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Regio- and stereoselective synthesis of pyrrolo or azepine-fused cyclopenta[d]isoxazolines from 2-p-tolylsulfinylcyclopent-2-en-1-one

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Regio- and stereoselective synthesis of pyrrolo or azepine-fused cyclopenta[*d*]isoxazolines from 2-*p*-tolylsulfinylcyclopent-2-en-1-one

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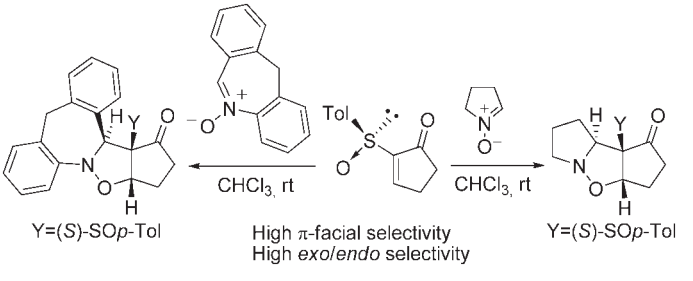
Reactions of enantiopure 2-*p*-tolylsulfinylcyclopent-2-en-1-one with cyclic nitrones afforded pyrrolo or azepine-fused cyclopenta[*d*]isoxazolidines in high yields under mild conditions. Comparison of these results with those obtained with cyclopent-2-en-1-one as the dipolarophile shows that the sulfinyl group increases the reactivity of the enonic system and efficiently controls the π-facial and *endo*/*exo* selectivities of the cycloadditions, which are also dependent on the easy cycloreversion of the resulting compounds. Results obtained in reactions with other dipoles (benzonitrile oxides and those resulting from allenoate and PPh_3) are also reported.



Keywords: 1,3-dipolar cycloadditions; cycloreversion; nitrones; benzonitrile oxide; vinyl sulfoxides; cyclopenta[*d*]isoxazolidines

1. Introduction

The [3 + 2] cycloaddition reaction is a useful method for obtaining heterocyclic (*1*) and carbocyclic (*2*) compounds. Several years ago, we initiated a program aimed at exploring the usefulness of vinyl sulfoxides in asymmetric 1,3-dipolar reactions (*3–9*). In all the reported studies, the most surveyed sulfinyldipolarophile was one of the epimers at C-5 of the 5-ethoxy-3-*p*-tolylsulfinylfuran-2(5*H*)-one. The results obtained in its reactions with diazoalkanes (*3a*), nitrile oxides (*4*), nitrones (*5*), azomethyne ylide (*6*), carbonyl ylide (*7*), and the dipoles generated from allenoates (*8*) or allenyl sulfones (*9*) in the presence of Ph_3P clearly demonstrated the beneficial

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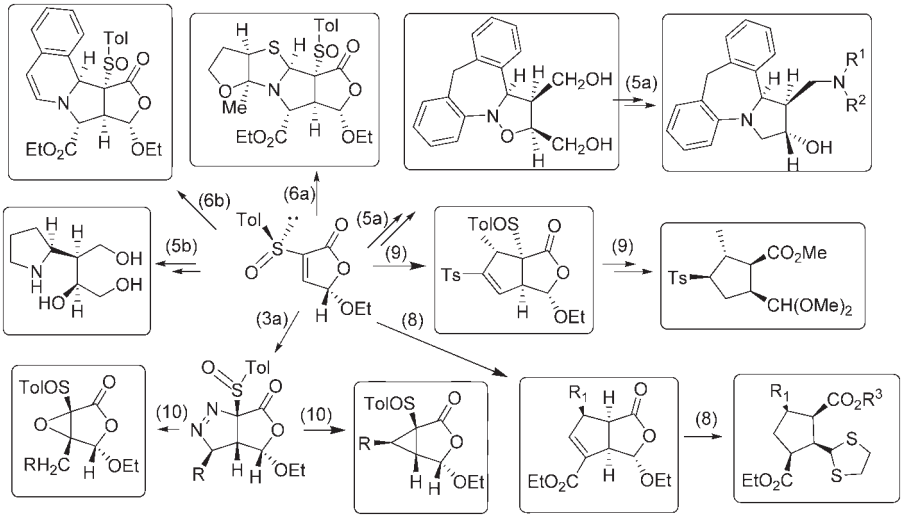
Dedicated to Professor Eric Block on the occasion of his 70th birthday.



Scheme 1. Compounds obtained by asymmetric [3+2] cycloadditions to 5-ethoxy-3-*p*-tolylsulfinylfuran-2(5*H*)-one.

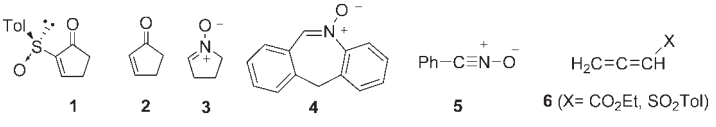


Figure 1. Dipolarophiles and dipoles used in this paper.

influence of the sulfinyl group in the reactivity and stereoselectivity of the butenolide reactive system, allowing the preparation of enantiomerically pure adducts which are interesting intermediates in the synthesis of different types of heterocycles or carbocycles (*5*, *8–10*). The structures of some compounds prepared from the 5-ethoxy-3-*p*-tolylsulfinylfuran-2(5*H*)-one are depicted in Scheme 1.

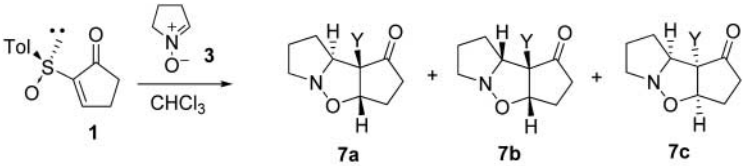
Saturated cyclopenta-fused heterocycles and pentalenes are interesting substrates with a large synthetic potential, which are present in the structure of many natural products (*11*) and biologically active compounds (*11b,c, 12*). These compounds would be available by reactions similar to those indicated at Scheme 1, by the use of 2-*p*-tolylsulfinylcyclopent-2-enone (**1**) as dipolarophile. However, surprisingly, only its reactions with diazoalkanes (*13*) and azomethine ylides (*14*) have been reported to date. In order to expand the scope of applicability of the cyclopentenone skeleton as dipolarophile, in this paper we describe the results obtained from the reactions of the cyclopentenone **1** with cyclic nitrones (**3** and **4**), nitrile oxide (**5**), and allenes **6** in the presence of nucleophiles such as Ph_3P (Figure 1). With comparative purposes, reactions with cyclopentenone **2**[1] have also been studied in those cases where they had not been reported previously (*15*).

2. Results and discussion

2.1. *Addition of cyclic nitrones to (S_S)-2-p-tolylsulfinylcyclopent-2-enone (1) and cyclopent-2-enone (2)*

Sulfinylcyclopentenone **1** (*16*), as well as nitrones **3** (*17*) and **4** (*18*), was prepared according to previously reported procedures. We first studied the reaction of 3,4-dihydro-2*H*-pyrrol 1-oxide (**3**)

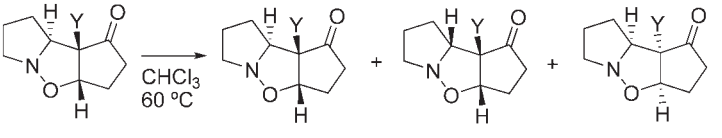
Table 1. Cycloaddition of nitrone **3** to sulfinylcyclopentenone **1**.



Entry	*T* (°C)	Time (h)	Products (%)	Yields
1	25	15	**7a** (86):**7b** (11):**7c** (3)	91%
2	25	20	**7a** (79):**7b** (16):**7c** (5)	92%
3	60	15	**7a** (49):**7b** (39):**7c** (12)	90%

with sulfinylcyclopentenone **1**[2] in $CHCl_3$ under different conditions (Table 1). Mixtures of three adducts (**7a**–**7c**), the ratio of which was dependent on the reaction conditions, were obtained in all cases. Adducts **7a** and **7b** were isolated diastereoisomerically pure by column chromatography. The highest selectivity was observed at room temperature (15 h, Entry 1), but it decreased at longer reaction times (Entry 2) or higher temperatures (Entry 3).

The regioselectivity of all the reactions was complete, exclusively yielding compounds with the oxygen atom of the nitrone bonded to C_3 in the cyclopentenone. The π-facial selectivity (defined as **7a**+**7b**:**7c**) was higher than 95:5 at room temperature (Entries 1 and 2) but it decreased when working at 60°C (Entry 3). Changes in the proportion of adducts could be explained assuming that cycloreversion is possible under reaction conditions. It was supported by the evolution with the time of a chloroformic solution of pure **7a** heated at 60°C (Scheme 2), which is transformed into a mixture of **7a**, **7b**, and **7c** along with traces of sulfinylcyclopentenone **1** and nitrone **3**. As we can see in Scheme 2, the composition of the reaction mixture after 14 h at 60°C is very similar to that indicated in Entry 3 in Table 1, where the reaction time and the temperature are almost identical.



Y=(*S*)-SOTol	**7a**		**7b**		**7c**
0 h:	100	:	0	:	0
1 h:	74	:	19	:	7
6 h:	62	:	29	:	9
14 h:	53	:	37	:	10

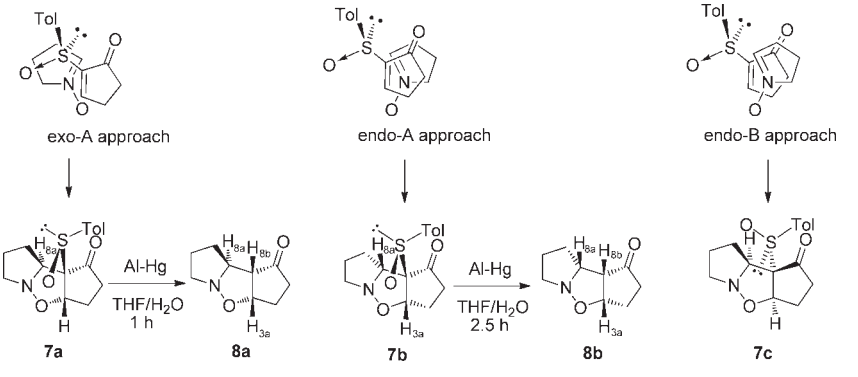
Scheme 2. Evolution with the time of a pure sample of **7a** in $CHCl_3$ at 60°C.

The structural and stereochemical assignment of the adducts **7** was performed taking into account: (a) their NMR parameters (Table 2) as well as those of desulfinylated compounds **8**,[3] obtained by the reaction of **7** with aluminum amalgam in THF/H_2O (Scheme 3); (b) the stereochemical proposal indicated in Scheme 3 for explaining the obtained results.

The regiochemistry of all adducts **7** (wherein the oxygen atom is bonded to C_3) was inferred from the high δ-$H_{\mathbf{3a}}$ value (>4.6 ppm) observed in all compounds **7** and **8** (Scheme 3). The relative stereochemistry of the protons $H_{\mathbf{8a}}$ and $H_{\mathbf{8b}}$ in compounds **8a** and **8b** was deduced from their $J_{\mathbf{8a,8b}}$

Table 2. Representative ^{1}H NMR data of adducts **7** and **8**.

	δ (ppm)			J (Hz)	
Compounds	H_{3a}	H_{8a}	H_{8b}	J_{3a-8b}	J_{8a-8b}
7a	5.19	3.84	–	–	–
7b	4.95	4.18	–	–	–
7c	4.63	3.92	–	–	–
8a	4.85	3.80	2.76	5.7	0.0
8b	4.72	3.97	3.08	5.5	10.0



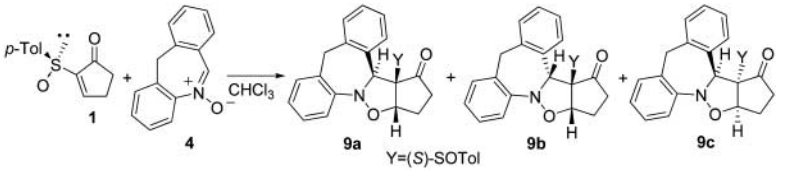
Scheme 3. Stereochemical course of the reaction of sulfinylcyclopentenone **1** with nitrone **3** and desulfinylation of adducts **7**.

values, which is close to zero for the *trans* arrangement in **8a** (*5b*, *19*), whereas for the *cis* one it is higher than 9 Hz (*5b*, *19b*). Taking into account that desulfinylation (Scheme 3) should not produce epimerization at C_{8b}, the spatial arrangement of the sulfinyl group in **7a** and **7b** must be identical to that of H_{8b} in **8a** and **8b**, respectively. Finally, the relative stereochemistry of H_{3a} and H_{8b} could not be unequivocally established in **8a** and **8b** from the $J_{3a,8b}$ values. However, the concerted character of these cycloadditions suggests that the sulfinyl group and H_{3a} must adopt the *cis* arrangement in **7a** and **7b**, and the same will be true for H_{8b} and H_{3a} in **8a** and **8b**.

The absolute configuration of the major compounds **7a** and **7b** was assigned as indicated in Scheme 3, by assuming that the facial selectivity of the reaction will be controlled by the orientation of the tolyl group at the starting cyclopentenone (*S*)-**1**, which must adopt the conformation depicted in Scheme 3 in order to minimize the electrostatic repulsion of the sulfinyl and carbonyl oxygen atom. The favored *exo*-**A**[4] and *endo*-**A** nitrone approaches will take place to the less hindered *si–si* face (**A**) of the cyclopentenone (*S*)-**1**, yielding **7a** and **7b**, respectively. The smaller steric interactions of the *exo*-**A** approach justify the formation of **7a** as the major isomer. The steric interactions between the sulfinyl group and the pyrrolidine ring in **7a** would justify the higher stability of **7b** and, therefore, its higher proportion under conditions favoring cycloreversion. Finally, the configuration of the minor adduct **7c** was tentatively assigned as indicated in Scheme 3 on the assumption that it must derive from the *endo*-**B** approach of the nitrone to the most hindered face (the *exo*-**B** approach must be sterically much more unstable).

We have also studied reactions of the cyclic nitrone **4** with sulfinylcyclopentenone **1** under different conditions. The obtained results, collected in Table 3, indicated the formation of three adducts (**9a**–**9c**). As it happened in the case of the cyclic nitrone **3** (Table 1), the diastereomeric ratio depends on the reaction time and the temperature, and the relative proportion of the major **9a** adduct decreases at longer times reaction and higher temperatures (Table 3), which evidences once

Table 3. Cycloaddition reactions of nitrone **4** to cyclopentenone **1**.



T (°C)	Time (h)	Cycloadducts (%)[a]	Yield (%)[b]
25	2.5	**9a** (62):**9b** (30):**9c** (8)	nd[c]
25	20	**9a** (57):**9b** (32):**9c** (11)	76%
60	2.5	**9a** (53):**9b** (33):**9c** (14)	93%

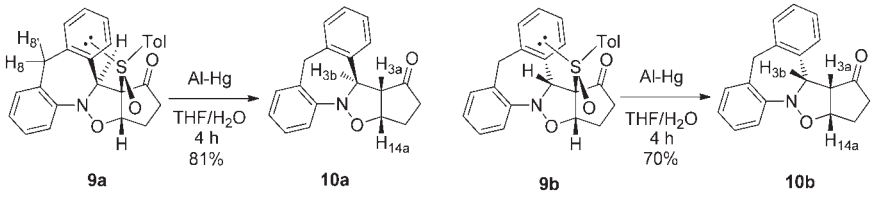
Notes: [a]Measured by ^{1}H-NMR.
[b]Overall yield.
[c]60% conversion.

Table 4. Representative NMR data of adducts **9** and **10**.

	δ (ppm)			
Compounds	H_{14a}	H_{3a}	H_{3b}	J_{3a-3b} (Hz)
9a	5.28	–	4.52	–
9b	5.21	–	4.95	–
10a	5.10	3.40	4.28	6.6
10b	5.17	3.47	4.53	6.5

more that cycloreversion is taking place. Nevertheless, the comparison of the results collected in Tables 1 and 3 reveals that, under similar conditions, reactions from **4** are less stereoselective (compare entries 2 in both tables) and present less marked variations of the diastereomeric ratios with the time or the temperature.

From the mixtures showed in Table 3, only the major **9a** isomer could be isolated as a diastereomerically pure compound by precipitation. Contrarily, **9b** could not be separated from their isomers and its NMR signals were obtained from a mixture where it was predominant. The minor isomer **9c** could not be completely characterized, and only some of its NMR signals could be assigned.

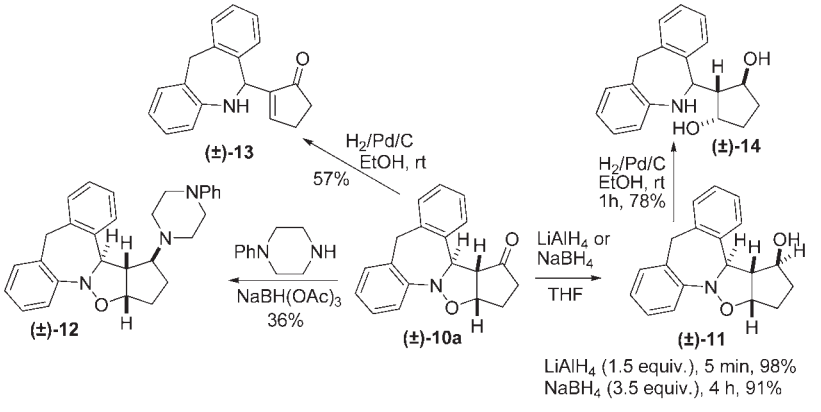


Scheme 4. Desulfinylation reaction of compounds **9**.

We could not unequivocally assign the structure and absolute configuration of **9a**–**9c**, despite they were submitted to studies similar to those used for establishing the structures of **7a**–**7c**. Thus, desulfinylation of **9a** with aluminum amalgam yielded compound **10a**, whereas a mixture of **9a**–**9c** (enriched in **9b**) afforded a mixture of two inseparable diastereoisomers (**10a** and **10b**) (Scheme 4) where the signals of both compounds were clearly assigned. The δ values of H_{14a}

(higher than 5.10 ppm) and the multiplicity of H_{3a} (singlet) for all adducts **9** (Table 4) allowed us unequivocally establish their regiochemistry, with the oxygen atom of the nitrone bonded to the β-carbon of the cycloalkenone (C_{14a} in the adduct). However, the *endo* or *exo* character of the cycloadducts **10a** and **10b** could not be unequivocally established from the J_{3a-3b} values (Table 4), which are about 6.5 Hz in both compounds and, therefore, intermediate between the values that unequivocally allow their assignment as *endo* or *exo* (*5b*, *19*). Thus, taking into account the similar behavior observed in reactions from nitrones **3** (Table 1) and **4** (Table 3), we have assigned the structure and absolute configuration of compounds **9** and **10** by assuming the same sterochemical course for both nitrones, which means that the major adduct **9a** will display the sulfinyl group in a *cis* arrangement with respect to the H_{3b} at the azepine ring (Scheme 4) as the result of the *exo* approach of the nitrone **4** to the less hindered face of 2-sulfinylcyclopentenone (see Scheme 3).[5]

We have also studied the reaction of **4** with cyclopent-2-enone **2**, which resulted completely stereoselective, only yielding compound **(±)-10a** in 72% yield after 18 h at room temperature. The comparison of this result with that obtained under similar conditions with the sulfinyl derivative **1** (Entry 1, Table 3) indicates that the presence of the sulfinyl group increases the dipolarophilic reactivity of the double bond, but it has a negative influence on the *exo*/*endo* selectivity.



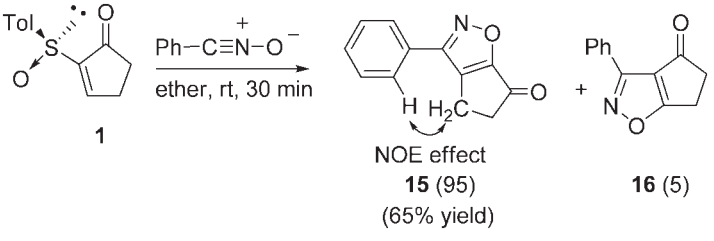
Scheme 5. Reactions of **(±)-10a**.

Taking into account the presumably high stereoselectivity of the reactions of different nucleophiles with the carbonyl group of compounds **9** and **10**, we assumed that they could be interesting scaffolds for the preparation of dibenzo[*c*,*f*]cyclopenta[4,5]isoxazolo[2,3-*a*]azepines or 2-(dibezo[*b*,*e*]azepin-6-yl)-cyclopentane derivatives. We confirmed this assumption by studying the chemoselective reduction of **10a** with $NaBH_4$ or $LiAlH_4$, which afforded the azepine derivative **11** as the only diastereoisomer in almost quantitative yield (Scheme 5). A similar behavior was observed in the reaction of **10a** with 4-phenylpiperazine and $NaBH(OAc)_3$ (*20*), which afforded, after 15 h, a mixture of the starting product **10a**, alcohol **(±)-11** (resulting from the direct reduction of the carbonyl group) and the amine **(±)-12** (as the only diastereoisomer), which were separated by column chromatography. The formation of the amine **12** involves the reduction of the iminium intermediate following a similar stereochemical course to that proposed for the carbonyl reduction.

Other interesting transformations concerned the hydrogenolysis of the N–O bonds. Pd(C)-catalyzed hydrogenation of **(±)-10a** gave, after 20 h and column chromatography purification, cyclopentenone **(±)-13** (57% yield) by spontaneous elimination of water of the β-hydroxyketone resulting from the cleavage of the N–O bond in the isoxazolidine. However, catalytic hydrogenation of hydroxyl compound **11** led to diol **14** in good yield (Scheme 5).

2.2. *Other cycloadditions of sulfinylcyclopentenone 1*

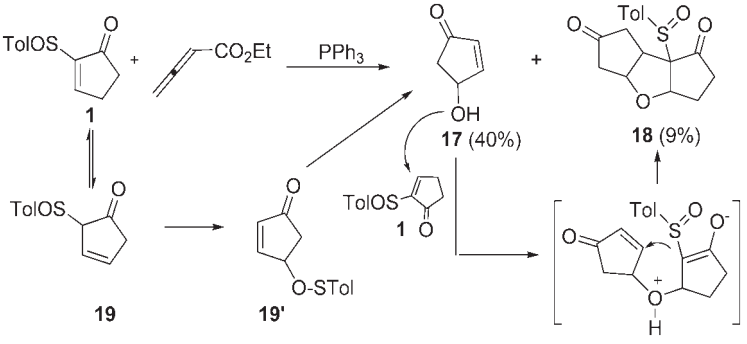
Reactions of cyclopent-2-enone **2** with benzonitrile oxide had been previously reported (*15c*). In order to know the influence of the sulfinyl group on the course of this reaction, we studied the reactions of this dipole with sulfinylcyclopentenone **1**. When we treated **1** with an excess amount of benzonitrile oxide (**5**), in ethyl ether at room temperature, we obtained, after 30 min, a 95:5 mixture of two regioisomeric isoxazoles **15** and **16** (Scheme 6). The major one (**15**) was isolated pure by column chromatography in 66% yield. The observed regioselectivity was not improved by lowering the temperature. The isoxazoline precursors of these isoxazoles were not detected, even at low temperatures, which is not surprising due to the easy desulfinylation of the adducts into the aromatic isoxazoles.



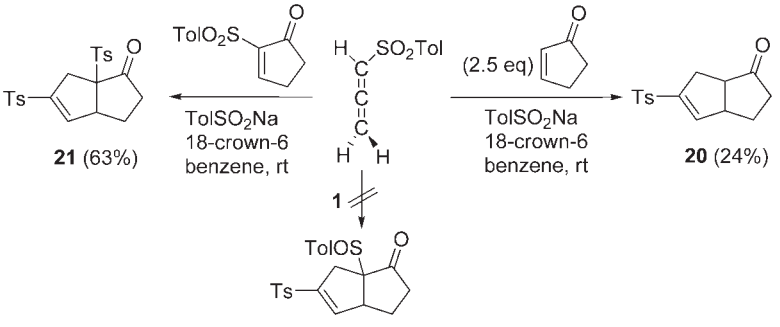
Scheme 6. Cycloaddition of benzonitrile oxide (**5**) to **1**.

The structure of the major regioisomer was assigned on the basis of the NOE effect observed between the phenyl and methylene groups, such as it is indicated in Scheme 6 (this NOE effect was not observed in **16**) and the comparison of the ^{13}C NMR data [$\Delta\delta$ (C_4–C_5)] of heterocyclic carbons of **15** with those of other isoxazoles (*4a, 21*) or pyrazoles (**3a**) previously reported. The comparison of the results obtained from compound **1** (Scheme 6) and those reported for **2**, which required 12 h at room temperature to react with **5** (*15c*), suggests that the sulfinyl group substantially improves the reactivity, which is in agreement with the results that we observed in reactions with other sulfinyl dipolarophiles and other dipoles. The regioselectivity is also affected, being higher for **1** (95:5) and opposite to that reported for cyclopentenone **2**, which yielded a 25:75 regioisomeric mixture (*15c*). This inversion of the regioselectivity produced by the sulfinyl group had also been observed in reactions of 5-alkoxyfuran-2(5*H*)-furanones and their 3-sulfinyl derivatives (*4a*). Other significant difference is the stability of primary adducts, high for those obtained from **2**, but very low for those derived from **1**; these adducts cannot be isolated not even detected due to the easier and spontaneous sulfinyl elimination (*4a*). This uncontrolled evolution precluded us to obtain any information about the influence of the sulfinyl group on the stereoselectivity of the reaction.

Finally, and taking into account our recent contributions to the asymmetric use of Lu's reaction (*8*), we have also studied the reactions of allenoates with sulfinylcyclopentenone **1**, because the resulting adducts would be promising starting materials for the regio- and stereoselective synthesis of polyfunctionalized pentalenes. However, reactions of dipolarophile **1** with ethyl 2,3-butadienoate in the presence of PPh_3 did not afford the expected adduct, but the hydroxyketone **17** (40%) and the tricyclic compound **18** (Scheme 7). Slightly better yields (45% and 13%, respectively) were obtained in the presence of 2,2,6,6-tetramethylpiperidine (10%) and phosphine (15%). The formation of **17** can be explained as the result of the migration of the double bond of **1** (favored by the base) to form the allylic sulfoxide **19** (Scheme 7) evolving through a sulfoxide–sulfenate rearrangement (*22*) to the sulfenate intermediate **19′** easily transformed into the carbinol **17** by cleavage of the S–O bond. The conjugate addition of alcohol **17** to sulfinylcyclopentenone



Scheme 7. Transformation of **1** under Lu's reaction conditions.



Scheme 8. Reactions of 2-*p*-tolylsulfonylallene with different cyclopent-2-enones.

1 (oxa-Michael) followed by intramolecular reaction of the intermediate (*exo-trig* cyclization) led to tricyclic compound **18**.

We also studied reactions of the sulfinylcyclopentenone **1** with *p*-tolylsulfonylallene, under the best conditions recently reported for reactions with sulfinyl furanones (*9*) (Scheme 8). Results were unsuccessful and only a complex mixture was obtained. It is interesting that reactions of the sulfonylallene with 2-cyclopentenone **2** and its 2-*p*-tolylsulfonyl derivative gave the expected adducts in low and moderate yields. It supports that the course indicated in Scheme 7 must be responsible for the results obtained with the sulfinyl derivative **1**.

In summary, we report herein the results of the reactions of 2-*p*-tolylsulfinylcyclopent-2-en-1-one (**1**) with different dipoles. They have provided a simple methodology for achieving new polyfunctionalized cyclopentaheterocyclic derivatives in a regio- and stereoselective manner, by using the [3+2] cycloadition as the key step. The positive influence of the sulfinyl group on the dipolarophilic reactivity of the 2-cyclopentenone, as well as on the regioselectivity of its reactions with some dipoles, can be inferred from the obtained results, which are not so good as those obtained from 5-ethoxy-3-*p*-tolylsulfinylfuran-2(5*H*)-one.

3. Experimental

3.1. *General*

All melting points were determined in open capillary tubes and are uncorrected. IR spectra were determined as indicated for each compound with a Bruker FTIR-Vector 22 spectrophotometer. The NMR spectra were determined using TMS as an internal reference on a Bruker AC-300

FT NMR spectrometer operating at 300 and 75 MHz for ^{1}H and ^{13}C NMR, respectively. High-resolution mass spectrometra were obtained using a Waters, VG AutoSpec, spectrometer by FAB technique. The optical rotations were measured at room temperature in the solvent and concentration (g/100 ml) indicated in each case. Silica gel 60 (230–400 mesh ASTM) and DC-Alufolien 60 F254 were used for flash column chromatography and analytical TLC, respectively. Microanalyses were carried out on a LECO CHNS-932 in Laboratory of Elemental Analyses of SIDI of Universidad Autónoma de Madrid and were in good agreement with the calculated values.

3.2. *Cycloaddition reactions of 3,4-dihydro-2H-pyrrol-1-oxide (3) to cyclopentenone 1*

To a stirred solution of **1** (300 mg, 1.4 mmol) in chloroform (5 ml), under argon atmosphere and at room the temperature, a solution of nitrone **3** (178 mg, 2.10 mmol) in 15 ml of chloroform was added. The reaction mixture was kept at room temperature or 60°C for 15 h. The reaction was monitored by TLC and ^{1}H NMR. The solvent was removed under reduced pressure and the residue was purified by column chromatography (hexane/ethyl acetate 4:1), to afford compounds **7a**, **7b**, and **7c** in decreasing order of R_f. Combined yield was 91% or 90%.

3.2.1. *8b-(p-Tolysulfinyl)octahydro-1H-cyclopenta[d]pyrrolo[1,2-b]isoxazol-1-ones (7).*

(3aS,8aS,8bR,SS)-isomer (7a): White solid, mp: 75–76°C. IR (KBr): 1731 (C=O), 1598, 1494, 1083, 1062, 815 cm^{-1}. $[\alpha]_D^{20}$:−34.8°(c=0.5, acetone). ^{1}H NMR ($CDCl_3$)δ 1.46–1.67 (m, 2H), 1.74–1.88 (m, 1H), 1.94–2.20 (m, 3H), 2.40 (s, 3H), 2.28–2.58 (m, 2H), 2.93–3.03 (m, 1H), 3.20–3.29 (m, 1H), 3.84 (t, 1H, J=7.8 Hz), 5.19 (d, 1H, J=5.0 Hz), 7.46 and 7.30 (AA′BB′ system, 4H). ^{13}C NMR ($CDCl_3$)δ 21.4 (CH_3), 24.1 (CH_2), 25.1 (CH_2), 27.0 (CH_2), 37.8 (CH_2), 55.0 (CH_2), 73.0 (CH), 77.3 (CH), 86.0 (C), 125.5 (CH), 129.9 (CH), 136.0 (C), 142.9 (C), 212.7 (C).

(3aS,8aR,8bR,SS)-isomer (7b): Recrystallized from ethyl acetate-diethyl ether, white solid, mp: 113–114 °C. $[\alpha]_D^{20}$: +258.2 (c=0.5, acetone). IR (KBr): 1728 (C=O), 1593, 1492, 1082, 1061, 815 cm^{-1}. ^{1}H NMR ($CDCl_3$)δ 0.93–1.19 (m, 1H), 1.67–2.10 (m, 6H), 2.32–2.52 (m, 1H), 2.42 (s, 3H), 2.82–3.02 (m, 1H), 3.23–3.41 (m, 1H), 4.14–4.28 (m, 1H), 4.95 (d, 1H, J=5.1 Hz), 7.48, and 7.31 (AA′BB′ system, 4H). ^{13}C NMR ($CDCl_3$)δ 21.6 (CH_3), 22.9 (CH_2), 24.8 (CH_2), 26.8 (CH_2), 38.6 (CH_2), 56.4 (CH_2), 72.9 (CH), 81.6 (CH), 83.7 (C), 125.3 (CH), 129.9 (CH), 136.0 (C), 142.9 (C), 212.4 (C). Anal. Calcd. for $C_{16}H_{19}NO_3S$: C, 62.93; H, 6.27; N, 4.9; S, 10.50. Found: C, 62.84; H, 6.62; N, 4.60; S, 10.96.

(3aR,8aS,8bS,SS)-isomer (7c): It was not isolated pure. The signals were assigned from the NMR spectrum of a mixture of **7c** and starting dipolarophile **1**. ^{1}H NMR ($CDCl_3$)δ 2.42 (s, 3H), 3.04 (dt, 1H, J=8.3 and 14.2 Hz), 3.34 (ddd, 1H, J=4.2, 7.8, and 14.2 Hz), 3.92 (t, 1H, J=8.2 Hz), 4.61–4.65 (m, 1H), 7.48 and 7.31 (AA′BB′ system, 4H). The remaining signals were not included because they overlap with the signals of compound **1**. ^{13}C NMR ($CDCl_3$) δ 21.5 (CH_3), 24.3 (CH_2), 25.7 (CH_2), 26.8 (CH_2), 38.1 (CH_2), 56.0 (CH_2), 73.6 (CH), 79.0 (CH), 82.7 (C), 125.4 (CH), 130.2 (CH), 135.9 (C), 143.4 (C), 210.3 (C).

3.3. *Transformation of adduct 7a by reflux in toluene*

A solution of 20 mg of diastereomerically pure sample of adduct **7a** in 5 ml of chloroform was heated at 60°C for 3, 6, or 14 h. After removal of the solvent, the residues, analyzed by ^{1}H NMR, were mixtures 74:19:7, 62:29:9, or 53:37:10 of **7a**:**7b**:**7c**, respectively.

3.4. *Desulfinylation of sufinyl adducts with aluminum amalgam*

Aluminum amalgam was prepared by immersing strips of aluminum foil in 10% hydrochloric acid. After rinsing with water, the strips were immersed in a 5% aqueous solution of mercuric chloride for 15–30 s, and the solution was decanted; the strips were rinsed with absolute ethanol, then with ether, and cut into pieces of ca. 1 cm^2.

To a stirred solution of sulfinyl adduct (0.23 mmol) in a 10:1 mixture of THF-H_2O (3 ml) at room temperature, an excess amount of aluminum amalgam was added. The reaction mixture was stirred at room temperature for 4 h and then filtered. The solid was washed with THF (50 ml), and the solution was evaporated at reduced pressure to dryness.

3.4.1. *Octahydro-1H-cyclopenta[d]pyrrolo[1,2-b]isoxazol-1-ones (**8**).*

(3aS,8aS,8bS)-isomer (8a): It was obtained after 1 h from adduct **7a**. It cannot be isolated pure by column chromatography (hexane/ethyl acetate 1:1). ^{1}H NMR ($CDCl_3$)δ 0.80–2.70 (m, 8H), 2.76 (d, 1H, J=5.7 Hz), 3.08–3.16 (m, 1H), 3.77–3.83 (m, 1H), 4.82–4.87 (m, 1H).

(3aS,8aR,8bS)-isomer (8b): It was obtained after 2.5 h from adduct **7b**. It cannot be isolated pure by column chromatography (hexane/ethyl acetate 2:1). ^{1}H NMR ($CDCl_3$) δ 1.60–2.63 (m, 8H), 2.79–2.93 (m, 1H), 3.08 (dd, 1H, J=5.5 and 10.0 Hz), 3.28–3.42 (m, 1H), 3.90–4.02 (m, 1H), 4.72 (t, 1H, J=4.8 Hz).

3.5. *Cycloadditions of 11H-dibenzo[b,e]azepine 5-oxide (4) to cyclopentenones 1 and 2*

To a solution of (*S*)-2-*p*-tolylsulfinyl-2-cyclopentenone (**1**) (1.4 mmol) in 10 ml of $CHCl_3$, under argon atmosphere and at the temperature indicated in Table 2, was added 11*H*-dibenzo[*b*,*e*]azepine 5-oxide (1.7 equiv.). The reaction was monitored by TLC. After the indicated time, the solvent was removed under reduced pressure and the residue analyzed by ^{1}H NMR. Yields and ratio of adducts are indicated in Table 2 for each case.

3.5.1. ***3a**-((S)-p-Tolylsulfinyl)-**3a,3b,8,14a**-tetrahydro-1H-dibenzo[c,f]cyclopenta[4,5] isoxazolo[2,3-a]azepin-3(2H)-ones (**9**).*

(3aR,3bS,14aS)-isomer (9a): It was obtained from sulfinylcyclopentenone 1 and nitrone 4 as the major stereoisomer. It was isolated as a pure diastereoisomer by precipitation with acetone from the crude reaction mixture. Additional amount of **9a** was isolated by column chromatography (hexane/ethyl acetate 9:1) of the residue resulting from concentrating the filtrate. White solid, mp: 135–137°C. (with decomposition). $[\alpha]_D^{20}$: +181.4 (c=0.5, $CHCl_3$. IR (KBr): 1734 (C=O), 1597, 1485, 1249, 1150 cm^{-1}. ^{1}H NMR ($CDCl_3$)δ 0.67–0.84 (m, 1H), 1.92–2.13 (m, 2H), 2.38 (s, 3H), 2.65–2.81 (m, 1H), 3.50 (d, 1H, J=13.9 Hz), 4.52 (s, 1H), 4.89 (d, 1H, J=13.9 Hz), 5.28 (d, 1H, J=6.1 Hz), 6.99–7.04 (m, 1H), 7.20 and 7.49 (AA′BB′ system, 4H), 7.22–7.36 (m, 6H), 7.94 (d, 1H, J=7.9 Hz). ^{13}C NMR ($CDCl_3$)δ 21.3 (CH_3), 23.2 (CH_2), 37.5 (CH_2), 39.4 (CH_2), 75.3 (CH), 78.9 (CH), 86.2 (C), 115.3 (CH), 124.5 (CH), 125.1 (CH), 126.2 (CH), 127.2 (CH), 127.4 (CH), 128.1 (CH), 130.0 (CH), 130,0 (CH), 130.2 (CH), 130.6 (C), 132.8 (C), 135.8 (C), 137.9 (C), 142.3 (C), 145.3 (C), 212.5 (C). Anal. Calcd. for $C_{26}H_{23}NO_3S$: C, 72.70; H, 5.40; N, 3.26; S, 7.46. Found: C, 72.44; H, 5.50; N, 3.35; S, 7.71.

(3aR,3bR,14aS)-isomer (9b): It was obtained from sulfinylcyclopentenone **1** and nitrone **4**. It was not isolated as a pure compound by column chromatography (hexane/ethyl acetate 9:1). Data

were measured from the mixture of **9b**+**9c**+**9a**. ^{1}H NMR ($CDCl_3$)δ 3.38 (d, 1H, J=14.8 Hz), 4.48 (d, 1H, J=14.8 Hz), 4.95 (s, 1H), 5.21 (d, 1H, J=6.7 Hz).

(3aS,3bS,14aR)-isomer (9c): It was obtained as minor stereoisomer from **1** and nitrone **4**. It was not isolated as a pure compound by column chromatography (hexane/ethyl acetate 9:1). Data were measured from the mixture of **9b**+**9c**+**9a**.^{1}H NMR ($CDCl_3$)δ 3.14 (d, 1H, J=14.5 Hz), 4.40 (d, 1H, J=14.5 Hz), 4.44 (s, 1H), 5.51 (d, 1H, J=4.4 Hz).

3.5.2. *(±)-(3aS,3bR,14aS)-3a,3b,8,14a-Tetrahydro-1H-dibenzo[c,f]cyclopenta[4,5] isoxazolo[2,3-a]azepin-3(2H)-one [(±)-10a].*

It was obtained diastereoisomerically pure from cyclopentenone **2** and nitrone **4** following the general procedure. It was isolated in 72% yield by column chromatography (hexane/ethyl acetate 9:1) of the crude reaction. White solid, mp: 158–159°C. IR (KBr): 1739 (C=O), 1591, 1488, 1150, 757, 725 cm^{-1}. ^{1}H NMR ($CDCl_3$)δ 2.04–2.32 (m, 1H), 2.37–2.60 (m, 2H), 2.73–2.98 (m, 1H), 3.40 (t, 1H, J=6.6 Hz), 3.69 (d, 1H, J=14.7 Hz), 4.28 (d, 1H, J=6.6 Hz), 4.60 (d, 1H, J=14.7 Hz), 5.07–5.13 (m, 1H), 6.98–7.06 (m, 1H), 7.15–7.33 (m, 5H), 7.42 (d, 1H, J=7.8 Hz), 7.63 (d, 1H, J=7.0 Hz). ^{13}C NMR ($CDCl_3$)δ 24.3 (CH_2), 35.9 (CH_2), 39.8 (CH_2), 63.4 (CH), 72.7 (CH), 80.4 (CH), 115.1 (CH), 124.2 (CH), 126.9 (CH), 127.3 (CH), 127.6 (CH), 128.1 (CH), 129.4 (CH), 130.4 (C), 132.8 (CH), 135.8 (C), 135.9 (C), 147.5 (C), 212.7 (C). Anal. Calcd. for $C_{19}H_{17}NO_2$: C, 78.33; H, 5.88; N, 4.81. Found: C, 78.10; H, 5.97; N, 4.73.

3.6. *Transformations of adducts 9a and 10a*

3.6.1. *3a,3b,8,14a-Tetrahydro-1H-dibenzo[c,f]cyclopenta[4,5]isoxazolo[2,3-a]azepin-3(2H)-ones (10).*

(3aS,3bR,14aS)-isomer (+)-10a. It was obtained by desulfinylation of **9a** with aluminum amalgam, following the above-indicated general procedure. The product was isolated by column chromatography (hexane/ethyl acetate 9:1) in 81% yield. White solid, mp: 158–159°C. $[\alpha]_D^{20}$: +95.7 (c=0.5, acetone).

(3aS,3bS,14aS)-isomer (−)-10b: It was obtained along with **(+)-10a** by desulfinylation of a 41:59 mixture **9a** and **9b** with aluminium amalgam, following the above-indicated general procedure. The product was isolated by column chromatography (hexane/ethyl acetate 9:1) as a white solid, mp: 165–167 °C. $[\alpha]_D^{20}$: −31.2 (c=0.18, $CHCl_3$). IR (KBr): 1739 (C=O), 1590, 1488, 757 and 725 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 2.10–2.33 (m, 2H), 2.39–2.53 (m, 1H), 2.75–2.89 (m, 1H), 3.42 (d, 1H, J=13.8 Hz), 3.47 (td, 1H, J=1.1 and 6.5 Hz), 4.53 (d, 1H, J=6.5 Hz), 4.56 (d, 1H, J=13.8 Hz), 5.13–5.20 (m, 1H), 7.03 (td, 1H, J=1.3 and 7.4 Hz), 7.15–7.32 (m, 6H), 7.46 (dd, 1H, J=1.2 and 7.8 Hz). ^{13}C NMR ($CDCl_3$)δ 30.4 (CH_2), 39.1 (CH_2), 39.3 (CH_2), 59.1 (CH), 73.5 (CH), 77.8 (CH), 115.4 (CH), 124.2 (CH), 126.1 (CH), 127.4 (CH), 127.5 (CH), 129.8 (CH), 129.9 (CH), 131.0 (C), 131.8 (C), 136.0 (C), 146.7 (C), 215.2 (CO).

3.6.2. *(±)- and (+)-(3S,3aR,3bR,14aS)-2,3,3a,3b, 8,14a-Hexahydro-1H-dibenzo [c,f]cyclopenta[4,5]isoxazolo[2,3-a]azepine-3-ol (11).*

To a solution of enantiopure or racemic compound **10a** (0.23 mmol) in anhydrous THF (5 ml), vigorously stirred at room temperature, was added $LiAlH_4$ (0.35 mmol) or $NaBH_4$ (0.81 mmol). The reaction mixture was stirred for 5 min ($LiAlH_4$) or 4 h ($NaBH_4$) and then ethyl acetate (10 ml)

and water (2 ml) were added. The layers were separated and the aqueous phase was extracted with ethyl acetate (3 × 20 ml). The organic phase was dried over Na_2SO_4 and evaporated at reduced pressure. Compound **11** was isolated by column chromatography (hexane/ethyl acetate 5:1) with 98% or 91% yield. White solid, mp: 145–147°C. IR (KBr): 3419, 1600, 1486, and 1070 cm^{-1}. ^1H NMR ($CDCl_3$)δ 1.72–1.86 (m, 1H), 1.93–1.99 (m, 1H), 2.00–2.14 (m, 3H), 3.34 (dt, 1H, J=6.7 and 7.9 Hz), 3.85 (d, 1H, J=14.7 Hz), 4.45 (d, 1H, J=14.7 Hz), 4.42–4.53 (m, 1H), 4.66 (d, 1H, J=6.7 Hz), 4.76–4.81 (m, 1H), 6.98 (td, 1H, J=1.3 and 7.5 Hz), 7.14–7.25 (m, 5H); 7.41 (dd, 1H, J=1.2 and 7.9 Hz), 7.44–7.48 (m, 1H). ^{13}C NMR ($CDCl_3$)δ 27.1 (CH_2), 33.7 (CH_2), 40.2 (CH_2), 58.6 (CH), 68.2 (CH), 76.6 (CH), 82.4 (CH), 116.5 (CH), 123.7 (CH), 126.6 (CH), 127.0 (CH), 127.5 (CH), 128.1 (CH), 129.1 (CH), 129.3 (CH), 130.3 (C), 136.9 (C), 137.1 (C), 148.1 (C). Enantiopure compound: $[\alpha]_D^{20}$: +116.7 (c=0.3, acetone).

3.6.3. *(**3S,3aS,3bR,14aS**)-3-(4-Phenylpiperazin-1-yl)-**2,3,3a,3b,8,14a**-hexahydro-1H-dibenzo[c,f] cyclopenta[4,5]isoxazolo[2,3-a]azepine[(±)-**12**].*

A mixture of **(±)-10a** (100 mg, 0.34 mmol), 4-phenylpiperazine (55 mg, 0.34 mmol), acetic acid (20 mg, 0.34 mmol) and $NaBH(OAc)_3$ (120 mg, 0.56 mmol) in 1,2-dichloroetane (5 ml) was stirred under argon at room temperature for 15 h. Then the reaction mixture was washed with a saturated aqueous solution of $NaHCO_3$. The layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 20 ml). The organic phase was dried over $MgSO_4$ and evaporated at reduced pressure. The residue analyzed by ^1H NMR was a mixture of the starting material (±)-**10a**, alcohol (±)-**11**, and amine (±)-**12**. Column chromatography (hexane/ethyl acetate 2:1) afforded (±)-**12** (20% or 36% based on the recovered starting material), **10a** (20 mg, 0.07 mmol), and (±)-**11** (15 mg, 0.05 mmol, 9%).

Compound [(±)-12]: White amorphous solid. ^1H NMR ($CDCl_3$)δ 1.66–2.15 (m, 4H), 2.46–2.65 (m, 4H), 2.70–2.80 (m, 1H), 2.87–3.04 (m, 4H), 3.72 (d, 1H, J=15.2 Hz), 3.71–3.79 (m, 1H), 4.65 (d, 1H, J=15.2 Hz), 4.76–4.83 (m, 1H), 5.58 (d, 1H, J=5.3 Hz), 6.78–6.88 (m, 4H), 7.04–7.28 (m, 8H), 7.54 (broad d, 1H, J=6.9 Hz). ^{13}C NMR ($CDCl_3$) δ 28.0 (CH_2), 30.5 (CH_2), 40.3 (CH_2), 48.9 (CH_2), 52.1 (CH), 52.6 (CH_2), 62.7 (CH), 68.9 (CH, C_{14b}), 81.8 (CH, $C_{\mathbf{3a}}$), 115.7 (CH), 119.5 (CH), 122.6 (CH), 122.8 (CH), 126.4 (CH), 126.8 (C), 126.9 (CH), 127.4 (CH), 127.9 (CH), 128.2 (CH), 129.0 (CH), 129.7 (CH), 134.7 (C), 141.1 (C), 146.5 (C), 151.2 (C).

3.6.4. *2-(6,11-Dihydro-5H-dibenzo[b,e]azepin-6-yl)cyclopent-2-en-1-one [(±)-**13**].*

A solution of **(±)-10a** (0.23 mmol) and Pd(C) 10% (5 mg) in ethanol (5 ml) was stirred under positive pressure of hydrogen at room temperature. After 20 h, the suspension was filtered through celite, the solid residue was washed with ethyl acetate, and the solvent was removed in vacuo. The residue was purified by column chromatography (hexane/ethyl acetate 3:2) to afford **13** in 57% yield as a yellow solid, mp: 136–138°C. IR (KBr): 1696 (C=O), 1626, 1603, 1240 cm^{-1}.^1H NMR ($CDCl_3$)δ: 2.37–2.57 (m, 4H), 3.97 (d, 1H, J=15.0 Hz), 4.29 (d, 1H, J=15.0 Hz), 4.47 (broad s, 1H), 5.52 (s, 1H), 6.61 (d, 1H, J=7.7 Hz), 6.79 (td, 1H, J=1.1 and 7.3 Hz), 6.94–7.04 (m, 3H), 7.09–7.27 (m, 4H). ^{13}C NRM ($CDCl_3$)δ: 26.4 (CH_2, C_4); 35.0 (CH_2, C_5); 40.0 (CH_2, $C_{11'}$), 55.3 (CH, $C_{6'}$), 119.9 (CH), 120.7 (CH), 126.4 (CH), 127.2 (CH), 127.5 (CH), 128.7 (CH), 129.0 (C), 129.2 (CH), 129.3 (CH), 136.5 (C), 138.1 (C), 145.3 (C), 148.2 (C), 160.2 (CH), 208.6 (CO).

3.6.5. *(±)-(1S,3S)-2-((R)-6,11-Dihydro-5H-dibenzo[b,e]azepin-6-yl)cyclopentane-1,3-diol (**14**).*

A solution of **(±)-11** (0.23 mmol) and Pd(C) 10% (5 mg) in ethanol (5 ml) was stirred under positive pressure of hydrogen at room temperature. After 1 h, the suspension was filtered through celite, the solid residue was washed with ethyl acetate, and the solvent was removed in vacuo. Yield 78%. ^{1}H NMR ($CDCl_3$)δ 1.87–2.08 (m, 4H), 2.20–2.40 (m, 1H), 3.82 (d, 1H, J=14.4 Hz), 4.05–4.15 (m, 1H), 4.41 (d, 1H, J=14.4 Hz), 4.54–4.68 (m, 1H), 5.09 (d, 1H, J=7.2 Hz), 6.70–6.80 (m, 2H), 6.90–7.25 (m, 6H) ^{13}C NMR ($CDCl_3$)δ 32.8 (CH_2), 33.9 (CH_2), 40.0 (CH_2), 55.5 (CH), 56.5 (CH), 74.0 (CH), 74.6 (CH), 119.4 (CH), 120.3 (CH), 126.8 (CH), 127.4 (CH), 127.6 (CH), 128.0 (C), 128.4 (CH), 128.9 (CH), 129.4 (CH), 137.3 (C), 139.0 (C), 143.9 (C).

3.7. *Reaction of 1 with benzonitrile oxide (5)*

To a stirred mixture of sodium hydroxide solution 10% (4.5 ml) and ether (4.5 ml), benzaldehyde chloroxime (7.5 mmol) was portionwise added during 10 min at 0°C. The ethereal layer was separated, quickly dried over $MgSO_4$, and added to a solution of the sulfinylcyclopentenone (1.4 mmol) in ether (10 ml). After stirring at room temperature for 30 min, the solvent was removed under reduced pressure and the residue analyzed by ^{1}H NMR was a 95:5 mixture of **15**:**16**. The major regioisomer **15** was isolated pure in a 66% yield by column chromatography (hexane/ethyl acetate 4:1).

3.7.1. *3-Phenyl-4,5-dihydro-6H-cyclopenta[d]isoxazol-6-one (**15**).*

Recrystallized from ethyl acetate–hexane, white solid, mp: 162–163°C. IR (KBr) 1715 (C=O), 1607, 1593 cm^{-1}. ^{1}H NMR ($CDCl_3$)δ 3.08–3.13 (m, 2H), 3.21–3.26 (m, 2H,), 7.46–7.57 (m, 3H), 7.78–7.88 (m, 2H). ^{13}C NMR ($CDCl_3$)δ 18.3 (CH_2), 43.3 (CH_2), 127.0 (CH), 127.7 (C), 129.3 (CH), 130.8 (CH), 146.0 (C), 159.0 (C), 171.5 (C), 186.5 (C=O). Anal. Calcd. for $C_{12}H_9NO_2$: C, 72.35; H, 4.55; N, 7.0. Found: C, 72.14; H, 4.55; N, 6.80.

3.7.2. *3-Phenyl-5,6-dihydro-4H-cyclopenta[d]isoxazol-4-one (**16**).*

It was not isolated as a pure compound. ^{1}H NMR ($CDCl_3$) δ 3.11–3.17 (m, 2H), 3.27–3.33 (m, 2H), 7.46–7.57 (m, 3H), 8.18–8.25 (m, 2H).

3.8. *Reaction of ethyl 2,3-butadienoate with sulfinylcyclopentenone 1 catalyzed by triphenylphosphine*

To a stirred solution 0.2 M of sulfinylcyclopentenone **1** (84 mg, 0.38 mmol), in benzene, under positive pressure of argon, commercial ethyl 2,3-butadienoate (64 mg, 0.29 mmol) was added at room temperature, and finally (32 mg, 0.12 mmol) of triphenylphosphine (solution 0.6 M) in benzene. The reaction was monitored by TLC. The solvent was removed *in vacuo* and the crude reaction, analyzed by ^{1}H NMR, was a complex mixture, which afforded compounds **17** and **18** by column chromatography.

3.8.1. *4-Hydroxycyclopent-2-enone (**17**) (23).*

It was obtained in 40% yield. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.25 (dd, 1H, J=2.3 and 18.4 Hz), 2.70 (dd, 1H, J=6.0 and 18.4 Hz), 4.08 (d, 2H, J=5.3 Hz), 4.99 (broad s, 1H), 6.14 (dd, 1H, J=1.3 and 5.7 Hz).

3.8.2. *7b-(p-Tolylsulfinyl)hexahydrodicyclopenta[b,d]furan-1,6(2H,7bH)-dione (**18**).*

It was isolated by column chromatography (dichloromethane/diethyl ether 6:1) as yellow oil in 9% yield. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.68–1.82 (m, 1H), 1.85–1.98 (m, 1H), 1.98–2.11 (m, 1H), 2.43 (s, 3H), 2.26–2.63 (m, 4H), 3.02 (dd, 1H, J=9.1 and 18.8 Hz), 3.17 (td, 1H, J=4.5 and 9.0 Hz), 4.52 (t, 1H, J=4.4 Hz), 5.29 (d, 1H, J=5.6 Hz), 7.33 and 7.45 (system AA′BB′, 4H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.6 (CH_3), 27.9 (CH_2), 37.6 (CH_2), 38.3 (CH_2), 43.6 (CH_2), 47.3 (CH), 80.9 (CH), 81.1 (CH), 82.6 (C), 125.3 (CH), 130.0 (CH), 143.2 (C), 153.8 (C), 213.2 and 214.0 (C=O). EM: 319.0 [M + H] (30%), 179 [M-SOTol] (100%).

3.9. *(±)-(3aR,6aR)-5-Tosyl-3,3a,6,6a-tetrahydropentalen-1(2H)-one (20)*

To a stirred 0.1 M solution in benzene of cyclopent-2-en-1-one (**2**) (85 mg, 1.03 mmol) at room temperature, *p*-tolyl-1-allenyl sulfone (100 mg, 0.52 mmol), 18-crown-6 ether (55 mg, 0.21 mmol) and anhydrous *p*-TolSO_2Na (37 mg, 0.21 mmol) were added. The reaction was monitored by TLC, the solvent was removed under vacuum, and the crude reaction was analyzed by ^{1}H NMR and purified by flash column chromatography (hexane/ethyl acetate 2:1) to afford **20** as colorless oil in 24% yield. ^{1}H NMR δ 2.12–2.00 (m, 2H), 2.13–2.27 (m, 1H), 2.28–2.38 (m, 1H), 2.44 (s, 3H), 2.88–2.63 (m, 3H), 3.60–3.74 (m, 1H), 6.61–6.65 (m, 1H), 7.33 and 7.73 (AA′BB′ system, 4H). ^{13}C NMR: DEPT 135 δ 21.7 (CH_3), 24.9 (CH_2), 35.1 (CH_2), 36.5 (CH_2), 47.8 (CH), 49.4 (CH), 128.0 (CH), 130.0 (CH), 143.7 (CH).

3.10. *(±)-(3aR,6aR)-5,6a-Ditosyl-3,3a,6,6a-tetrahydropentalen-1(2H)-one (21)*

It was obtained following the above procedure starting from 2-*p*-tolylsulfonylcyclopent-2-en-1-one (24 mg, 0.10 mmol), *p*-tolyl 1-allenyl sulfone (29 mg, 0.15 mmol), 18-crown-6 ether (18 mg, 0.07 mmol) and anhydrous *p*-TolSO_2Na (13 mg, 0.07 mmol). It was isolated by flash column chromatography (hexane/ethyl acetate 2:1) as colorless oil in 63% yield. ^{1}H NMR δ 1.95–2.06 (m, 1H), 2.15–2.30 (m, 1H), 2.44 (s, 3H), 2.47 (s, 3H), 2.62–2.76 (m, 2H), 3.06 (dt, 1H, *J*=2.2 and 16.4 Hz), 4.36 (dt, 1H, *J*=2.4 and 8.6 Hz), 6.54 (td, 1H, *J*=1.4 and 2.3 Hz), 7.30–7.37 (m, 4H), 7.56–7.61 (m, 2H), 7.65–7.71 (m, 2H). ^{13}C NMR δ 21.7, 21.8, 24.0, 37.0, 37.5, 50.5, 79.2, 127.9, 129.8, 130.0, 130.1, 132.6, 135.4, 141.8, 142.9, 145.2, 146.1, 209.7.

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Notes

1. The cyclopent-2-en-1-one (**2**) has been less studied as dipolarophile than furan-2(5*H*)-one. For cycloadditions to cyclopentenone **2**, see (*15a, b*) for nitrones, (*15c*) for nitrile oxides. For selected examples of azomethine ylides, see (*15d–f*) and references cited therein. For diazomethane, see (*12*).

2. Lee et al. (*15a*) report the results obtained in reaction of cyclopent-2-en-1-one (**2**) with a five-membered cyclic nitrone. However, to our knowledge, reactions of **2** with nitrone **3**, or with any seven-membered cyclic nitrones, such as **4**, have never been reported.
3. Although the desulfinylated compounds **8** could not be isolated pure, the ^{1}H NMR data indicated in Scheme 3 could be measured.
4. The *endo* or *exo* terms indicate, respectively, the *cis* or *trans* arrangement adopted by cyclopentanone and pyrrolidine (for adducts **7**) or azepine (for adducts **9** and **10**) moieties at the isoxazolidine ring formed in the reactions from nitrones. They are related to the *endo* and *exo* dipole addition modes, using the carbonyl group at cyclopentenone ring as a reference.
5. The higher δ of H-3b and the smaller $\Delta\delta$ (δH8–δH8′) observed for adduct **9b** (*endo*), when compared with those corresponding to adduct **9a** (*exo*), support the assigned stereochemistry.

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