selectivity and total *endo* selectivity were attained with 1,1-disubstitued dienophiles, though the 1,2-disubstituted ones afforded poorer results. In contrast, (*S*)-[2-(*p*-tolylsulfinyl)phenyl] vinyl ketones **9–11** reacted readily at low temperature (–40 °C) with complete *endo* selectivity and high facial selectivity in the presence of Yb(OTf)<sub>3</sub> as a chelating reagent of sulfinyl and carbonyl oxygen atoms. Concerning furan reactions, β-trifluoromethyl enone **14** afforded Diels–Alder adducts with high facial selectivity in the presence of the Lewis acid, but β-non-substituted enones **9** and **12** yielded products of furan conjugate addition to the double bond.

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#### 1. Introduction

The generation of asymmetric centers with a high control of the stereoselectivity constitutes an important goal in organic synthesis. In this context, the Diels–Alder reaction<sup>1</sup> has always been considered as indispensable for the construction of cyclohexane frameworks in a regio- and stereochemically defined manner, being possible to control the absolute configuration of cycloadducts as it has been exemplified by the use of chiral auxiliaries (bonded to the dienophile<sup>2</sup> or the diene<sup>3</sup> moieties), chiral Lewis acid catalysts<sup>4</sup> or organocatalysts,<sup>5</sup> and even with chiral solvents.<sup>6</sup> Among the asymmetric inductors profusely employed in Diels–Alder reaction, the sulfinyl group plays a preponderant role.<sup>7</sup> On the other hand, the application of modern synthetic techniques, as microwave activation,<sup>8,9</sup> sonication<sup>10</sup> or high pressure,<sup>11</sup> sometimes combined with solvents as water,<sup>8b,10b,12</sup> fluorous media,<sup>11b</sup> ionic liquid-s<sup>8b,10a,13</sup> or supercritical CO<sub>2</sub>,<sup>14</sup> allows to increase the reaction rate or to obtain better selectivities.

Some years ago we initiated a program to investigate the efficiency of the sulfinyl group to control the stereoselectivity of reactions taking place at remote positions.<sup>7a</sup> We have mainly studied 1.4-asymmetric induction processes controlled by the sulfinyl group at the nucleophilic moiety,<sup>15,16</sup> and we have observed that these reactions proceed with an almost complete control of the stereoselectivity. Besides, in the presence of Yb(OTf)<sub>3</sub>, an excellent result was also obtained in 1,4-17 and 1,5-asymmetric induction processes<sup>18</sup> being the sulfur function at the electrophile, usually a carbonyl compound. The efficiency of this catalyst seems to be due to the formation of stable chelated species with the sulfinyl and carbonyl oxygen atoms, which are highly reactive and show a strong facial discrimination toward the attack of nucleophiles. On the other hand, hetero Diels-Alder reactions of oxygenated dienes with (S)-2-[2-(p-tolylsulfinyl)phenyl]acetaldehyde (1) provided sulfinyl dihydropyranones<sup>19</sup> with a high level of *trans* selectivity in the presence of Yb(OTf)<sub>3</sub>, according to a 2 step mechanism involving the Mukaiyama's type reaction where chelated species formed from the aldehyde and the Lewis acid are acting as electrophiles.

Taking into account our experience in asymmetric cycloaddition reactions mediated by sulfoxides,<sup>7a,20,21</sup> as well as in the use of the sulfinyl group at 2-*p*-tolylsulfinylphenyl moiety as remote chiral inducer of many nucleophilic additions<sup>16</sup> we wondered the possible influence of this moiety on the stereoselectivity of the



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Diels–Alder reactions of double bonds containing it,<sup>19,22</sup> being 2-*p*-tolylsulfinyl styrene (**2**) our model substrate. However, as this compound is presumably a bad dienophile, we decided to incorporate EWG (electron withdrawing groups) to different positions of the double bond. In this sense, we have also studied 1,2-disubstituted *E*-sulfinylstyrenes **3–5**, and 1-acylstyrenes **6–8** (Scheme 1), differing in the relative position of the CO and SO groups. Finally, sulfinylated vinyl arylketones **9–12** and **14**, with the arylsulfinyl group no directly joined to the dienophilic system, complete the series of compounds whose behavior in their Diels–Alder reactions with cyclopentadiene have been studied and described in this paper.



**3**: Z = COMe **5**: Z = NO<sub>2</sub>





9 ( $R_1$ =H,  $R_2$ =H,  $R_3$ =H)12 ( $R_1$ =CH<sub>3</sub>,  $R_2$ =H,  $R_3$ =H)10 ( $R_1$ =H,  $R_2$ =CH<sub>3</sub>,  $R_3$ =H)14 ( $R_1$ =H,  $R_2$ =H,  $R_3$ =CF<sub>3</sub>)11 ( $R_1$ =H,  $R_2$ =H,  $R_3$ =CH<sub>3</sub>)

Scheme 1. Dienophiles studied in this paper.

#### 2. Results and discussion

The synthesis of compounds  $2^{23}$  and  $6-8^{18d}$  had been previously reported. The (*S*)-2-*p*-tolylsulfiny benzaldehyde<sup>17</sup> was used as starting material for the rest of dienophiles considered in this paper. Enantiomerically pure compounds **3** and **4** resulted by its reaction with the corresponding diethyl phosphonate, whereas nitroaldol reaction was used to synthesize **5** (see Scheme 2). Finally, **9–12** were prepared by reaction of the aldehyde with the corresponding vinyl magnesium bromide and further oxidation of the resulting diastereoisomeric mixtures of alcohols with MnO<sub>2</sub> at rt (Scheme 2).

A different approach, consisting in the aldolic condensation under acidic conditions of the trifluoroacetaldehyde aminal<sup>24</sup> with the silylenolether derived from (*S*)-2-(*p*-tolylsulfinyl)phenylethanone<sup>25</sup> **13**, was used to prepare the trifluoromethyl ketone **14** (Scheme 3).

Reactions of the 2-*p*-tolylsulfinyl styrene **2** were unsuccessful in all the studied conditions. Reactions of compounds **3–5** with cyclopentadiene, performed under multiple conditions (reaction time, temperature, and Yb(OTf)<sub>3</sub> as Lewis acid), were also unsuccessful. Thus we studied the influence of high pressure conditions.<sup>11</sup>

Reactions of **3**–**5** were carried out in acetonitrile at room temperature with 10 equiv of cyclopentadiene in a high pressure apparatus at 8.2 kbar. The obtained results are depicted at Table 1.

In the absence of a Lewis acid, the cycloaddition of sulfinylketone **3** needs two days to completion and proceeds with good yield but very low stereoselectivity (*endo–exo* and facial). The presence of Yb(OTf)<sub>3</sub> as Lewis acid substantially increases the reactivity (only 10 min were needed to completion) but has scarce



**Scheme 2.** Synthesis of (*S*)-[2-(*p*-tolylsulfinyl)]styrenes **3**–**5** and (*S*)-[2-(*p*-tolylsulfinyl)phenyl] vinyl ketones.



Scheme 3. Synthesis of E-(S)-[2-(p-tolylsulfinyl)phenyl] trifluoromethylvinyl ketone.

Table 1Reaction of sulfinylstyrenes 3, 4 and 5 with cyclopentadiene at 8.2 kbar



Entry	Dienophile	Yb(OTf)₃ (equiv)	Time (h)	Adduct (endo/exo) <sup>a</sup>	endo A/B	Yield (%) <sup>b</sup>
1	3	_	48	<b>15</b> (67/33)	55/45	78
2	3	1	10 min	15 (40/60)	67/33	80
3	4	_	3+3+12 <sup>c</sup>	<b>16</b> (70/30)	35/65	80
4	4	1	3+3+12 <sup>c</sup>	<b>16</b> (70/30)	75/25	90
5	5	_	6,5	<b>17</b> (100/0)	60/40	90
6	5	1	4	<b>17</b> (100/0)	64/36	91

<sup>a</sup> Measured by <sup>1</sup>H NMR.

<sup>b</sup> Global yield.

<sup>c</sup> Cyclopentadiene (10 equiv) were added after each period.

positive influence on both types of selectivity, being the predominance of the *exo* adducts the most relevant feature of these reactions. Similar behavior was observed in reactions with the ester derivative **4** (Table 1, entries 3 and 4). The best stereoselective behavior was showed by the nitro functionalized dienophile **5** (Table 1, entries 5 and 6), that exclusively affords *endo* adducts, but with poor facial selectivity. Reactivity and sense of the facial selectivity for *endo* adducts are not significantly increased by the catalyst.

Separation of the *endo* and *exo* adducts was possible in all the cases, as well as *endo*-**15A** and *endo*-**15B**. *endo* and *exo* adducts are clearly differentiated by NOESY experiments and vicinal J values of head-bridge protons. The classification as *endo* adducts of the two inseparable major diastereoisomers of adduct **16** as well as those of adduct **17**, was effected by *m*-CPBA oxidation of the mixture of sulfoxides into a mixture of the corresponding enantiomeric sulfones (undistinguished by <sup>1</sup>H NMR). The absolute configuration for the *endo* adducts was based in the unequivocal assignment of compound *endo*-**15A**, performed by X-ray diffraction studies,<sup>26</sup> and the comparison of the chemical shifts of the olefinic protons of the *endo*-**15**-**17** adducts, resonating at lower field than those corresponding to the *endo* **A** structures.

We then studied the reactivity of the 1,1-disubstituted alkenes **6–8**, with a presumably better relative arrangement of the carbonyl and sulfinyl groups to become chelated by the Lewis acid [this chelation had been proposed to explain the stereoselective reduction with NaBH<sub>4</sub> in the presence of Yb(OTf)<sub>3</sub><sup>18d</sup>]. Reactions of ketones **6** (*R*=Me), **7** (*R*=*n*-Pr) and **8** (*R*=*i*-Pr) with cyclopentadiene were unsuccessfully attempted in acetonitrile under thermal and catalytic [Yb(OTf)<sub>3</sub>] conditions, making necessary the use of high pressure conditions (8.2 kbar) to obtain the corresponding adducts. The results for complete conversion of the dienophile are shown in Table 2.

#### Table 2

Diels-Alder cycloaddition of enones 6, 7 and 8 with cyclopentadiene

0=	O S pTol + R 10 e	Yb(OTf) <sub>3</sub> CH <sub>3</sub> CN 8.2 Kbar quiv	NOE		Tolues +	
R= I r	Ие (6), л-Pr (7), <i>i-</i> Pr (8)		endo-	18A-20A	endo-1	8B-20B
Entry	Dienophile	Yb(OTf) <sub>3</sub> (equiv)	Time (h)	Adduct	endo A/B <sup>a</sup>	Yield <sup>b</sup> (%)
1	6		3	18	86/14	75
2	6	1	6.5	18	93/7	79
3	7	_	3	19	90/10	73
4	7	1	6.5	19	90/10	73
5	8	_	3	20	83/17 <sup>c</sup>	—
6	8	1	6.5	20	90/10	83

<sup>a</sup> Measured by <sup>1</sup>H NMR.

<sup>b</sup> Yield of the major **A** adduct.

<sup>c</sup> A 30% of an *exo* adduct was also obtained.

The *endo* structure assigned to compounds **18–20** was based on the NOESY experiment carried out with adduct **18A**, that suggest the existence of n.O.e. effect between the *R* group and the headbridged hydrogen, only understandable with the acetyl group placed at *endo* position. The assignment of the adducts as belonging to the series **A** or **B** was effected by comparison of <sup>1</sup>H NMR chemical shifts of both olefinic protons, with closer values in adducts **B** than in **A** ones. Finally, the absolute configuration, which is not unequivocal, was deduced from the mechanistic model proposed for these reactions (see later). Two main conclusions can be obtained from the results at Table 2, the complete *endo* selectivity<sup>27</sup> (with the sole exception of enone **8** without Yb(OTf)<sub>3</sub>, entry 5) and the high facial selectivity, both scarcely dependent of the presence of the Lewis acid.

The results obtained from Diels-Alder reaction of enones 9-12 with cyclopentadiene are depicted in Table 3. Contrasting with the previously studied ketones, these enones are good dienophiles and react with cyclopentadiene at atmospheric pressure, even at -40 °C. Complete endo selectivity was attained from 9-11, whereas the exo adducts were also obtained in reactions, catalyzed or not, from compound 12 (entries 10 and 11). In all the cases, very low (<10%) facial selectivity was observed in the absence of Lewis acid (Table 3, entries 1, 3, 6 and 10), but the presence of Yb(OTf)<sub>3</sub> improves it very much with monosubstitued (9) and (E)-disubstituted (10) ketones (Table 3, entries 2 and 5), being the influence less significant with (Z)-disubstituted (11) and gemdisubstituted (12) ketones (entries 9 and 11). This improvement suggests the formation of a stable chelate, with the Lewis acid associated to the sulfinyl and carbonyl oxygen atoms, restricting the conformational preferences of the dienophile and thus increasing the stereoselectivity (see later).

 Table 3

 Diels-Alder cycloaddition of enones 9–12 with cyclopentadiene



Entry	Dienophile	Yb(OTf)3 equiv	Time (h)	Temp (°C)	endo A/B <sup>a</sup>	Yield <sup>b</sup> (%)
1	9	_	1	-40	<b>21</b> (55/45)	86 <sup>c</sup>
2	9	1.2	10 min	-40	<b>21</b> (96/4)	94
3	10	_	12 days	rt	<b>22</b> (55/45)	_
4	10	1.2	23	-10	<b>22</b> (93/7)	83
5	10	1.2	72	-40	<b>22</b> (96/4)	85
6	11	_	14 days	rt	<b>23</b> (53/47)	_
7	11	1.2	3	rt	<b>23</b> (80/20)	_
8	11	1.2	36	-10	<b>23</b> (85/15)	75
9	11	1.2	48	-40	<b>23</b> (85/15)	_
10	12	_	14 days	rt	<b>24</b> (50/50) <sup>d</sup>	_
11	12	1.2	96	$-40^{e}$	<b>24</b> (75/25) <sup>f</sup>	80 <sup>c</sup>

<sup>a</sup> Measured by <sup>1</sup>H NMR.

<sup>b</sup> Yield of the major **A** adduct.

<sup>c</sup> Global yield.

<sup>d</sup> A 40% of an *exo* adduct was obtained.

<sup>e</sup> No reaction in 48 h at -78 °C.

<sup>f</sup> A 20% of an *exo* adduct was obtained.

Configurational assignment of these adducts was also performed by <sup>1</sup>H NMR (see S. I.) and then, confirmed by X-ray diffraction<sup>26</sup> in the case of the adduct *endo*-**21A**.

The good results obtained in reactions of sulfinylenones **9–12** and cyclopentadiene, prompted us to study their reactions with other less reactive dienes, as 1-methoxy-1,3-cyclohexadiene, furan, 2-methylfuran and 2,5-dimethylfuran. The first reactions were performed with 1-methoxy-1,3-cyclohexadiene, with the aim of determining their regioselectivity (see Table 4). Then, *E*-enone **10** reacted at rt with 5 equiv of the above diene, in the presence of

cyclohexadiene			5
	OCH <sub>3</sub> 5 equiv CH <sub>3</sub> CN, rt Yb(OTf) <sub>3</sub>	R 3CO H + TolOS +	3CO HR
<i>E</i> -10 or <i>Z</i> -11 : F <i>E</i> -14 : R =CF <sub>3</sub>	c =CH <sub>3</sub>	endo <b>-25A</b> endo <b>-26A</b>	exo <b>-25A</b> exo- <b>26A</b>

Diels-Alder cycloaddition of enones 10. 11 and 14 with 1-methoxy-1.3-

Entry	Dienophile	Time (h)	Temp (°C)	Adduct (endo/exo) <sup>a</sup>	Yield <sup>b</sup> (%)
1	10	40	rt	<b>25</b> (75/25)	70 (48) <sup>c</sup>
2	11	40	rt	<b>25</b> (75/25)	68
3	14	20	-30	<b>26</b> (70/30) <sup>d</sup>	_
4	14	8	rt	<b>26</b> (60/40)	75

<sup>a</sup> Measured by <sup>1</sup>H NMR.

<sup>b</sup> Global yield.

<sup>c</sup> Yield of the major *endo* adduct.

<sup>d</sup> A 40% of conversion was attained.

a stoichiometric quantity of ytterbium triflate as Lewis acid catalyst, to yield a 75:25 diastereoisomeric mixture of the adducts 25, although 40 h were necessary to complete the cycloaddition (Table 4, entry 1). The obtained adducts were easily separated by flashcolumn chromatography to afford a 48% of the major diastereomer. Identical conditions were applied to the reaction of the methoxy diene with the Z-enone **11** and, surprisingly, the same adducts 25, also in 75:25 ratio, were obtained (Table 4, entry 2). This result clearly indicated that an isomerisation from Z-enone 10 to *E*-enone **11** was occurring during the cycloaddition,<sup>28</sup> which is much easier for the *E*-isomer **10**. Taking into account that Z-Eequilibration is not observed in reactions with cyclopentadiene, it must be a consequence of the lower reactivity of the 1-methoxy-1,3-cyclohexadiene, requiring higher temperatures and longer reaction times (compare Tables 3 and 4), and facilitated by the presence of the Lewis acid. The reaction of this diene with the more reactive trifluoromethyl derivative 14, under the same experimental conditions used with 10 and 11, yielded a 60:40 mixture of the diastereoisomeric adducts 26 (Table 4, entry 4). Stereoselectivity was slighly larger by decreasing the temperature (a 70:30 diastereoisomeric mixture was obtained at -30 °C, Table 4, entry 3) though the conversion was only a 40% for a reaction time of 20 h.

We must remark that the two adducts formed in the reactions of methoxycyclohexadiene (both exhibiting the regiochemistry expected from the orientation rules) result in its *endo* and *exo* approach to the less hindered face of the dienophile, whereas those formed with cyclopentadiene are the result of the *endo* approach to both diastereotopic faces.<sup>29</sup>

Reactions with the furan presented a special interest due to the profuse applicability of the obtained adducts.<sup>30</sup> However, it is less reactive than the cyclopentadiene and its reactions with **10** and **11** were unfruitful. Reactions of furan with **9** and **12** at room temperature in the presence of the Lewis acid exclusively yielded the Friedel–Crafts alkylation products **27** and **28**<sup>31</sup> (Scheme 4).

The only cycloadduct obtained with furan resulted in its reaction with the trifluoromethyl derivative **14** affording the Diels–Alder products with an excellent facial selectivity but only moderated *endo* selectivity, as it was the case with methoxycyclohexadiene. The easy separation of the reaction mixture allowed the preparation of the diastereomerically pure major component, *endo*-**29A**,<sup>32</sup> in 60% yield (Scheme 5). Its structure was unequivocally assigned by X-ray diffraction studies<sup>26</sup> and resulted to be identical to that of the major adducts obtained from **8–11** with cyclopentadiene.



Scheme 4. Conjugated addition reactions of furan to enones 9 and 12 in the presence of Yb(OTf)<sub>3</sub>.

Reaction of the enone **14** with the symmetric 2,5-dimethylfuran does not work, even under forced experimental conditions (reflux with 10 equiv of the diene). Finally, the reaction of **14** with 2-methylfuran at rt cleanly afforded a 80:20 diastereisomeric mixture of the corresponding Friedel–Crafts alkylation products **30** (Scheme 5).



**Scheme 5.** Reactions of trifluoromethyl substituted enone **14** with furan and 2-methylfuran in the presence of Yb(OTf)<sub>3</sub>.

Results obtained in Table 1 indicate that the only influence of the Lewis acid on the reaction course is related to the increase of reactivity, which remains very low in any condition. The endo selectivity observed in the absence of Lewis acid is a consequence of the lower endo-directing character of the 2-p-tolylsulfinylphenyl group with respect to that of the electron withdrawing one (W), which is very large in the case of NO<sub>2</sub>. The association of the catalyst to the substituents is not able to produce chelated species, probably due to the long distance existing between the sulfinyl and the W group adopting the *trans* arrangement (*a* in Scheme 6). In accordance with the results observed in Table 2, indicating that the facial selectivity is not modified by the presence of the Yb(OTf)<sub>3</sub>, we must conclude that the evolution of the reaction through the chelated species like **b** (Scheme 6) is highly improbable, despite the distance between the sulfinyl and carbonyl oxygen atoms in compounds 6–8 would allow their formation. The instability of species **b** provoked by the lost of conjugation and/or their low reactivity due to the steric destabilization of the approaches of the cyclopentadiene to both diastereotopic faces (the plane containing the CO group is orthogonal to that of the double bond), would explain this fact. The endo approach of the cyclopentadiene to the less hindered face of the presumably most stable non-chelated conformation **b**' (Scheme 6) would explain the formation of adducts endo-18A-20A (Table 2) as the major ones in these reactions. Finally, the chelated forms from compounds 8–12 and 14 ( $R_1$ ,  $R_2$  y  $R_3$  have not been represented in Scheme 6) will adopt the chair-like conformation c with the CO conjugated with the double bond, but orthogonal to the aromatic ring. The lower face of the double bond will be hindered by the sulfinyl group, and then, the favored approaches of cyclopentadiene (Table 3) and furan (Scheme 5) will take place to the upper face, affording essentially compounds *endo*-**21A**-**24A** and *endo*-**29A**, respectively.



Scheme 6. Favored approach of cyclopentadiene to enones 6–12.

In summary, we have demonstrated that a 2-*p*-tolylsulfinylphenyl moiety at the dienophile is able to control the facial selectivity of the Diels—Alder reactions when the sulfinyl oxygen atom can interact, via a chelation agent as the Yb(OTf)<sub>3</sub>, with another electron withdrawing group present at the double bond.

#### 3. Experimental section

#### 3.1. General methods

Melting points were determined using a Gallenkamp apparatus in open capillary tubes. The IR spectra were recorded on a Bruker Vector 22 spectrometer and the frequencies are given in  $cm^{-1}$ . NMR spectra were acquired on a Brucker AC-300 instrument at 300 and 75.5 MHz for <sup>1</sup>H and <sup>13</sup>C NMR, respectively. Chemical shifts ( $\delta$ ) are reported in parts per million relative to residual solvent signals (CHCl<sub>3</sub>, 7.26 ppm for <sup>1</sup>H NMR, CDCl<sub>3</sub>, 77.0 ppm for <sup>13</sup>C NMR spectra). <sup>13</sup>C NMR spectra were acquired on a broad-band decoupled mode. Optical rotations were measured on a Perkin-Elmer 241 polarimeter. Microanalyses were carried out on a LECO CHNS-932. High resolution mass spectra were obtained by ESI<sup>+</sup> (MeoH+0,1% formic acid) with a QSTAR (Applied Biosystems) apparatus. Silica gel 60 (230-400 mesh ASTM) and DC-Alufolien 60 F254 were used for flash-column chromatography and analytical TLC, respectively. All reactions were carried out in anhydrous solvents. THF was dried with molecular sieves. iPr<sub>2</sub>NH was distilled from KOH. Freshly distilled cyclopentadiene was always used. Other commercially available starting materials were used without purification. n-BuLi (2.5 M solution in hexanes) was purchased from Aldrich. Reactions under high pressure conditions were carried out using Unipress Equipment 101LV Synthesis of compounds  $1^{17}$   $2^{23}$   $6^{18d}$   $7^{18d}$   $8^{18d}$  and  $13^{25}$  have been previously described.

#### 3.2. Synthesis of styrenes 3-5

To a solution of NaH (4.17 mmol) in anhydrous THF (10 mL) was added the corresponding phosphonate (4.17 mmol). The resulting mixture was stirred for 30 min at rt under argon atmosphere. The solution was cooled at -78 °C, and sulfinyl aldehyde **1** (3.8 mmol) in THF anhydrous (5 mL) was added via

syringe. The resulting solution was stirred for 12 h at room temperature and then, the reaction mixture was hydrolyzed (saturated NH<sub>4</sub>Cl), extracted (3x5 mL DCM), washed (saturated NaCl), dried (MgSO<sub>4</sub>) and the solvent evaporated under reduced pressure. The residue was purified by flash-column chromatography. The eluent and the obtained yield in each case are indicated below.

3.2.1. (*S*,*E*)-4-[2-(*p*-Tolylsulfinyl)phenyl]but-3-en-2-one (**3**). Compound **3** obtained from **1** and diethyl (2-oxopropyl)-phosphonate. Chromatography: *n*-hexane:AcOEt, 3:1. Yield: 77%; white solid; *mp*: 65–67 °C; the *ee* was determined by HPLC (Chiralcel OD, 1.0 mL/min, *i*-PrOH/hexane 30/70,  $\lambda$ =254 nm,  $t_{R}$ =(*S*) 8.1 (*R*) 9.1 min), 98% *ee*; [ $\alpha$ ]<sub>D</sub><sup>20</sup>–391 (*c* 1, CHCl<sub>3</sub>); <sup>1</sup>H NMR  $\delta$  8.06 (dd, *J*=8.1, 1.51 Hz, 1H), 8.00 (d, *J*=16.1 Hz, 1H), 7.61–7.57 (m, 2H), 7.51–7.49 (m, 1H), 7.45 (d, *J*=8.15 Hz, 2H), 7.22 (d, *J*=8.15 Hz, 2H), 6.55 (d, *J*=16.1 Hz, 1H), 2.36 (s, 3H), 2.34 (s, 3H); <sup>13</sup>C NMR  $\delta$  198.0, 145.0, 142.2, 141.8, 137.5, 133.3, 131.6, 131.3, 130.4, 130.3, 127.4, 125.6, 125.5, 27.9, 21.7. IR (KBr)  $\delta$  3055, 2875, 1672, 1610, 1465, 1398, 1277, 1084. MS (ESI) *m/z*: 337 [M+Na]<sup>+</sup> (29), 285 [M+H]<sup>+</sup> (100), 243 (23), 149 (92), 145 (26), 139 (22); Anal. Calcd for C<sub>17</sub>H<sub>16</sub>O<sub>2</sub>S: C, 71.80; H, 5.67; S, 11.28. Found: C, 71.35; H, 4.82; S, 11.11.

3.2.2. (*S*,*E*)-*Ethyl* 3-[2-(*p*-tolylsulfinyl)phenyl]acrylate (**4**). Compound **4** was obtained from **1** and triethyl phosphonoacetate. Chromatography: *n*-hexane:AcOEt, 3:1. Yield: 70%; white solid; *mp* 98–100 °C; the *ee* was determined by HPLC (Chiralcel OD, 1.0 mL/ min, *i*-PrOH/hexane 30/70,  $\lambda$ =254 nm,  $t_R$ =(*S*) 13.7 (*R*) 10.1 min), 98% *ee*; [ $\alpha$ ]<sub>D</sub><sup>20</sup>–408 (*c* 1, CHCl<sub>3</sub>); <sup>1</sup>H NMR  $\delta$  8.12 (d, *J*=15.7 Hz, 1H), 8.10–8.07 (m, 1H), 7.55–7.61 (m, 2H); 7.48 (d, *J*=8.1 Hz, 2H), 7.49–7.45 (m, 1H), 7.20 (d, *J*=8.1 Hz, 2H), 6.31 (d, *J*=15.7 Hz, 1H), 4.29 (q, *J*=7.2 Hz, 1H), 4.28 (q, *J*=7.1 Hz, 1H), 1.35 (t, *J*=7.1 Hz, 3H); <sup>13</sup>C NMR  $\delta$  166.3, 142.3, 142.1, 142.0, 138.8, 132.9, 131.4, 131.3, 130.4, 127.2, 125.7, 124.8, 122.1, 61.1, 21.7, 14.6. IR (KBr)  $\delta$  3956, 2981, 1714, 1637, 1466, 1316, 1277, 1181, 1035. MS (ESI) *m/z*: 337 [M+Na]<sup>+</sup> (54), 315 [M+H]<sup>+</sup> (46), 269 (88), 149 (31), 139 (100); Anal. Calcd for C<sub>18</sub>H<sub>18</sub>O<sub>3</sub>S: C, 68.76; H, 5.77; S, 10.20. Found: C, 68.56; H, 5.92; S, 10.10.

3.2.3. (S,E)-1-(2-Nitrovinyl)-2-(p-tolylsulfinyl)benzene (5). To a solution of aldehyde 1 (1.02 mmol) and t-BuOH (4 mL) in THF (4 mL), nitromethane (1.54 mmol) was added and the mixture was cooled at 0 °C. Then, t-BuOK (0.11 mmol) was added and the resulting mixture was stirred for 12 h at rt. The mixture was diluted, extracted (Et<sub>2</sub>O:AcOEt, 1:1), washed (saturated NaCl), dried (MgSO<sub>4</sub>), the solvent evaporated under reduced pressure and the residue purified by flash cromatography (DCM:AcOEt 10:1) before the addition of dichloromethane (5 mL) and trifluoroacetic anhydride (0.85 mmol) at -10 °C. The resulting solution was allowed to stir 2 min and then triethylamine (1.70 mmol) was dropwise added over a period of 15 min The reaction mixture was stirred at -10 °C for an additional period of 30 min and the resulting mixture was poured into dichlomethane and washed with saturated NH<sub>4</sub>Cl solution. The aqueous layers were extracted with the same solvent, the combined organic layers dried (MgSO<sub>4</sub>) and the solvent removed under reduced pressure. The residue was purified by flash cromatography using as eluent *n*-hexane:AcOEt, 2:1. Yield: 75%; yellow solid; mp: 122-124 °C; the ee was determined by HPLC (Chiralcel IC, 0.8 mL/min, *i*-PrOH/hexane 30/70,  $\lambda$ =254 nm,  $t_{R}$ =(S) 40.2 (*R*) 64.8 min), 98% *ee*;  $[\alpha]_D^{20}$  – 274 (*c* 1, CHCl<sub>3</sub>); <sup>1</sup>H NMR  $\delta$  8.49 (d, *J*=13.5 Hz, 1H), 8.15 (d, *J*=7.9 Hz, 1H), 7.72–7.69 (m, 1H), 7.53–7.54 (m, 2H), 7.47 (d, J=8.1 Hz, 2H). 7.36 (d, J=13.5 Hz, 1H), 7.23 (d, J=8.1 Hz, 2H); 2.34 (s, 3H); <sup>13</sup>C NMR  $\delta$  146.5, 142.6, 141.4, 139.2, 133.5, 132.9, 131.8, 130.6, 128.4, 128.1, 125.9, 125.7, 21.7. IR (KBr)  $\delta$  3114, 2921, 1717, 1522, 1341, 1084, 1039, 960; MS (ESI) m/z: 310 [M+Na]<sup>+</sup> (14), 288 [M+H]<sup>+</sup> (85), 149 (100). Anal. Calcd

for C<sub>15</sub>H<sub>13</sub>NO<sub>3</sub>S: C, 63.98; H, 4.70; N, 4.66; S, 10.68. Found: C, 63.58; H, 4.68; N, 4.73; S, 10.75.

#### 3.3. Synthesis of sulfinyl $\alpha$ , $\beta$ -unsaturated ketones 9–12 and 14

A vinyl magnesium bromide solution (3.3 mmol) in anhydrous THF was added to aldehyde **1** (1.65 mmol) in anhydrous THF (10 mL) at -78 °C. The solution was stirred for 5 h at -78 °C. Then, the reaction mixture was hydrolyzed (saturated NH<sub>4</sub>Cl), extracted (3×5 mL DCM), washed (saturated NaCl), dried (MgSO<sub>4</sub>) and the solvent evaporated under reduced pressure. The obtained two epimeric allylic alcohols were purified by flash-column chromatography using as eluent DCM:AcOEt, 8:1. Then, MnO<sub>2</sub> (16 mmol) in DCM was added, and the reaction mixture was stirred for 36 h at rt, and filtered through Celite. The filtrate was evaporated under reduced pressure and the residue was purified by flash-column chromatography. The eluent and the obtained yield in each case are indicated below.

3.3.1. (*S*)-1-[2-(*p*-Tolylsulfinyl)phenyl]prop-2-en-1-one (**9**). Compound **9** was obtained from **1** and vinyl magnesium bromide. Chromatography: DCM:AcOEt, 5:1. Yield: 82%; yellow solid; *mp*: 98–100 °C;  $[\alpha]_D^{20}$ –270 (*c* 1, CHCl<sub>3</sub>); <sup>1</sup>H NMR  $\delta$  8.49 (d, *J*=7.2 Hz, 1H), 7.85–7.79 (m, 2H), 7.66 (d, *J*=8.3 Hz, 2H), 7.60–7.55 (m, 1H), 7.18 (d, *J*=7.9 Hz, 2H), 7.04 (dd, *J*=17.1, 10.6 Hz, 1H), 6.35 (dd, *J*=17.1, 1.3 Hz, 1H), 5.97 (dd, *J*=10.6, 1.2 Hz, 1H), 2.32 (s, 3H); <sup>13</sup>C NMR  $\delta$  190.7, 149.4, 143.8, 141.3, 134.9, 133.9, 132.7, 132.2, 130.5, 130.1, 129.9, 126.7, 125.8, 21.7; IR (KBr)  $\delta$  3060, 2922, 2360, 1658, 1606, 1402, 1260, 1029, 1015, 750; MS (ESI) *m/z*: 293 [2M+Na]<sup>+</sup> (13), 271 [M+H]<sup>+</sup> (100), 179 (48), 149 (38); Anal. Calcd for C<sub>16</sub>H<sub>14</sub>O<sub>2</sub>S: C, 71.08; H, 5.22; S, 11.86. Found: C, 70.77; H, 5.32; S, 11.79.

3.3.2. (*E*,*S*)-1-[2-(*p*-Tolylsulfinyl)phenyl]but-2-en-1-one (**10**). Compound **10** was obtained from **1** and (*E*)-prop-1-en-1-yl magnesium bromide. Chromatography: DCM:AcOEt 7:1. Yield: 82%. Yellow solid;  $[\alpha]_D^{2D}$ -259 (*c* 1.1, CHCl<sub>3</sub>). <sup>1</sup>H NMR  $\delta$  8.45–8.42 (m, 1H), 7.80–7.75 (m, 2H), 7.67–7.64 (m, 2H), 7.58–7.52 (m, 1H), 7.19–7.16 (m, 2H), 6.97 (dq, *J*=15.4, 7.0 Hz, 1H), 6.76 (dq, *J*=15.4, 1.4 Hz, 1H), 2.32 (s, 3H), 1.97 (dd, *J*=7.0, 1.5 Hz, 3H).<sup>13</sup>C NMR  $\delta$  190.19, 148.6, 143.6, 140.9, 135.4, 133.1, 130.1, 129.6, 129.3, 127.9, 126.3, 125.4, 21.4, 18.8. IR (KBr)  $\delta$  3060, 2919, 2361, 1663, 1617, 1439, 1300, 1224, 1022, 920, 810, 764. MS (ESI) *m*/*z*: 285 [M+H]<sup>+</sup> (100), 227 (10). Anal. Calcd for C<sub>17</sub>H<sub>16</sub>O<sub>2</sub>S: C, 71.80; H, 5.67; S, 11.28. Found: C, 71.83; H, 5.74; S, 11.13.

3.3.3. (*Z*,*S*)-1-[2-(*p*-Tolylsulfinyl)*phenyl*]*but*-2-*en*-1-*one* (**11**). Compound **11** was obtained from **1** and (*Z*)-prop-1-en-1-yl magnesium bromide followed by the oxidation with MnO<sub>2</sub>. Chromatography: DCM:AcOEt, 7:1. Yield: 85%; yellow oil;  $[\alpha]_D^{20} - 236$  (*c* 0.9, CHCl<sub>3</sub>); <sup>1</sup>H NMR  $\delta$  8.5 (dd, *J*=1.0, 8.0 Hz, 1H), 7.85–7.75 (m, 2H), 7.70–7.66 (m, 2H), 7.54 (dt, *J*=7.5, 1.2 Hz, 1H), 7.18–7.15 (m, 2H), 6.72 (dq, *J*=1.8, 11.5 Hz, 1H), 6.46 (dq, *J*=11.5, 7.2 Hz, 1H), 2.33 (s, 3H), 2.07 (dd, *J*=7.2, 1.8 Hz, 3H); <sup>13</sup>C NMR  $\delta$  191.7, 149.2, 146.0, 144.26, 141.1, 136.3, 133.6, 130.4, 129.9, 129.8, 126.8, 125.6, 125.3, 21.7, 16.6; IR (NaCl)  $\delta$  3060, 2919, 1659, 1610, 1435, 1230, 1007, 918, 809, 760; MS (ESI) *m/z*: 569 [2M+H]<sup>+</sup> (10), 285 [M+H]<sup>+</sup> (100); Anal. Calcd for C<sub>17</sub>H<sub>16</sub>O<sub>2</sub>S: C, 71.80; H, 5.67; S, 11.28. Found: C, 72.17; H, 5.96; S, 11.01.

3.3.4. (*S*)-2-*Methyl*-1-[2-(*p*-tolylsulfinyl)phenyl]prop-2-en-1-one (**12**). Compound **12** was obtained from **1** and prop-1-en-2-yl magnesium bromide followed by the oxidation with MnO<sub>2</sub>. Chromatography: DCM:AcOEt, 7:1. Yield: 79%; colorless oil;  $[\alpha]_D^{20} - 94$  (*c* 1.2, CHCl<sub>3</sub>). <sup>1</sup>H NMR  $\delta$  8.20 (d, *J*=7.4 Hz, 1H), 7.70–7.62 (m, 3H), 7.52–7.43 (m, 2H), 7.21–7.19 (m, 2H), 5.95 (s, 1H), 5.50 (s, 1H), 2.33 (s, 3H), 2.03 (s, 3H); <sup>13</sup>C NMR  $\delta$  196.9, 147.4, 144.1, 142.7, 141.1, 136.6, 132.1, 129.9, 129.7,

129.7, 129.5, 125.8, 125.3, 21.3, 17.8; IR (NaCl)  $\delta$  3056, 2924, 2361, 1652, 1450, 1328, 1198, 1062, 810, 763; MS (ESI) m/z: 569 [2M+H]+ (14), 285 [M+H]+ (100); Anal. Calcd for C17H16O2S: C, 71.80; H, 5.67; S, 11.28. Found: C, 72.17; H, 5.96; S, 11.01.

3.3.5. (E,S)-4,4,4-Trifluoro-1-[2-(p-tolylsulfinyl)phenyl]but-2-en-1one (14). To a solution of HMDSLi (0.31 mmol. 1 M heptane) in anhydrous THF (0.5 mL) under argon atmosphere was dropwise added a solution of 13 (0.31 mmol) in anhydrous THF (2.5 mL). The resulting mixture was stirred 20 min at rt. Then, TMSCI (0.372 mmol) was added and the resulting solution was stirred 3 h. After this time the solvent was directly removed. To a solution of the residue in dry DCM (2.5 mL) at 0 °C under argon atmosphere was added 1,1-bis(dimethylamino)-2,2,2-trifluoroethane (0.23 mmol) and BF<sub>3</sub>.OEt<sub>2</sub> (0.23 mmol). The resulting solution was stirred for 3 h at room temperature and then, the reaction mixture was quenched (saturated NaHCO<sub>3</sub>), extracted (3×5 mL DCM), washed (saturated NaCl), dried (MgSO<sub>4</sub>) and the solvent evaporated under reduced pressure. The residue was purified by flash-column chromatography: AcOEt-n-hexane 1:1. Yield: 65%; white solid; mp: 102-104 °C; the ee was determined by HPLC (Chiralcel IC, 0.8 mL/min, *i*-PrOH/hexane 30/70,  $\lambda$ =254 nm,  $t_{R}$ =(S) 24.7 (*R*) 27.6 min), 98% *ee*;  $[\alpha]_{D}^{20}$  – 228 (*c* 0.96, CHCl<sub>3</sub>); <sup>1</sup>H NMR  $\delta$  8.59 (dd, J=7.9, 1.1 Hz, 1H), 7.94–7.86 (m, 2H), 7.68–7.61 (m, 3H), 7.40 (dq, J=15.6, 1.9 Hz, 1H), 7.26–7.17 (m, 2H), 6.72 (dq, J=15.6, 6.5 Hz, 1H), 2.33 (s, 3H); <sup>13</sup>C NMR δ 187.4, 149.9, 143.2, 141.4, 134.6, 133.2, 131.7, 131.2, 130.5 (c), 130.4, 130.1, 129.7, 126.7, 125.9, 21.33; IR (NaCl)  $\delta$  3090, 2924, 1736, 1680, 1303, 1277, 1211, 1019, 863; MS (ESI) m/z; 699 [2M+Na]<sup>+</sup> (98), 361 [M+Na]<sup>+</sup> (90), 339 [M+H]<sup>+</sup> (100); HRMS *m*/*z* calcd for C<sub>17</sub>H<sub>14</sub>F<sub>3</sub>O<sub>2</sub>S [M+H<sup>+</sup>]: 339.0661, found: 339.0655. Anal. Calcd for C<sub>17</sub>H<sub>13</sub>F<sub>3</sub>O<sub>2</sub>S: C, 60.35; H, 3.90; S, 9.48. Found: C, 60.12; H, 4.10; S, 9.34.

## 3.4. Diels—Alder reaction under high pressure conditions. General procedure

A solution of the corresponding dienophile (0.1 mmol) and Yb(OTf)<sub>3</sub> (0.11 mmol) in CH<sub>3</sub>CN (1.8 mL) was stirred at rt for 45 min. Then, freshly distilled cyclopentadiene (10 mmol) was added and the resulting solution was placed in a Teflon ampoule. The ampoule was placed in the high pressure apparatus and compressed up to the indicated pressure for the indicated time. Following decompression, the mixture was hydrolyzed (saturated NH<sub>4</sub>Cl), extracted ( $3 \times 5$  mL DCM), washed (saturated NaCl), dried (MgSO<sub>4</sub>) and the solvent evaporated under reduced pressure. The residue was purified by flash-column chromatography. The eluent and the obtained yield in each case are indicated below.

3.4.1.  $1-\{(15,2R,3R,4R)-3-[2-((S)-p-Tolylsulfinyl)phenyl]bicyclo[2.2.1]$ hept-5-en-2-yl}ethanone (endo-**15A**). Compound endo-**15A** was obtained as major diastereomer from **3** in absence of Yb(OTf)<sub>3</sub>. Chromatography: Et<sub>2</sub>O:n-hexane, 3:2. Yield: 20%; white solid; *mp*: 113–115 °C;  $[\alpha]_D^{2D}-213$  (*c* 0.55, CHCl<sub>3</sub>); <sup>1</sup>H NMR  $\delta$  8.02–7.99 (m, 1H), 7.59–7.57 (m, 2H), 7.43–7.40 (m, 2H), 7.36–7.33 (m, 1H), 7.26–7.23 (m, 2H), 6.48 (dd, J=5.7, 3.1 Hz, 1H), 6.06 (dd, J=2.0, 5.7 Hz, 1H), 3.55 (br s, 1H), 3.37 (br s, 1H), 3.36 (br s, 1H), 2.94 (br s, 1H), 2.34 (s, 3H), 1.90 (s, 3H), 1.80 (d, J=9.0 Hz, 1H), 1.53 (dd, J=8.9, 1.7 Hz, 1H); <sup>13</sup>C NMR  $\delta$  206.9, 144.9, 141.8, 141.5, 140.9, 138.9, 133.6, 131.0, 130.0, 127.8, 126.0, 125.7, 125.5, 57.3, 52.0, 46.2, 46.1, 42.0, 28.7, 21.4. IR (NaCl)  $\delta$  3056, 2973, 1707, 1594, 1440, 1331, 1082, 1031. MS (ESI) *m/z*: 753 [2M+Na]<sup>+</sup> (15), 351 [M+H]<sup>+</sup> (100). HRMS *m/z* calcd for C<sub>22</sub>H<sub>23</sub>O<sub>2</sub>S [M+H]<sup>+</sup>: 351.1413, found: 351.1399.

3.4.2. 1-{(15,25,35,4R)-3-[2-((S)-p-Tolylsulfinyl)phenyl]bicyclo[2.2.1] hept-5-en-2-yl}ethanone (exo-**15A**). Compound exo-**15A** was obtained as major diastereomer from **3** in presence of Yb(OTf)<sub>3</sub>. Chromatography: Et<sub>2</sub>O:*n*-hexane, 3:2. Yield: 35%; colorless oil.  $[\alpha]_D^{20}$  – 559 (*c* 1.0, CHCl<sub>3</sub>); <sup>1</sup>H NMR  $\delta$  8.20–8.19 (m, 1H), 7.55–7.52 (m, 2H), 7.49–7.43 (m, 2H), 7.40–7.37 (m, 1H), 7.26–7.23 (m, 2H), 6.06 (dd, *J*=5.5, 3.1 Hz, 1H), 6.01 (dd, *J*=5.5, 2.7 Hz, 1H), 3.27 (br s, 1H), 3.24 (dd, *J*=8.2, 3.4 Hz, 1H), 3.17 (dd, *J*=4.9, 1.5 Hz, 1H), 2.37 (s, 3H), 2.14 (s, 3H), 2.13 (br s, 1H), 1.85 (d, *J*=8.9 Hz, 1H), 1.46 (dd, *J*=8.9, 1.5 Hz, 1H); <sup>13</sup>C NMR  $\delta$  207.1, 143.7, 142.3, 141.8, 141.6, 138.2, 134.4, 130.9, 130.0, 127.5, 127.2, 126.5, 124.7, 60.8, 49.2, 46.8, 46.2, 41.6, 29.6, 21.5; IR (NaCl)  $\delta$  3059, 2978, 1706, 1594, 1441, 1331, 1083, 1060. MS (ESI) *m/z*: 753 [2M+Na]<sup>+</sup> (8), 373[M+Na]<sup>+</sup> (10), 351 [M+H]<sup>+</sup> (100); HRMS *m/z* calcd for C<sub>22</sub>H<sub>23</sub>O<sub>2</sub>S [M+H]<sup>+</sup>: 351.1379, found: 351.1396.

3.4.3. (1S,2R,3R,4R)- and (1R,2S,3S,4S) Ethyl 3-[2-((S)-p-tolylsulfinyl) phenyl]bicyclo[2.2.1]hept-5-ene-2-carboxylate (endo-**16A**)+(endo-16B). Compounds endo-16A and endo-16B were obtained as a 75:25 diastereoisomers mixture from 4. Chromatography: Et<sub>2</sub>O:nhexane 3:2. Yield: 65%; colorless oil; <sup>1</sup>H NMR  $\delta$  7.93–7.85 (m, 1H), 7.58-7.54 (m, 2H), 7.42-7.33 (m, 3H) 7.24-7.21 (m, 2H), 6.53 (dd, J=5.6, 3.1 Hz, 1H, **A**), 6.44 (dd, J=5.6, 3.3 Hz, 1H, **B**), 6.13 (dd, J=2.7, 5.6 Hz, 1H, A), 5.89 (dd, J=5.5, 2.8 Hz, 1H, B), 4.25 (dd, J=5.2, 3.4 Hz, 1H, **B**), 4.10–3.88 (m, 2H), 3.60 (dd, *J*=5.0 1.4 Hz, 1H, **A**), 3.37 (br s, 1H, A), 3.33-3.30 (m, 1H), 3.19 (br s,1H, B), 3.00 (br s,1H, A), 2.56 (dd, J=1.5, 5.2 Hz, 1H, B), 2.34 (s, 3H), 1,91 (d, J=8.8 Hz, 1H, B), 1.78 (d, J=8.9 Hz, 1H, A), 1.56–1.49 (m, 1H), 1.14 (t, J=7.0 Hz, 3H, A), 0.89 (t, I=7.2 Hz, 3H, **B**); <sup>13</sup>C NMR  $\delta$  174.46, 173.42, 144.6, 142.3, 142.0, 141.2, 140.6, 139.0, 137.0, 135.6, 134.4, 131.1, 130.6, 129.9, 129.8, 127.9, 127.8, 126.7, 125.9, 125.7, 125.4, 125.3, 124.8, 60.7, 60.5, 60.4, 52.1, 50.0, 49.3, 48.8, 48.6, 48.4, 46.5, 46.0, 44.34, 43.7, 21.3, 14.2, IR (NaCl) δ 3060, 2957, 2925, 2807, 1727, 1594, 1464, 1377, 1262, 1182, 1083, 1057, 1030. MS (ESI) *m/z*: 783 [2M+Na]<sup>+</sup> (27), 381 [M+H]<sup>+</sup> (100). HRMS *m*/*z* calcd for C<sub>23</sub>H<sub>25</sub>O<sub>3</sub>S [M+H]<sup>+</sup>: 381.1518, found: 381.1507.

3.4.4. (1R,4S,5R,6S)- and (1S,4R,5S,6R)-5-Nitro-6-[2-((S)-p-tolylsulfinyl)phenyl]bicyclo[2.2.1]hept-2-ene (endo-17A)+(endo-17B). Compounds endo-17A and endo-17B were obtained, in the absence of Yb(OTf)<sub>3</sub>, as a 60:40 diastereoisomeric mixture from 5. Chromatography: Et<sub>2</sub>O:*n*-hexane, 3:2. Yield: 90%; colorless oil; <sup>1</sup>H NMR δ 8.23 (dd, J=7.8, 1.53 Hz, 1H, **B**), 8.01–7.98 (m, 1H, **A**), 7.52–7.46 (m, 5H), 7.28–7.24 (m, 2H), 6.74 (dd, J=5.7, 3.2 Hz 1H, A), 6.31 (dd, J=5.8, 3.2 Hz, 1H, **B**), 6.12 (dd, J=5.7, 2.7 Hz, 1H, **A**),6.06 (dd, J=5.8, 2.7 Hz, 1H, **B**), 5.35 (t, *J*=4.1 Hz, 1H, **A**), 5.19 (t, *J*=4.1 Hz, 1H, **B**), 3.87 (dd, J=4.1, 2.4 Hz, 1H, A), 3.68 (br s, 1H, A), 3.60 (br s, 1H, B), 3.56 (dd, J=4.1, 2.4 Hz, 1H, B), 3.09 (br s, 1H, A), 2.39 (s, 3H, B), 2.35 (s, 3H, A),2.14 (s, 1H, B), 1.93 (d, J=9.6 Hz, 1H, B), 1.91 (d, J=9.6 Hz, 1H, **A**), 1.71 (dd, *J*=9.6, 2.3 Hz, 1H); <sup>13</sup>C NMR δ 144.8, 142.6, 141.9, 140.8, 140.7, 138.4, 132.9, 132.7, 131.4, 131.2, 130.1, 128.6, 128.2, 127.2, 126.2, 126.1, 125.6, 125.5, 125.4, 91.2 (B), 88.9 (A), 51.9, 49.7, 48.1, 48.0, 45.5, 45.4, 45.0, 44.5, 21.5, 21.4; IR (NaCl) δ 3061, 2989, 1574, 1335, 1059, 1015, 810, 756. MS (ESI) *m*/*z*: 729 [2M+Na]<sup>+</sup> (12), 707 [M+H]<sup>+</sup> (14), 376 [M+Na]<sup>+</sup> (15), 354 [M+1]<sup>+</sup> (100); Anal. Calcd for C<sub>20</sub>H<sub>19</sub>NO<sub>3</sub>S: C, 67.97; H, 5.42; N, 3.96; S, 9.07. Found: C, 67.71; H, 5.59; N, 3.84; S, 8.78.

3.4.5.  $1-\{(15,25,45)-2-(2-((S)-p-Tolylsulfinyl)phenyl)bicyclo[2.2.1]$ hept-5-en-2-yl}ethanone (endo-**18A**). Compound endo-**18A** was obtained as major diastereomer from **6**. Chromatography: Et<sub>2</sub>O:n-hexane, 3:2. Yield: 79%; colorless oil;  $[\alpha]_D^{20}-344$  (c 1.8, CHCl<sub>3</sub>). <sup>1</sup>H NMR  $\delta$  7.76 (dd, *J*=7.9, 1.5 Hz, 1H), 7.69 (d, *J*=7.8 Hz, 1H), 7.50 (dt, *J*=7.3, 1.5 Hz, 1H), 7.42–7.34 (m, 3H), 7.23–7.20 (m, 2H), 6.44 (dd, *J*=5.7, 3.1 Hz, 1H), 5.89 (dd, *J*=5.7, 2.9 Hz, 1H), 3.76 (br s, 1H), 3.07–3.03 (m, 2H), 2.35 (s, 3H), 2.14 (dd, *J*=11.9, 3.7 Hz, 1H), 1.83 (s, 3H), 1.69–1.67 (m, 2H). <sup>13</sup>C NMR  $\delta$  206.8, 147.9, 143.9, 142.3, 141.5, 141.4, 132.4, 131.1, 130.1, 129.6, 129.1, 126.9, 125.9, 65.2, 49.9, 48.6, 44.9, 39.7, 27.8, 21.7. IR (NaCl)  $\delta$  3059, 2975, 2868, 1709, 1464, 1221, 1081, 1041, 1025, 756. MS (ESI) m/z: 721  $[2M+Na]^+$  (41), 701  $[2M+H]^+$  (23), 351  $[M+H]^+$  (100), 285 (79), 307 (57). HRMS m/z calcd for C<sub>22</sub>H<sub>23</sub>O<sub>2</sub>S  $[M+H]^+$ : 351.1413, found: 351.1412.

3.4.6. 1-{(1S,2S,4S)-2-[2-((S)-p-Tolylsulfinyl)phenyl]bicyclo[2.2.1] hept-5-en-2-yl}butan-1-one (endo-19A). Compound endo-19A was obtained as major diastereomer from 7. Chromatography: Et<sub>2</sub>O:*n*hexane, 3:1. Yield: 73%; colorless oil;  $[\alpha]_D^{20}$  –334 (*c* 0.95, CHCl<sub>3</sub>). <sup>1</sup>H NMR & 7.83 (dd, J=1.5, 7.8 Hz, 1H), 7.70 (d, J=7.1 Hz, 1H), 7.50 (dt, J=7.3, 1.5 Hz, 1H), 7.40 (dt, J=7.8, 1.3 Hz, 1H), 7.36-7.34 (m, 2H), 7.22-7.19 (m, 2H), 6.42 (dd, J=5.7, 3.1 Hz, 1H), 5.82 (dd, J=5.7, 3.0 Hz, 1H), 3.78 (br s, 1H), 3.12-3.06 (m, 2H), 2.35 (s, 3H), 2.36-2.25 (m, 1H), 2.12 (ddd, J=18.1, 8.8, 5.3 Hz, 1H), 1.85-1.73 (m, 1H), 1.63-1.61 (m, 1H), 1.36-1.31 (m, 1H), 1.15-1.12 (m, 1H), 0.89–0.88 (m, 1H), 0.72 (t, J=7.4 Hz, 3H). <sup>13</sup>C NMR  $\delta$  208.1, 147.4, 143.8, 141.8, 141.2, 141.0, 131.9, 130.8, 129.7, 129.0, 128.5, 126.7, 125.9, 64.5, 50.0, 48.2, 44.5, 41.8, 39.7, 21.3, 16.7, 13.6. IR (NaCl) δ 3061, 2968, 2873, 1708, 1463, 1337, 1114, 1082, 1046, 1030, 810. MS (ESI) m/z: 779  $[2M+Na]^+$  (58), 757  $[2M+H]^+$  (86), 401  $[M+Na]^+$  (26), 379  $[M+H]^+$  (100); HRMS m/z calcd for  $C_{24}H_{27}O_2S$   $[M+H^+]$ : 379.1692, found: 379.1710.

3.4.7. 2-Methyl-1-{(15,25,45)-2-[2-((5)-p-tolylsulfinyl)phenyl]bicyclo [2.2.1]hept-5-en-2-yl]propan-1-one (endo-**20A**). Compound endo-**20A** was obtained as major diastereomer from **8** in the presence of Yb(OTf)<sub>3</sub>. Chromatography: Et<sub>2</sub>O:n-hexane, 2:1. Yield: 83%; white solid; 118–120 °C. [ $\alpha$ ]<sub>D</sub><sup>20</sup>–114 (c=0.9, chloroform). <sup>1</sup>H NMR  $\delta$  7.80–7.74 (m, 1H), 7.53–7.50 (m, 2H), 7.46 (dt, J=7.9, 1.5 Hz, 1H), 7.37 (dt, J=7.9, 1.4 Hz, 1H), 6.42 (dd, J=5.7, 3.1 Hz, 1H), 5.90 (dd, J=5.5, 2.9 Hz, 1H), 3.9 (br s, 1H), 3.16–3.14 (m, 2H), 2.89 (sept, J=6.7 Hz, 1H), 2.36 (s, 3H), 2.30 (dd, J=12.0, 3.8 Hz, 1H), 0.99 (d, J=6.6 Hz, 3H), 0.21 (d, J=6.8 Hz, 3H). <sup>13</sup>C NMR  $\delta$  212.6, 148.4, 142.9, 141.9, 141.3, 140.5, 131.8, 131.1, 129.6, 129.4, 128.1, 126.8, 126.1, 65.6, 49.6, 48.1, 44.3, 40.4, 37.1, 21.4, 21.1, 19.7. IR (KBr)  $\delta$  3063, 2974, 2872, 1704, 1463, 1339, 1081, 1045, 1031, 813. MS (ESI) m/z: 779 [2M+Na]<sup>+</sup> (100), 757 [2M+H]<sup>+</sup> (47), 401 [M+Na]<sup>+</sup> (20), 379 [M+H]<sup>+</sup> (53); HRMS m/z calcd for C<sub>24</sub>H<sub>27</sub>O<sub>2</sub>S [M+H<sup>+</sup>]: 379.1692, found: 379.1710.

## 3.5. Reaction of enones 9–12 and 14 under atmospheric pressure. General procedure

A solution of the corresponding enone (0.1 mmol) and Yb(OTf)<sub>3</sub> in CH<sub>3</sub>CN (1.8 mL) was stirred at rt for 45 min The solution was cooled at the corresponding temperature and then the diene (5–10 mmol) was added. After the indicated time, the mixture was hydrolyzed (saturated NH<sub>4</sub>Cl), extracted ( $3 \times 5$  mL DCM), washed (saturated NaCl), dried (MgSO<sub>4</sub>) and the solvent evaporated under reduced pressure. The residue was purified by flash-column chromatography. The eluent used and the obtained yield in each case are indicated below.

3.5.1. (15,25,4S)-Bicyclo[2.2.1]hept-5-en-2-yl[2-((S)-p-tolylsulfinyl) phenyl]methanone (endo-**21A**). Compound endo-**21A** was obtained as major diastereomer from **9** and cyclopentadiene. Chromatography: Et<sub>2</sub>O:*n*-hexane 3:1. Yield: 94%; white solid; *mp*: 99–101 °C;  $[\alpha]_D^{20}$ -250 (*c* 0.4, CHCl<sub>3</sub>). <sup>1</sup>H NMR  $\delta$  8.54 (dd, *J*=7.9, 1.2 Hz, 1H), 8.03 (dd, *J*=7.9, 1.2 Hz, 1H), 7.81 (dt, *J*=7.3, 1.3 Hz, 1H), 7.59 (dt, *J*=7.6, 1.2 Hz, 1H), 7.55–7.52 (m, 2H), 7.15–7.13 (m, 2H), 5.97 (dd, *J*=5.6, 3.1 Hz, 1H), 5.05 (dd, *J*=5.6, 2.8 Hz, 1H), 3.77 (dt, *J*=9.0, 4.1 Hz, 1H), 3.11 (br s, 1H), 2.90 (br s,1H), 2.31 (s, 3H), 1.93 (ddd, *J*=11.7, 9.0, 3.7 Hz, 1H), 1.50 (dd, *J*=11.7, 4.1 Hz, 1H), 1.39 (d, *J*=1.4 Hz, 2H); <sup>13</sup>C NMR  $\delta$  200.2, 148.8, 143.8, 140.8, 137.1, 134.1, 133.3, 131.5, 130.0, 129.9, 129.3, 126.9, 125.2, 49.8, 47.6, 47.2, 42.8, 31.0, 29.1, 21.3; IR (NaCl)  $\delta$  2975, 2833, 1672, 1585, 1337, 1218, 1023, 810, 757; MS (ESI)

 $m/z:\ 673\ [M+Na]^+$  (18), 337  $[M+H]^+$  (100). Anal. Calcd for  $C_{21}H_{20}O_2S:$  C, 74.97; H, 5.99; S, 9.53. Found: C, 75.22; H, 6.11; S, 9.54.

3.5.2. [(1S,2S,3R,4R)-3-Methylbicyclo[2.2.1]hept-5-en-2-yl][2-((S)-ptolylsulfinyl)phenyl]methanone (endo-22A). Compound endo-22A was obtained as major diastereomer from **10** and cyclopentadiene. Chromatography: Et<sub>2</sub>O:*n*-hexane, 2:1. Yield: 85%; colorless oil;  $[\alpha]_{D}^{20}$ -318 (c 0.4, CHCl<sub>3</sub>); <sup>1</sup>H NMR  $\delta$  8.54 (dd, J=7.9, 1.2 Hz, 1H), 8.03-8.00 (m, 1H), 7.85-7.79 (m, 1H), 7.60 (dt, J=7.6, 1.3 Hz, 1H), 7.52-7.49 (m, 2H), 7.15-7.13 (m, 2H), 6.07 (dd, J=5.6, 3.1 Hz, 1H), 4.83 (dd, *J*=5.6, 2.8 Hz, 1H), 3.28 (t, *J*=3.8 Hz, 1H), 2.99 (br s, 1H), 2.48 (br s, 1H), 2.30 (s, 3H), 2.01 (ddt, *J*=6.8, 3.8, 1.5 Hz, 1H), 1.67 (d, *J*=8.6 Hz, 1H), 1.38 (dd, *J*=8.6, 1.6 Hz, 1H), 1.13 (d, *J*=7.0 Hz, 3H); <sup>13</sup>C NMR δ 200.2, 148.7, 143.8, 140.9, 138.4, 134.3, 133.2, 131.1, 130.1, 130.0, 129.3, 127.0, 125.3, 56.2, 49.3, 48.6, 46.7, 35.7, 21.3, 20.7; IR (NaCl) δ 2963, 2868, 1668, 1586, 1436, 1218, 1062, 1017, 808, 759; MS (ESI) m/z: 723  $[2M+Na]^+$  (19), 701  $[2M+H]^+$  (32), 351  $[M+H]^+$ (100), 285 (50); HRMS *m*/*z* calcd for C<sub>22</sub>H<sub>23</sub>O<sub>2</sub>S [M+H]<sup>+</sup>: 351.1315, found: 351.1303.

3.5.3. [(1S,2S,3S,4R)-3-Methylbicyclo[2.2.1]hept-5-en-2-yl][2-((S)-ptolylsulfinyl)phenyl]methanone (endo-23A). Compound endo-23A was obtained as major diastereomer from **11** and cyclopentadiene. Chromatography: Et<sub>2</sub>O:*n*-hexane, 3:1. Yield: 75%; colorless oil;  $[\alpha]_D^{20}$  – 191 (*c* 0.7, CHCl<sub>3</sub>). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  8.55 (dd, *J*=8.0, 1.2 Hz, 1H), 7.94 (dd, J=8.0, 1.0 Hz, 1H), 7.82 (dt, J=7.8, 1.2 Hz, 1H), 7.61-7.56 (m, 1H), 7.49-7.46 (m, 2H), 7.09-7.06 (m, 2H), 6.48 (dd, *I*=5.6, 3.0 Hz, 1H), 5.83 (dd, *I*=5.5, 2.8 Hz, 1H), 3.79 (dd, *I*=10.0, 2.8 Hz, 1H), 3.03 (br s, 1H), 2.77-2.70 (m, 1H), 2.68 (br s, 1H), 2.28 (s, 3H), 1.46 (dt, *J*=8.4, 1.7 Hz, 1H), 1.19 (m, 1H), 0.02 (d, *J*=6.9 Hz, 3H); <sup>13</sup>C NMR δ 201.4, 149.1, 143.7, 140.6, 137.0, 135.1, 133.3, 132.3, 130.0, 129.9, 129.1, 127.0, 125.0, 52.4, 49.0, 48.9, 46.4, 39.1, 21.2, 15.4; IR (NaCl) δ 3059, 2962, 2925, 1670, 1437, 1211, 1081, 1062, 1024, 807; MS (ESI) *m*/*z*: 723 [2M+Na]<sup>+</sup> (10), 701 [2M+H]<sup>+</sup> (37), 351 [M+H]<sup>+</sup> (100), 285 (33); HRMS *m*/*z* calcd for C<sub>22</sub>H<sub>23</sub>O<sub>2</sub>S [M+H]<sup>+</sup>: 351.1413, found: 351.1303.

3.5.4. (1*R*,2*S*,3*R*,4*R*)-1-Methoxy-3-methylbicyclo[2.2.2]oct-5-en-2yl-{2-[(*S*)-p-tolylsulfinyl]phenyl}methanone (endo-**25A**). Compound endo-**25A** was obtained as major diastereomer from **10** or **11** and 1methoxycyclohexadiene. Chromatography: *n*-hexane:AcOEt 3:1. Yield: 48%; colorless oil;  $[\alpha]_D^{20}$ -217 (*c* 1.2, CHCl<sub>3</sub>). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  8.36 (d, *J*=7.7 Hz, 1H), 8.06 (d, *J*=7.7 Hz, 1H), 7.73 (t, *J*=7.5 Hz, 1H), 7.62–7.53 (m, 3H), 7.14 (d, *J*=8.3 Hz, 2H), 6.41 (dd, *J*=6.6, 8.8 Hz, 1H), 3.25 (d, *J*=6.5 Hz, 1H), 3.00 (s, 3H), 2.31 (s, 3H), 2.29–2.26 (s, 1H), 2.00–1.88 (m, 2H), 1.71–1.57 (m, 2H), 1.55–1.45 (m, 1H), 1.01 (d, *J*=7.0 Hz, 3H); <sup>13</sup>C NMR  $\delta$  202.5, 148.1, 143.8, 140.4, 137.1, 134.1, 132.9, 130.8, 130.5, 130.0, 129.3, 126.4, 125.0, 81.4, 58.4, 51.0, 39.4, 36.1, 29.8, 21.2, 19.3, 18.8; MS (ESI) *m/z*: 789 [2M+Na]<sup>+</sup> (11), 417 [M+Na]<sup>+</sup> (19), 395 [M+H]<sup>+</sup> (52), 137 (100); HRMS *m/z* calcd for C<sub>24</sub>H<sub>27</sub>O<sub>3</sub>S [M+H]<sup>+</sup>: 395.1675, found: 395.1681.

3.5.5. (1R,2S,3R,4R)and (1S,2S,3R,4S)-1-Methoxy-3-(trifluoromethyl)bicyclo[2.2.2]oct-5-en-2-yl-{2-[(S)-p-tolylsulfinyl]phenyl}methanone (endo-26A)+(exo-26A). Compounds endo-26A and exo-26A were obtained as 60:40 diastereomers mixture from 14 and 1-methoxycyclohexadiene. Chromatography: *n*-hexane:AcOEt 3:1. Global yield: 75%; colorless oil. <sup>1</sup>H NMR  $\delta$  8.41 (m, 1H), 8.08-8.03 (m, 1H), 7.78-7.71 (m, 1H), 7.56-7.44 (m, 3H), 7.09-7.06 (m, 2H), 6.35–6.30 (m, 1H), 6.18–6.13 (m, 1H, *exo*), 5.72 (d, *J*=8.7 Hz, 1H, endo), 3.76 (d, J=7.1 Hz, 1H, endo), 3.54 (d, J=7.1 Hz, 1H, exo), 2.83 (s, 3H, exo), 2.82 (s, 3H, endo), 2.84-2.80 (m, 1H), 2.24 (s, 3H, endo), 2.23 (s, 3H, exo), 2.02–1.94 (m, 1H), 1.77–1.43 (m, 4H); <sup>13</sup>C NMR & 200.0, 199.36, 148.3, 148.2, 143.8, 143.7, 140.7, 140.6, 135.5, 135.5, 134.2, 133.5, 133.4, 132.9, 131.7, 131.6, 131.4, 131.2, 130.0, 129.9, 129.3, 129.2, 26.9, 126.9, 125.3, 125.1, 51.2, 80.7, 51.33, 51.1, 49.7, 48.8, 47.5, 47.1, 46.8, 46.4, 46.1, 46.1, 29.7, 29.2, 28.6, 25.4, 21.3, 20.4, 19.9; MS (ESI) *m*/*z*: 471 [M+Na]<sup>+</sup> (100), 449 [M+H]<sup>+</sup> (50). HRMS *m*/*z* calcd for C<sub>24</sub>H<sub>24</sub>F<sub>3</sub>O<sub>3</sub>S [M+H]<sup>+</sup>: 449.1392, found: 449.1397.

3.5.6. (*S*)-3-(*Furan-2-yl*)-1-[2-(*p*-tolylsulfinyl)phenyl]propan-1-one (**27**). Compound **27** was obtained from **9** and furan. Chromatography: Et<sub>2</sub>O:*n*-hexane, 3:1. Yield: 69%; white solid; <sup>1</sup>H RMN  $\delta$  8.56 (dd, *J*=1.1, 7.9 Hz, 1H), 7.90 (dd, *J*=7.8, 1.2 Hz, 1H), 7.84 (dt, *J*=7.6, 1.3 Hz, 1H), 7.63–7.55 (m, 3H), 7.29–7.25 (m, 1H), 7.18–7.05 (m, 2H), 6.20 (dd, *J*=3.2, 1.9 Hz, 1H), 5.95 (dd, *J*=3.2, 0.8 Hz, 1H), 3.35–3.16 (m, 2H), 3.03–2.98 (m, 2H), 2.32 (s, 3H); <sup>13</sup>C RMN  $\delta$  198.3, 154.0, 148.8, 143.8, 141.2, 140.6, 133.8, 133.8, 130.23, 128.7, 129.5, 126.7, 125.3, 110.3, 105.6, 37.4, 22.4, 21.4; MS (ESI) *m*/*z*: 361 [M+Na]<sup>+</sup> (17), 407 [M+H]<sup>+</sup> (100); HRMS *m*/*z* calcd C<sub>20</sub>H<sub>18</sub>O<sub>3</sub>S [M+H<sup>+</sup>]: 339.1049, found: 339.1045.

3.5.7. (*R*)- and (*S*)-3-(*Furan-2-yl*)-2-methyl-1-[2-((*S*)-p-tolylsulfinyl) phenyl]propan-1-one (**28**). Compound **28** was obtained as a 60(**A**):40(**B**) epimers mixture from **12** and furan. Chromatography: Et<sub>2</sub>O:*n*-hexane, 3:1. Global yield: 64%; <sup>1</sup>H RMN  $\delta$  8.55 (dd, *J*=7.8, 1.2 Hz, 1H), 7.82 (dd, *J*=7.8, 1.1 Hz, 1H), 7.77 (dt, *J*=7.6, 1.3 Hz, 1H), 7.65–7.52 (m, 3H), 7.30–7.26 (m, 1H), 7.20–7.08 (m, 2H), 6.21 (dd, *J*=3.2, 1.9 Hz, 1H, **B**), 6.15 (dd, *J*=3.1, 1.9 Hz, 1H, **A**), 5.98 (dd, *J*=3.2, 0.7 Hz, 1H, **B**), 5.77 (dd, *J*=3.2, 0.7 Hz, 1H, **A**), 3.35–3.16 (m, 2H), 3.04 (dd, *J*=14.8, 6.6 Hz, 1H, **B**), 2.95 (dd, *J*=15.2, 6.6 Hz, 1H, **A**), 2.72 (dd, *J*=15.0, 7.2 Hz, 1H, **B**), 2.62 (dd, *J*=15.1, 7.4 Hz, 1H, **A**), 2.33 (s, 3H, **A**), 2.32 (s, 3H, **B**), 1.19 (d, *J*=7.0 Hz, 3H, **A**), 0.96 (d, *J*=6.9 Hz, 3H, **B**).

3.5.8. (15,25,35,4R)-[2-((S)-p-Tolylsulfinyl)phenyl]{3-(trifluoromethyl)-7-oxabicyclo[2.2.1]hept-5-en-2-yl]methanone (endo-**29A**). Compound endo-**29A** was obtained as major diastereomer from **14** and furan. Chromatography: Et<sub>2</sub>O:*n*-hexane, 3:1. Yield: 60%; white solid; *mp*: 108–110 °C;  $[\alpha]_D^{2D}$ –239 (*c* 0.45, CHCl<sub>3</sub>). <sup>1</sup>H NMR  $\delta$  8.68 (dd, *J*=7.9, 1.1 Hz, 1H), 8.15 (d, *J*=7.1 Hz, 1H), 7.97 (t, *J*=7.5 Hz, 1H), 7.72 (dt, *J*=7.5, 0.9 Hz, 1H), 7.45–7.42 (m, 2H), 7.17–7.14 (m, 2H), 6.21 (dd, *J*=5.3, 1.7 Hz, 1H), 5.11–5.09 (m, 2H), 4.74 (dd, *J*=5.8, 1.2 Hz, 1H) 4.04 (t, *J*=4.4 Hz, 1H), 2.96 (dq, *J*=9.6, 4.3 Hz, 1H), 2.32 (s, 3H); <sup>13</sup>C NMR  $\delta$  193.3, 149.9, 143.4, 141.4, 136.1, 134.5, 132.5, 132.3, 130.6, 130.5, 129.3, 127.7, 125.9, 80.3, 79.5, 49.2, 45.2 (c), 21.3; IR (NaCl)  $\delta$  3083, 3061, 2921, 1677, 1334, 1284, 1271, 1141, 1082, 845; MS (ESI) *m/z*: 835 [2M+Na]<sup>+</sup> (90), 813 [2M+H]<sup>+</sup> (15), 407 [M+H]<sup>+</sup> (37), 361 (100); HRMS *m/z* calcd for C<sub>21</sub>H<sub>18</sub>F<sub>3</sub>O<sub>3</sub>S [M+H]<sup>+</sup>: 407.0923, found: 407.0925.

3.5.9. (R)- and (S)-4,4,4-Trifluoro-3-(5-methylfuran-2-yl)-1-(2-[(S)*p-tolylsulfinyl]phenyl)butan-1-one* (**30**). Compounds **30** were obtained from 14 and 2-methylfuran as an inseparable 80:20 diastereomers mixture. Chromatography: n-hexane:AcOEt 3:1. Global yield: 83%; colorless oil; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 8.56–8.55 (m, 1H), 7.94 (d, J=7.6 Hz, 1H), 7.85 (t, J=7.5 Hz, 1H), 7.60 (t, J=7.6 Hz, 1H), 7.50 (d, J=8.3 Hz, 2H), 7.16 (d, J=7.9 Hz, 2H, minor), 7.06 (d, J=8.2 Hz, 2H, major), 6.18 (d, J=3.1 Hz, 1H, minor), 6.06 (d, J=3.1 Hz, 1H, major), 5.89-5.88 (m, 1H, minor), 5.83-5.82 (m, 1H, major), 4.28–4.16 (m, 1H), 3.67 (dd, J=9.3, 17.4 Hz, 1H, minor), 3.60 (dd, J=9.3, 17.6 Hz, 1H, major), 3.40 (dd, J=4.2, 17.6 Hz, 1H, major), 3.27 (dd, J=3.9, 17.4 Hz, 1H, minor) 2.32 (s, 3H, minor), 2.29 (s, 3H, major), 2.22 (s, 3H, minor), 2.16 (s, 3H, major). <sup>13</sup>C NMR  $\delta$  (major) 194.9, 152.3, 149.5, 144.9, 143.5, 140.8, 134.3, 133.1, 130.3, 129.7, 129.5, 129.4, 126.5, 126.4, 125.3, 110.27, 106.5, 38.6 (c), 36.4, 29.7, 21.3, 13.4; (ESI) *m/z*: 863 [2M+Na]<sup>+</sup> (26), 841 [2M+H]<sup>+</sup> (21), 443 [M+Na]<sup>+</sup> (100), 421 [M+H]<sup>+</sup> (71); HRMS *m*/*z* calcd for C<sub>22</sub>H<sub>20</sub>F<sub>3</sub>O<sub>3</sub>S [M+H]<sup>+</sup>: 421.1079, found: 421.1076.

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#### Supplementary data

NMR spectra (<sup>1</sup>H, <sup>13</sup>C) of compounds **3**, **4**, **5**, **9**, **10**, **11**, **12**, **14**, *endo*-**15A**, *exo*-**15A**, *endo*-**16B**, *endo*-**17A**+*endo*-**17B**, *endo*-**18A**, *endo*-**19A**, *endo*-**20A**, *endo*-**21A**, *endo*-**22A**, *endo*-**23A**, *endo*-**25**, *endo*-**26**+*exo*-**26**, **27**, *endo*-**29A** and **30** and X-ray ORTEP of compounds *endo*-**15A**, *endo*-**21A** and *endo*-**29A**. Supplementary data related to this article can be found online at doi:10.1016/j.tet.2012.03.112.

#### **References and notes**

- Diels-Alder reaction reviews: (a) Fringuelli, F.; Taticchi, A. The Diels-Alder Reaction: Selected Practical Methods; John Wiley & Sons: Chichester, UK, 2002; (b) Mamedov, E. G.; Klabunovskii, E. I. Russian J. Org. Chem. 2008, 44, 1097; (c) Pellisier, H. Tetrahedron 2009, 65, 2839.
- For review see: (a) Gnas, Y.; Glorius, F. Synthesis 2006, 1899; (b) Lait, S. M.; Rankic, D. A.; Keay, B. A. Chem. Rev. 2007, 107, 767 For recent references see: (c) Liu, X.; Snyder, J. K. J. Org. Chem. 2008, 73, 2935; (d) Sarotti, A. M.; Spanevello, R. A.; Suárez, A. G. Tetrahedron 2009, 65, 3502; (e) Broeker, J.; Knollmueller, M.; Gaertner, P. Tetrahedron: Asymmetry 2009, 20, 273; (f) Lam, Y.; Cheong, P. H.-Y.; Blasco Mata, J. M.; Stanway, S. J.; Gouverneur, V.; Houk, K. N. J. Am. Chem. Soc. 2009, 131, 1947; (g) Henderson, J. R.; Parvez, M.; Keay, B. A. Org. Lett. 2009, 11, 3178; (h) Henderson, J. R.; Chesterman, J. P.; Parvez, M.; Keay, B. A. J. Org. Chem. 2010, 75, 988.
- (a) Trost, B. M.; O'Krongly, D.; Belletire, J. L. J. Am. Chem. Soc. 1980, 102, 7595; (b) Monbaliu, J.-C.; Robiette, R.; Peeters, D.; Marchand-Brynaert, J. Tetrahedron Lett. 2009, 50, 1314; (c) Agopcan, S.; Celebi-Ölcüm; Ücısık, M. N.; Sanyal, A.; Aviyente, V. Org. Biomol. Chem. 2011, 9, 8079; (d) Fernández de la Pradilla, R.; Tortosa, M.; Castellanos, E.; Viso, A.; Baile, R. J. Org. Chem. 2010, 75, 1517.
- For reviews see: (a) Harada, T.; Kusukawa, T. Synlett 2007, 1823; (b) Mellah, M.; Voituriez, A.; Schulz, E. Chem. Rev. 2007, 107, 5133; (c) Pellisier, H. Tetrahedron 2007, 63, 1297; (d) Corey, E. J. Angew. Chem. Int. Ed. 2002, 41, 1650; (e) Kagan, H. B; Riant, O. Chem. Rev. 1992, 92, 1007 Selected recent references: (f) Boersma, A. J.; Feringa, B. L.; Roelfes, G. Org. Lett. 2007, 9, 3647; (g) Harada, S.; Toudou, N.; Hiraoka, S.; Nishida, A. Tetrahedron Lett. 2009, 50, 5652; (h) Mukherjee, S.; Corey, E. J. Org. Lett. 2010, 12, 632.
- Reviews in asymmetric organocatalysis: (a) Pellisier, H. Tetrahedron 2007, 63, 9267; (b) Notz, W.; Tanaka, F.; Barbas, C. F., III. Acc. Chem. Res. 2004, 37, 580
   Selected references: (c) Northrup, A. B.; MacMillan, D. W. C. J. Am. Chem. Soc. 2002, 124, 2458; (d) Karsten, J.; Jorgensen, K. L. Angew. Chem., Int. Ed. 2003, 42, 1498; (e) Hayashi, Y.; Samanta, S.; Gotoh, H.; Ishikawa, H. Angew. Chem., Int. Ed. 2008, 47, 6634 and references cited therein; (f) Li, Q.; Wong, W.-Y.; Chan, W.-H.; Lee, A. W. M. Adv. Synth. Catal. 2010, 352, 2142.
- (a) Winkel, A.; Reddy, P. V. G.; Wilhelm, R. Synthesis 2008, 999; (b) Nguyen Van Buu, O.; Aupoix, A.; Vo-Thanh, G. Tetrahedron 2009, 65, 2260.
- 7. For a recent review of the sulfinyl group as chiral auxiliary in Diels-Alder reaction see: (a) García Ruano, J. L; Alemán, J.; Cid, M. B.; Fernández-Ibáñez, M. A.; Maestro, M. C.; Martín, M. R.; Martín Castro, A. M. In Organosulfur Chemistry in Asymmetric Synthesis; Toru, T., Bolm, C., Eds.; Wiley-VCH: Weinheim, 2008; p 55; For a recent reference see: (b) Lanfranchi, D. A.; Bour, C.; Hanquet, G. Eur, J. Org. Chem. 2011, 2818 For a review about the sulfinyl group as ligand in asymmetric catalysis see: (c) Fernández, I.; Khiar, N. In Organosulfur Chemistry in Asymmetric Synthesis; Toru, T., Bolm, C., Eds.; Wiley-VCH: Weinheim, 2008; p 265; (d) Senanayake, C. H.; Han, Z.; Krishnamurthy, D. In Organosulfur Chemistry in Asymmetric Synthesis; Toru, T., Bolm, C., Eds.; Wiley-VCH: Weinheim, 2008; p 233.
- (a) Kappe, C. O. Chem. Soc. Rev. 2008, 37, 1127; (b) Chen, I.-O.; Young, J.-N.; Yu, S. J. Tetrahedron 2004, 60, 11903.
- 9. Dallinger, D.; Kappe, C. O. Chem. Rev. 2007, 107, 2563.
- (a) Bravo, J. L.; López, I.; Cintas, P.; Silvero, G.; Arévalo, M. J. Ultrason. Sonochem. 2006, 13, 408; (b) Timko, M. T.; Allen, A. J.; Danheiser, R. L.; Steinfeld, J. I.; Smith, K. A.; Tester, J. W. Ind. Eng. Chem. Res. 2006, 45, 1594; (c) Cella, R.; Stefani, H. A. Tetrahedron 2009, 65, 2619.
- 11. (a) Jenner, G. Tetrahedron Lett. 2002, 58, 5185; (b) Jenner, G.; Gacem, B. J. Phys. Org. Chem. 2003, 16, 265 (and references cited therein). For recent articles on synthesis via Diels–Alder reaction under high pressure conditions see: (c) Minuti, L; Ballerini, E. J. Org. Chem. 2011, 76, 5392 (and references cited therein); (d) Waalboer, D. C. J.; Schaapman, M. C.; van Delft, F. L.; Rutjes, F. P. J. T.

Angew. Chem., Int. Ed. 2008, 47, 6576; (e) Pichon, N.; Harrison-Marchand, A.; Toupet, L.; Maddaluno, J. J. Org. Chem. 2006, 71, 1892.

- 12. Pan, C.; Wang, Z. Coord. Chem. Rev. 2008, 252, 736.
- 13. Vidis, A.; Küsters, E.; Sedelmeier, G.; Dyson, P. J. J. Phys. Org. Chem. 2008, 21, 264. 14. Oakes, R. S.; Heppenstall, T. J.; Shezad, N.; Clifford, A. A.; Rayner, C. M. Chem.
- Commun. **1999**, 1459. 15. For a review see: (a) García Ruano, J. L.; Martín-Castro, A. M. Heteroat. Chem.
- 2007, 18, 537 (and references cited therein).
  16. (a) Garcia Ruano, J. L.; Torrente, E.; Martin-Castro, A. M. J. Org. Chem. 2011, 76, 3597; (b) García Ruano, J. L.; Marcos, V.; Alemán, J. Angew. Chem., Int. Ed. 2008, 47, 6836; (c) Garcia Ruano, J. L.; Schoepping, C.; Alvarado, C.; Aleman, J. Chem. –Eur. J. 2010, 16, 8968; (d) Arroyo, Y.; Sanz-Tejedor, M. A.; Alonso, I.; Garcia-Ruano, J. L. 007. Lett. 2011, 13, 4534; (e) Garcia Ruano, J. L.; Parra, A.; Alonso, I.;
- Fustero, S.; del Pozo, C.; Arroyo, Y.; Sanz-Tejedor, A. Chem.—Eur. J. 2011, 17, 6142.
   García Ruano, J. L.; Martín-Castro, A. M.; Tato, F.; Cárdenas, D. J. Tetrahedron: Asymmetry 2005. 16, 1963.
- (a) García Ruano, J. L.; Fernández-Ibáñez, M. A.; Maestro, M. C.; Rodríguez-Fernández, M. M. J. Org. Chem. 2005, 70, 1796; (b) García Ruano, J. L.; Fernández-Ibáñez, M. A.; Maestro, M. C.; Rodriguez-Fernández, M. M. Tetrahedron 2006, 62, 1245; (c) García Ruano, J. L.; Fernández-Ibáñez, M. A.; Maestro, M. C. Tetrahedron 2006, 62, 12297; (d) García Ruano, J. L.; Fernández-Ibáñez, M. A.; Fernández-Salas, J. A.; Maestro, M. C.; Márquez-López, P.; Rodríguez-Fernández, M. M. J. Org. Chem. 2009, 74, 1200.
- García Ruano, J. L.; Fernández-Ibáñez, M. A.; Maestro, M. C. J. Org. Chem. 2006, 71, 7683.
- Recent results of 1,3-dipolar cycloaddition to sulfinyl dipolarophiles: (a) Cruz Cruz, D.; Yuste, F.; Martín, M. R.; Tito, A.; García Ruano, J. L. J. Org. Chem. 2009, 74, 3820; (b) García Ruano, J. L.; Nuñez, A., Jr.; Martín, M. R.; Fraile, A. J. Org. Chem. 2008, 73, 9366; (c) García Ruano, J. L.; Fraile, A.; Martín, M. R.; González, G.; Fajardo, C. J. Org. Chem. 2008, 73, 8484.
- 21. (a) Garcia Ruano, J. L.; Cid de la Plata, B. In *Topics in Current Chemistry*; Page, P. G. B., Ed.; Springer: Berlin, 1999; vol. 204; p 1; (b) Garcia Ruano, J. L.; Martín Castro, A. M.; Rodríguez Ramos, J. H. *Heteroat. Chem.* 2002, *13*, 453; (c) Garcia Ruano, J. L.; Alemparte, C. J. Org. Chem. 2004, *69*, 1405 and references cited therein; (d) Arribas, C.; Carreño, M. C.; García Ruano, J. L.; Rodríguez, J. F.; Santos, M.; Sanz-Tejedor, M. A. Org. Lett. 2000, *2*, 3165; (e) Garcia Ruano, J. L.; González Gutierrez, L.; Martín Castro, A. M.; Yuste, F. *Tetrahedron: Asymmetry* 2002, *13*, 2003; (f) Aranda, M. T.; Aversa, M. C.; Barattucci, A.; Bonaccorsi, P.; Carreño, M. C.; Cid, M. B.; García Ruano, J. L. *Tetrahedron: Asymmetry* 2000, *11*, 1217.
- For other Diels–Alder reactions of substrates containing remote sulfinyl groups see: (a) Arai, Y.; Masuda, T.; Masaki, Y. J. Chem. Soc., Perkin Trans. 1 1999, 2165; (b) Arai, Y.; Masuda, T.; Masaki, Y. Chem. Pharm. Bull. 1998, 46, 1078.
- García Ruano, J. L.; Aleman, J.; Aranda, M. T.; Arevalo, M. J.; Padwa, A. Org. Lett. 2005, 7, 19.
- 24. Xu, Y.; Dolbier, W. R., Jr. J. Organomet. Chem. 2000, 65, 2134.
- Garcia Ruano, J. L.; Martin-Castro, Ana, M.; Tato, F.; Pastor, C. J. J. Org. Chem. 2005, 70, 7346.
- 26. CCDC 862077, CCDC 862078 and CCDC 862079 contain the supplementary crystallographic data of compounds *endo*-**15A**, *endo*-**21A** and *endo*-**29A**, respectively. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data\_request/cif.
- Complete *endo* selectivity has been also described for the reaction of 3phenylbut-3-en-2-one with cyclopentadiene in the presence of Me<sub>2</sub>AlCl. See: Davies, H. M. L.; Dai, X. J. Org. Chem. **2005**, 70, 6680.
- 28. In order to prove the transformation of Z-enone 11 in *E*-enone 10 under the reaction conditions, a 1:1 mixture of Yb(OTf)<sub>3</sub> and compound 11 in acetonitrile was maintained under stirring at room temperature for 20 h. Then, both *E* and *Z* isomers 10 and 11 in 1:2 ratio, respectively, appeared at the resulting mixture (<sup>1</sup>H NMR).
- 29. To ascertain this result, besides the <sup>1</sup>H NMR analysis of the reaction mixtures, we have carried out a careful oxidation of the 60:40 mixture of adducts obtained from the trifluoromethyl dienophile **14** and 1-methoxy-1,3-cyclohexadiene, to transform the sulfinyl group into sulfone moiety. The formation of a 60:40 mixture of the corresponding diastereoisomeric sulfones indicated that the facial selectivity produced by the sulfnyl group is complete but the Diels–Alder reaction occurred with low *endo–exo* selectivity.
- (a) Leroy, J.; Fischer, N.; Wakselman, C. J. Chem. Soc., Perkin Trans. 1 1990, 1, 1281;
   (b) Benjamin, N. M.; Martin, S. F. Org. Lett. 2011, 13, 450.
- 31. Diels–Alder cycloadditions and Friedel–Crafts alkylation of furan derivatives with non aromatic ketones catalyzed by chiral Lewis acids have been recently reported: (a) Singh, R. S.; Adachi, S.; Tanaka, F.; Yamauchi, T.; Inui, C.; Harada, T. J. Organomet. Chem. 2008, 73, 212; (b) Adachi, S.; Tanaka, F.; Watanabe, K.; Harada, T. Org. Lett. 2009, 11, 5206.
- 32. Reaction of the dienophile with similar structure than **14**, but lacking of the sulfinyl group, afforded the adduct with *exo* configuration as the major one. See: Leuger, J.; Blond, G.; Frohlich, R.; Billard, T.; Haufe, G.; Langlois, B. R. *J. Organomet. Chem.* **2006**, *71*, 2735.