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Asymmetric 1,3-dipolar cycloadditions of diazoalkanes to (5*S*,S_S)-5-[(*1R*)-menthyloxy]-4-phenylsulfinyl (and phenylsulfonyl)furan-2(5*H*)-ones†

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Abstract—The behavior of the title compounds in their reactions with diazomethane and diazoethane is reported. The reactivity of the 5-alkoxyfuran-2(5*H*)-ones as dipolarophiles is dramatically enhanced by the presence of sulfur functionalities at C-4. The regioselectivity of the cycloadditions of diazomethane is opposite to that observed with diazoethane, due to control by the carbonyl group in the first case and by the sulfur function in the second case, with the sulfonyl group exhibiting a higher regio-orientating ability than the sulfinyl one. The π-facial selectivity is moderate, being controlled mainly by steric factors in the reactions involving the formation of N_{dipole}–$C(4)_{furanone}$ bonds, whereas the predominant role of electronic factors, modulated by the polarity of the solvent, leads to high stereoselectivities in processes involving the formation of N_{dipole}–$C(3)_{furanone}$ bonds. Finally, the *endo*/*exo* ratios from reactions with diazoethane can be rationalized on steric grounds. © 2002 Elsevier Science Ltd. All rights reserved.

1. Introduction

α,β-Unsaturated sulfoxides have been widely used in asymmetric synthesis due to the ability of the sulfinyl group to differentiate the diastereotopic faces of the double bond.[1] Among the processes most studied, the Diels–Alder reactions with sulfinyl dienes[2,3] and activated vinyl sulfoxides,[2] deserve special attention due to the high levels of stereoselectivity achieved in many cases. In contrast, the number of papers concerning the use of homochiral vinyl sulfoxides as dipolarophiles is lower,[2,4] despite the fact that in some of these reactions the influence of the sulfinyl group seems to be even more significant than that observed in Diels–Alder reactions. This is the case with (*Z*)-*p*-tolylsulfinylacrylonitriles, which exhibit the best features as chiral dienophiles among the monoactivated vinyl sulfoxides hitherto reported,[5] but have shown even more outstanding behavior as dipolarophiles.[6] A clearer example can be found in (5*R*,S_S)- and (5*S*,S_S)-5-ethoxy-3-(*p*-tolylsulfinyl)furan-2(5*H*)-ones, **1a** and **1b**, which have moderately interesting features as chiral dienophiles,[7] but have interesting chiral dipolarophile behaviour.[8,9] The results shown in Scheme 1 for compound **1a** reveal moderate stereoselectivity and reactivity in reactions with cyclopentadiene, but complete control of the stereoselectivity (*endo–exo* and π-facial) with diazoalkanes under milder conditions.

We have recently reported the synthesis and reactions of (5*S*,S_S)-5-[(1*R*)-menthyloxy]-4-(phenylsulfinyl)furan-2(5*H*)-one **2**[10] (differing from **1a** in the alkoxy group at C-5 and in the position of the sulfinyl group at the furanone ring) with cyclopentadiene. The stereochemical evolution of the substrates **1a** and **2** was completely different (see Scheme 1). Compound **1a** afforded the adduct with *endo*,*anti* stereochemistry as the major product, whereas **2** mainly evolved into the *exo*,*syn* isomer despite the fact that the configuration at C-5 is identical for both dienophiles. Taking into account the very similar results obtained in the reactions of cyclopentadiene with the 5-methoxy- and (5*S*)-[(1*R*)-

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† Dedicated to the memory of Professor Jesús H. Rodríguez Ramos.

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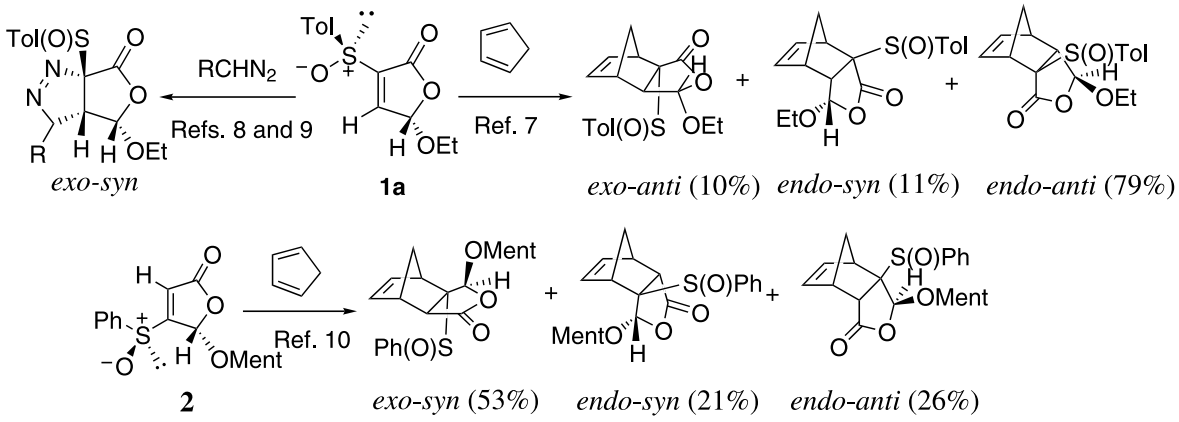


Scheme 1.

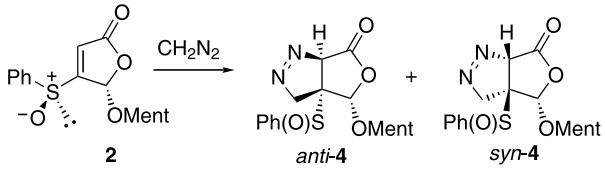
menthyloxy]furan-2(5*H*)-ones (93:7 and 92:8 of *endo*,*anti*:*exo*,*anti*, respectively),[10] the differing results obtained from **1a** and **2** could be due to the different position of the sulfinyl group in the furanone ring.

These results prompted us to study the addition of diazoalkanes to sulfinylfuranone **2**, to check the influence of the relative position of the sulfinyl group at the furanone ring on the stereochemical course of the 1,3-dipolar cycloaddition reaction. The study was performed with diazomethane and diazoethane to attain information on the π-facial (*syn* and *anti*) and *endo*–*exo* selectivity. The results obtained from this study are potentially interesting from a synthetic point of view, since complete control of the stereochemistry of the adducts could be achieved simply by choosing the position of the sulfur function at the furanone skeleton. We have also extended this study to sulfonylfuranone **3**, obtained by oxidation of **2**, in order to corroborate the isolated effect of the configuration at C-5 on the stereoselectivity.

2. Results

(5*S*,S_S)-5-[(1*R*)-Menthyloxy]-4-(phenylsulfinyl)furan-2(5*H*)-one **2** was prepared following the previously reported procedure.[10] Its reaction with an excess of diazomethane, as an ethereal solution, afforded a mixture of the pyrazolines *anti*-**4** and *syn*-**4** resulting from the approach of the dipole to both diastereotopic faces of the dipolarophile.[11] As expected, their relative ratio, indicative of the facial selectivity of the reactions, increased slightly as the temperature decreased (Table 1), rising to 70% at −50°C. The facial selectivity was even higher at −78°C (entry 6) but complete conversion required reaction times which were too long to be practicable. The reactions proceeded quantitatively (except under the conditions of entry 6) and were completely regioselective, yielding only the adduct resulting from formation of the N_{dipole}–$C(3)_{furanone}$ bond, which indicates that the influence of the carbonyl group in the control of the regioselectivity is clearly

Table 1. Cycloaddition of diazomethane to sulfinylfuranone **2**



Entry	*T* (°C)	Catalyst	Time	Products ratio[a] *anti*-4:*syn*-4[b]	De (%)
1	0	–	5 min	65:35	30
2	−20	–	15 min	68:32	36
3	−20[c]	–	15 min	100:0[d]	100
4	−33	–	30 min	74:26	48
5	−50	–	5 h	85 (70):15 (10)	70
6	−78	–	8 h	95:5[e]	92
7	0	$ZnBr_2$	1 min	100:0[d]	100
8	−78 to −33	$ZnBr_2$	1 h	100 (72):0	100
9	−78	$ZnBr_2$	7 h	100 (79):0	100

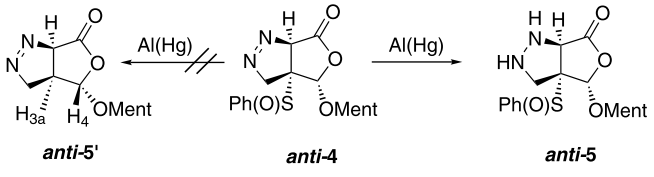
[a] Determined by ^1H NMR of the crude reaction mixture.
[b] Isolated yield (%).
[c] CH_3CN as solvent.
[d] Other unidentified compounds could be detected.
[e] 80% of the starting compound **2** was recovered.

higher than that of the sulfinyl function. The facial selectivity increased sharply in acetonitrile (entry 3) or in the presence of catalytic $ZnBr_2$. Under these conditions only one adduct (*anti*-**4**) was obtained, which proves a complete control of the π-facial selectivity. The preferential formation of the *anti* adduct starting from **2** contrasts with the results obtained in reactions from **1a** with diazomethane, which afforded the *syn* adduct as the sole product (Scheme 1).

The major adduct, *anti*-4, was isolated as a white solid by filtration after addition of cool ether to the crude reaction mixture and the minor product, *syn*-**4**, was isolated from the filtrate resulting from successive removal of the *anti*-isomer. Despite the fact that adducts *anti*-**4** and *syn*-**4** are stable at room temperature for several months, their partial transformation into the 4-formylpyrazol-3-carboxylic acid could be observed during attempts to isolate them by flash column chromatography.

The regiochemistry of the adducts was established from the small value observed for $J_{3,6a}$ (2.1–1 Hz) and the δ value for C-3a (70.8 and 70.4 ppm). All attempts to obtain suitable crystals for X-ray analysis of the adducts **4**, which would allow the unequivocal assignment of the configurations at C-3a and C-6a, were unsuccessful. Moreover, efforts to achieve C–S hydrogenolysis by reaction of the *anti*-**4** with aluminium amalgam, afforded pyrazolidine *anti*-**5** (Scheme 2) instead of the expected desulfinylated compound *anti*-**5′**, whose relative configuration at C-3a could have been assigned from the $J_{3a,4}$ value, thereby allowing the relationship (*cis* or *trans*) between the menthyloxy and sulfinyl groups present in compound *anti*-**4** to be determined.

The configurations at C-4 and sulfur for both adducts were assigned as $4S,S_S$ on the basis of the known configurations of the starting dipolarophile, which presumably did not change during the reaction. The *anti* and *syn* character of the obtained adducts is based on intensive NMR analysis. The most relevant data are the relative δ values of the acetalic protons (it is higher for the *syn* adduct due to deshielding effect of the sulfinyl group in a *cis* arrangement) and the $\Delta\delta$ values for the H-3 protons (1.28 and 0.33 ppm for *anti*-**4** and *syn*-**4**, respectively) influenced by the phenyl group and the sulfinyl oxygen, as indicated in Fig. 1. The increase in the π-facial selectivity observed in reactions of **2** with diazomethane under $ZnBr_2$ catalysis (entries 7–9) provides additional support to the configurational assignment of compound *anti*-**4** (vide infra).



Scheme 2.

The times required for reactions of diazomethane with sulfoxide **2** to reach completion (5 min at 0°C, entry 1, Table 1) are shorter than those with 5-alkoxy-furan-2(5*H*)-ones lacking sulfur functions (ca. 12 h at 0°C[9,12]). It reveals that the presence of the sulfinyl group at C-4 strongly increases the dipolarophilic reactivity of the furanone, although this influence is slightly lower than that exerted by the sulfinyl group at C-3 (substrate **1a** is more reactive than **2** at low temperatures[9]). On the other hand, a comparison of the results shown in Scheme 1 and Table 1 indicates that the influence of the sulfur function on the π-facial selectivity is markedly dependent on the position of the sulfinyl group. Thus, the stereoselectivity for $(5S,S_S)$-5-ethoxy-(3-*p*-tolylsulfinyl)furan-2(5*H*)-one **1a** is complete and the *syn* adduct is exclusively formed,[8,9] whereas for $(5S,S_S)$-5-menthyloxy-3-(phenylsulfinyl)furan-2(5*H*)-one **2** the *anti* adduct is the major one, the stereoselectivity being complete in the presence of $ZnBr_2$ (entries 7–9, Table 1).

The addition of diazomethane to sulfone **3** in ether proceeded readily, affording two pairs of regioisomeric adducts (Scheme 3), each resulting from the approach of the dipole to both diastereotopic faces at the dipolarophile. Changing the reaction temperature between 0 and −78°C barely altered the regioisomeric ratio (**6**/**7** ∼ 60/40) or the diastereofacial selectivity (*syn*-**6**/*anti*-**6** ∼ 8/1 and *syn*-**7**/*anti*-**7** ∼ 4/5). The use of acetonitrile as the solvent led to a decrease in the amount of *syn*-**6**, as a consequence of an inversion in the regioselectivity (the adducts **7** were now obtained as the major products).

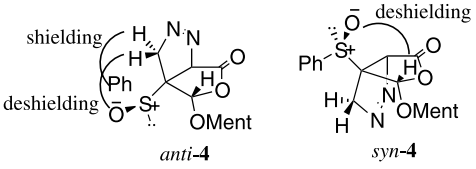
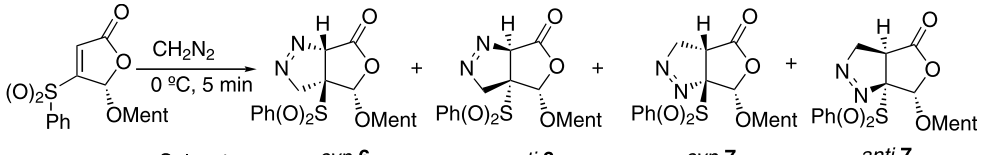


Figure 1. Shielding effects of the phenylsulfonyl group for adducts **4**.



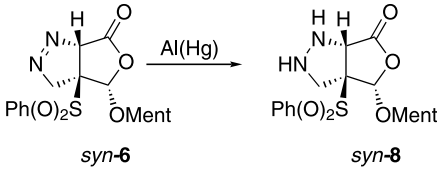
3	Solvent	*syn*-**6**	*anti*-**6**	*syn*-**7**	*anti*-**7**
	Ether	52	6	19	23
	CH_3CN	26	6	32	36

Scheme 3.

All attempts to isolate the obtained adducts by flash column chromatography failed. Diastereomerically pure compound *syn*-**6** was isolated as a white solid by precipitation from a toluene solution of the crude product by addition of hexane. The ^{1}H NMR signals corresponding to the minor *anti*-**6** adduct were identified from the crude reaction spectra, which were confirmed by oxidation of *anti*-**4** with *m*-CPBA. Compounds **7** were characterized from the ^{1}H NMR spectra of the crude product after removal of a considerable amount of *syn*-**6** by filtration.

As the crystals obtained for compound *syn*-**6**, as well as those of pyrazolidine *syn*-**8** (derived from *syn*-**6** by reaction with Al(Hg), Scheme 4), were not suitable for X-ray analysis, the stereochemistry of the adducts **6** and **7** was assigned from their NMR data. Additionally, compounds **6** were also chemically correlated with the sulfinyl derivatives **4**.

Comparison of the results obtained from the reactions of diazomethane with sulfoxide **2** (Table 1) and sulfone



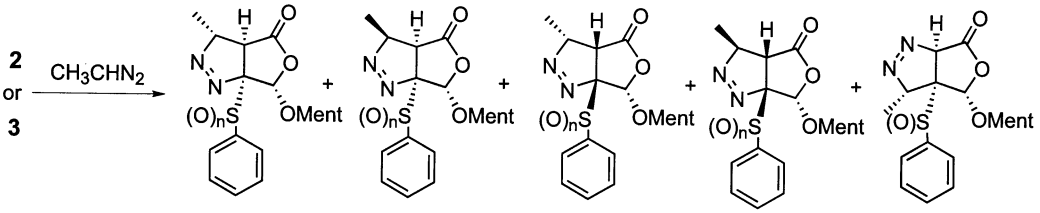
syn-**6** *syn*-**8**

Scheme 4.

3 (Scheme 3) revealed the expected higher reactivity of the latter and the lower regioselectivity of its reactions, which is easily explained by assuming a higher regioorientating ability of the sulfone group, thus competing with that of the ester group at compound **3**. With respect to the π-facial selectivity, we observed very different results depending on the regiochemistry of the cycloaddition. For reactions involving the formation of the N_{dipole}–$C(3)_{furanone}$ bond, the *syn* adduct was obtained as the major product from sulfone **3**, whereas the *anti*-adduct was predominant in reactions from sulfoxide **2**. Reactions evolving with the opposite regiochemistry (only observed for sulfone **3**) showed a slight predominance of the *anti*-adduct. From these results and those reported for the reactions of diazomethane with 5-alkoxyfuran-2(5*H*)-ones bearing no sulfur functionality, we can conclude that the introduction of a sulfinyl group at C-4 of the furanone ring (sulfoxide **2**) favours the formation of the *anti*-adducts, particularly in acetonitrile where they are exclusively obtained (Table 1, entry 3). In contrast, the presence of the sulfonyl group at C-4 markedly favoured the formation of the *syn* adducts in ether (Scheme 3).

We have also studied the reactions of furanones **2** and **3** with diazoethane under different conditions (Table 2). The reactions proceeded quantitatively in all cases, yielding $^1\Delta$-pyrazolines **9** and **11** (as mixtures of the four possible stereoisomers),[13] respectively, as the major

Table 2. Cycloaddition of diazoethane to sulfoxide **2** and sulfone **3**



anti,exo-**9**: n=1 *anti,exo*-**11**: n=2 | *anti,endo*-**9**: n=1 *anti,endo*-**11**: n=2 | *syn,endo*-**9**: n=1 *syn,endo*-**11**: n=2 | *syn,exo*-**9**: n=1 *syn,exo*-**11**: n=2 | **10**

Substrate	*T* (°C)	Solvent	Time (min)	Adducts ratio (%)[a]				
				anti,exo-**9**	*anti,endo*-**9**	*syn,endo*-**9**	*syn,exo*-**9**	*anti,exo*-**10**
2	−20	Ether	5	59	14	4	8	15
		CH_3CN	5	53	14	6	8	19
		Ether/$ZnBr_2$	5	62	16	4	8	10
	−33	Ether	15	58	14	4	8	16
		CH_3CN	15	54	11	7	8	20
		Ether/$ZnBr_2$	5	66	13	4	7	10
	−78	Ether	60	61	11	3	6	19
		Ether/$ZnBr_2$	15	65	9	3	6	17
				anti,exo-**11**	*anti,endo*-**11**	*syn,endo*-**11**	*syn,exo*-**11**	
3	−20	Ether	5	48	13	17	22	
		CH_3CN	5	56	14	14	16	
	−33	Ether	10	49	11	18	22	
		CH_3CN	10	58	14	13	15	
	−78	Ether	30	51	11	17	21	

[a] Determined by ^{1}H NMR of the crude reaction mixture.

or sole regioisomers. In the reaction of sulfoxide **2**, one stereoisomer exhibiting the opposite regiochemistry, adduct **10**, was also detected. The influence of the temperature, solvent and catalysts on the diastereomeric ratio of the pyrazolines obtained from **2** and **3**, as well as on the regioselectivity is minimal, which contrasts with the significant influence of these factors in the reactions with diazomethane (see Table 1 and Scheme 3).

Diastereomerically pure sulfoxide *anti*,*exo*-**9** was isolated in 54% yield by flash column chromatography from the reaction conducted in ether at −20°C without catalyst, but the other adducts had to be characterized from the ^{1}H NMR spectra of partially separated mixtures (see Section 3). This was also the case for the adducts obtained from sulfone **3**. The major adduct *anti*,*exo*-**11** was isolated in analytically pure form (34% yield) by precipitation with hexane from an *anti*,*exo*-**11**–*syn*,*exo*-**11** mixture or by *m*-CPBA oxidation of the corresponding sulfoxide *anti*,*exo*-**9** (96% yield). Moreover, the *m*-CPBA oxidation of mixtures of adducts **9** into sulfones **11** allowed their chemical correlation from their ^{1}H NMR spectra.

The regiochemistry of compounds **9**–**11** was established from the values of the $J_{3,3a}$ coupling constant, which is larger than 2.6 Hz (indicating the presence of vicinal protons) for compounds **9** and **11**, but nearly zero (no vicinal protons) for **10**. The chemical shift of C-6a (114.5–117.5 ppm) for compounds **9** and **11** supports such an assignment. The stereochemistry corresponding to the *endo* and *exo* approaches (*cis* and *trans* relationship between the methyl and ester groups at the pyrazoline ring) was also determined from the $J_{3,3a}$ values in compounds **9** and **11** (smaller than 4.4 Hz for the *exo* adducts and larger than 8.9 Hz for the *endo* adducts). Finally, the *syn* or *anti* character of the adducts **9** and **11** can be deduced from the relative δ values of their acetalic protons, which are higher for the *syn* adducts due to the deshielding effect of the sulfinyl group in a *cis* arrangement (see Fig. 1). The *S* configuration at C-6 of the adducts derives from the 5*S* configuration of the substrate. The unequivocal assignment of the adduct *anti*,*exo*-**11**—and therefore that of its corresponding sulfoxide *anti*,*exo*-**9**—was established by X-ray analysis (Fig. 2).[14]

The structure and configuration of compound **10** have been tentatively assigned as depicted in Table 2. The appearance in the ^{1}H NMR spectrum of three singlets, each corresponding to one proton, after irradiation at the methyl signal, suggests the existence of three protons with no visible coupling constant, which is in agreement with the postulated regiochemistry and suggests *exo* character (the $J_{3,6a}$ value is closer to zero for the proton at C-3 adopting a *trans* arrangement with respect to H-6a in compounds **4**, which exhibit the same regiochemistry as **10**).[15] The *anti* character of adduct **10** has been assigned (see Table 2) on the basis of mechanistic considerations (vide infra) and the chemical shift of the acetalic proton.

On comparison of the results depicted in Tables 1 and 2, and Scheme 3 it can be concluded that the change in the structure of the dipole causes a significant change in the regioselectivity. In the case of diazoethane, the regioselectivities of its reactions with sulfoxide **2** and

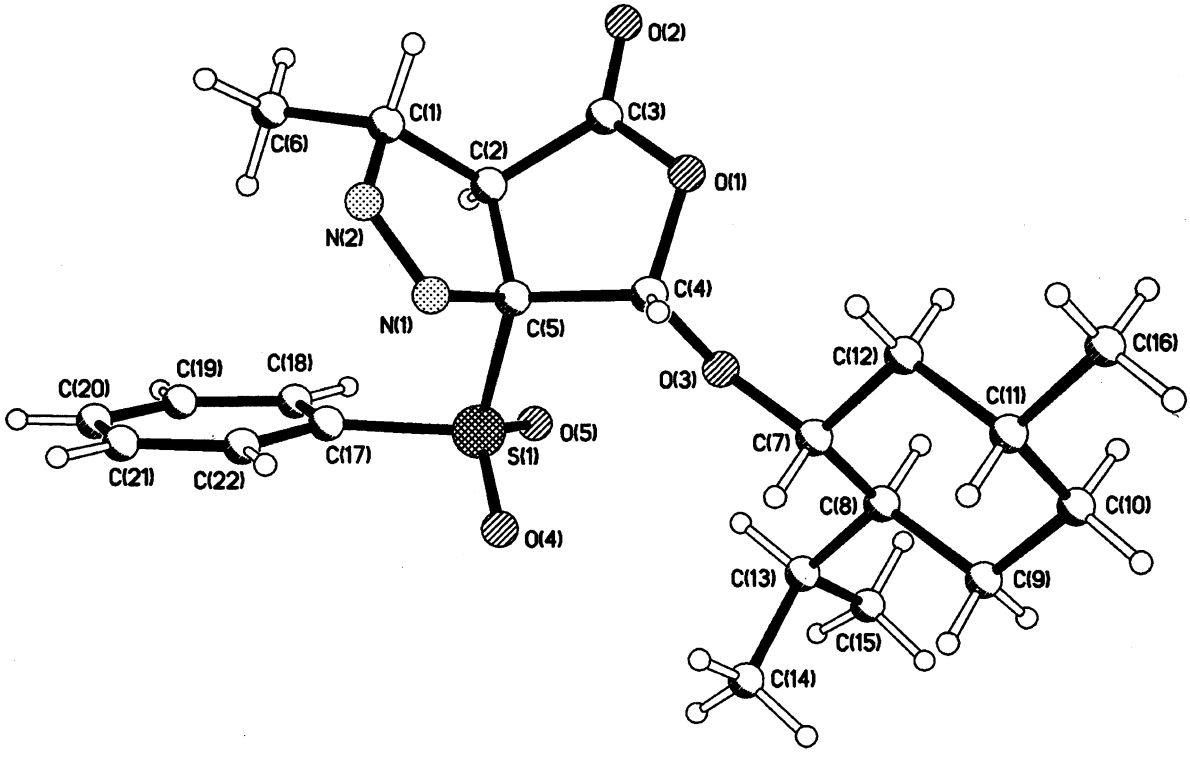


Figure 2. X-Ray structure for adduct *anti*,*exo*-**11**.

sulfone **3** range from high to complete, respectively, yielding as the major (or the only) adducts those exhibiting the same regiochemistry as the minor adduct formed in reaction of sulfone **3** with diazomethane. The greater size of the carbon chain of diazoethane and the fact that C-4 of compound **2** and **3** is more sterically hindered than C-3, explain the inversion in the regioselectivity observed for the two dipoles.

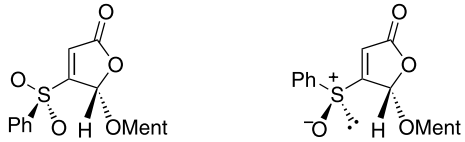
With respect to the facial selectivity, the major adducts obtained with diazoethane derive from attack of the dipole to the face opposite the one bearing the menthyloxy group in both sulfoxide **2** and sulfone **3**, the *anti*/*syn* stereoselectivity being lower in reactions from sulfone **3**. This is in contrast with the results obtained from diazomethane which gave the opposite π-facial selectivity for sulfoxide **2** (the *anti* approach is clearly favoured) and sulfone **3** (the *syn* adduct is the major one).

The π-facial selectivity of the reactions reported herein can be rationalised by assuming a significant role of both steric and electrostatic grounds and a clear dependence on the regiochemistry, which determines important differences between the interactions controlling the relative stability of the possible approaches. Recently, we have suggested a significant contribution of the electronic interactions (electrostatic or hydrogen bonding) between the alkoxy oxygen at C-5 of the furan-2(5*H*)-one and the alkyl group of the diazoalkane, in order to explain the high proportion for the *syn*-adducts obtained in the reactions of these dipoles with **1a**, as well as its decrease with increasing solvent polarity.[9] These interactions could also be responsible for the spatial arrangement of the sulfinyl oxygen. The presumably most populated conformations for substrates **2** and **3** taking into account steric and stereoelectronic factors are depicted in Fig. 3.[16]

For reactions involving the formation of the N_{dipole}–$C(3)_{furanone}$ bond (regiochemistry 1, Fig. 3) *syn*-approach of the dipole to conformation A of sulfone **3** will be favoured on electrostatic grounds, whereas the steric interactions would be similar for both faces (the steric hindrance of the Ph group must be equivalent to that produced by both oxygenated functions), thus a clear predominance of the *syn*-adduct results. This preference decreases slightly in acetonitrile, where polar interactions must be less important. By contrast, the *anti*-approaches will be favoured in reactions with B-**2** mainly due to the greater size of the menthyloxy group with respect to the sulfinyl oxygen (the electrostatic contributions must be now compensated). The fact that the stereoselectivity of the reactions with **2** was complete in acetonitrile could be a consequence of the greater role of steric interactions in more polar solvents, while the influence of the $ZnBr_2$ catalyst in increasing the stereoselectivity could also be related to the increase in the size of the oxygenated functions after associating with $ZnBr_2$. On the basis of these assumptions, the addition of diazoethane to sulfoxide **2** evolving with this regiochemistry must exhibit a higher *anti*-selectivity (which would become even higher in acetonitrile), because of the greater size of the dipole, increasing the significance of steric factors in the control of the π-facial selectivity. This is the reason why we have postulated the *anti* stereochemistry to the adduct **10**, the only isomer detected with this regiochemistry from the reactions of **2**.

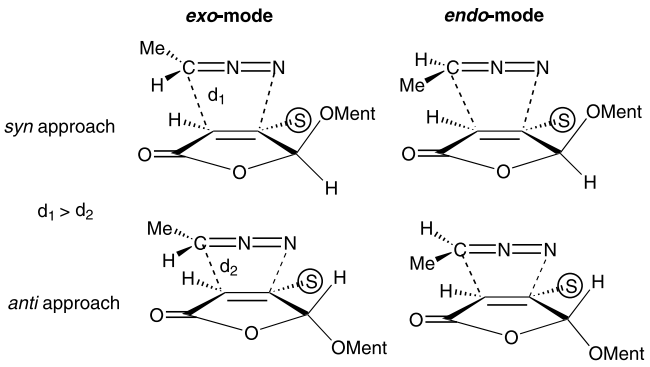
For reactions involving the formation of the N_{dipole}–$C(4)_{furanone}$ bond (regiochemistry 2 in Fig. 3) electrostatic interactions are barely significant (the distance between the carbon chain at the dipole and the oxygens of the dipolarophile is greater) and only steric factors need to be considered. They clearly differentiate diastereotopic faces for B-**2** (*O*-menthyl>*O*-sulfinyl) thus resulting in an *anti*/*syn* ratio ca. 84:16. This is not the case in the reactions on A-**3** (Ph ~ *O*-sulfinyl+*O*-menthyl) which exhibit a 60/40 *anti*/*syn* ratio as a result.

The last topic to be discussed in this paper concerns the *endo*/*exo* selectivity observed in reactions with diazoethane. It was similar for sulfoxide **2** and sulfone **3** (Table 2) and slightly higher for the *anti* approaches of both substrates, the *exo* adducts being the major ones. The most important factor controlling the *exo*-selectivity of these reactions must be related mainly to the steric interactions between the substituents at C-3 (CO and H for both dipolarophiles) and those of diazoethane (Me and H) during the approach of both reactants (Scheme 5). Therefore, the similar *endo*/*exo* ratio obtained for the sulfoxide and sulfone is not



	syn/anti	*syn/anti*
Regiochemistry 1 (Reactions with CH_2N_2)	52/6 (Ether) 26/6(CH_3CN)	35/65 (Ether) 0/100(CH_3CN, or $ZnBr_2$)
Regiochemistry 2 (Reactions with $MeCHN_2$)	~40/60 (Ether) ~30/70 (CH_3CN)	~14/86 (Ether) ~17/83 (CH_3CN)

Figure 3. Reactive conformations of the substrates **2** and **3** and *syn*/*anti* ratios obtained in their reactions with diazoalkanes according their regiochemistry (see text).



Scheme 5.

unexpected. The differences detected between the *anti* (~3.5:1) and *syn* (~2:1) approaches could be attributed to the different position of the corresponding transition states at the reaction coordinate, earlier for the *syn* approach due to steric reasons which determines that the incipient N_{dipole}–$C(4)_{furanone}$ bond must be longer than that of the *anti* approach ($d_1 > d_2$, Scheme 5), thus leading to a lower magnitude and, therefore, lower significance of the interactions at their respective TSs.

In conclusion, from the results obtained in this paper we can state that the reactivity of 5-alkoxy-2(5*H*)-furanones towards diazoalkanes is strongly enhanced by sulfinyl and sulfonyl groups at C-4. The regioselectivity of these reactions depends on both the regio-orientating ability of the substituents ($SO_2Ph \sim CO_2R > SOPh$), mainly controlling the regiochemistry of the reactions with diazomethane, and the steric interactions, which favor the regiochemistry involving the formation of the bond between nitrogen (the less hindered end of the dipole) and $C(4)_{furanone}$ (the bulkiest end of the dipolarophile), which predominate in reactions with diazoethane. The π-facial selectivity (*syn*/*anti* relationship) can be completely controlled in the reactions of the sulfoxide, which affords the regiochemistry involving the formation of the N_{dipole}–$C(3)_{furanone}$ bond, with the *anti* adducts formed as the only products of the reactions, mainly in polar solvents. By contrast, sulfone yielded mainly the *syn*-adducts in apolar solvents. Reactions involving the formation of the N_{dipole}–$C(4)_{furanone}$ bond exhibit a moderate *anti* selectivity (higher for sulfoxide). From a mechanistic point of view, the obtained results evidence that the position of the sulfur function plays a significant role on the stereochemical course of these 1,3-dipolar reactions, which can be advantageously applied for synthetic purposes.

3. Experimental

3.1. General methods

Melting points were determined in a Gallenkamp apparatus in open capillary tubes and are uncorrected. Microanalyses were performed with a Heraeus analyser. IR spectra were recorded on a Perkin–Elmer 681 grating spectrophotometer. ν values are given in cm^{-1}. NMR spectra were determined with a Bruker AC-200 spectrometer, in $CDCl_3$ solutions at 200 and 50.3 MHz for ^1H and ^{13}C NMR, respectively. Chemical shifts are reported in ppm (δ) downfield from Me_4Si. J values are given in H. Silica gel Merck 60 (230–400 mesh ASTM) and DC-Alufolien 60 F_{254} were used for flash column chromatography and analytical TLC, respectively. The optical rotations were measured at room temperature (20–23°C) using a Perkin–Elmer model 241 MC polarimeter (concentration in g/100 mL).

3.2. General procedures

3.2.1. Cycloaddition of diazoalkanes to sulfoxide 2 and sulfone 3. Method A: To a solution of furanone **2** or **3** (0.40 mmol) in diethyl ether or acetonitrile (20 mL) at the temperature indicated in Tables 1 and 2 and Scheme 3, was added an ethereal solution of diazomethane or diazoethane (1.5 mL, concentration 0.6 mmol/mL). The reaction was kept at the same temperature for the time indicated in Tables 1 and 2. The solvent was removed and the residue was analysed by ^1H NMR and purified as indicated in each case.

Method B: To a stirred solution of $ZnBr_2$ (94.6 mg, 0.42 mmol) in THF (0.4 mL) at room temperature was added a solution of sulfinylfuranone **2** (100 mg, 0.28 mmol) in diethyl ether (20 mL). The mixture was stirred for 1 h and then cooled to the temperature indicated in Tables 1 and 2. After addition of an ethereal solution of diazoalkane (1.5 mL, concentration 0.6 mmol/mL), the reaction mixture was stirred at room temperature for the time indicated in Tables 1 and 2. Water was added to the reaction mixture and the aqueous layer was extracted several times with dichloromethane. The combined organic extracts were dried over dry magnesium sulfate and the solvent removed in vacuo. The resulting residue was analysed by ^1H NMR.

3.3. Oxidation of sulfinyl adducts

To a stirred solution of pure sulfoxide (*anti*-**4**, *anti*,*exo*-**9**) or mixtures of stereoisomeric sulfinyl cycloadducts (**4**, **9**) in dichloromethane (0.1 M) was added an equal volume of a solution of *m*-CPBA in dichloromethane (0.22 M) at 0°C. The mixture was allowed to stand for 2.5 h, and then it was washed with saturated aqueous sodium bicarbonate until pH 7. The aqueous layer was extracted several times with dichloromethane. The combined organic layers were dried and the solvent evaporated to dryness. ^1H NMR analysis of crude reaction mixtures revealed the presence of the corresponding sulfones in the same ratio of the starting sulfoxides.

3.4. Reduction with aluminium amalgam

To a solution of *anti*-**4** or *syn*-**6** (0.05 mmol) in a 9:1 mixture of THF–H_2O (2.5 mL) was added freshly prepared aluminium amalgam (obtained from 32 mg of aluminium kitchen foil). The reaction mixture was stirred for 2 h at room temperature and then filtered.

The solid was washed with THF, and the solution was concentrated to dryness.

3.4.1. (3a*R*,4*S*,6a*S*)-4-{(1*R*,2*S*,5*R*)-[2-Isopropyl-5-methylcyclohexyl]oxy}-3a-[(S_S)-phenylsulfinyl)-3,3a,4,6a-tetrahydro-6*H*-furo[3,4-*c*]pyrazol-6-one, *anti*-4. Prepared by cycloaddition of diazomethane to **2**. It was isolated by filtration after addition of cool diethyl ether to the crude reaction mixture, mp 144–146°C (white solid). $[\alpha]_D=-149$ (*c* 1.0, chloroform). IR (KBr): 1780, 1550, 1460, 1445, 1145, 1040. δ_H 7.63–7.48 (m, 5H), 5.73 (d, 1H, *J* 19.8), 5.71 (d, 1H, *J* 1.7), 5.56 (s, 1H), 4.45 (dd, 1H, *J* 19.8 and 1.7), 3.68 (dt, 1H, *J* 10.6 and 4.4), 2.55–0.80 (m, 18H). δ_C 164.1, 138.5, 132.7, 129.5, 125.0, 105.0, 90.5, 84.4, 80.9, 70.8, 48.2, 42.3, 33.9, 31.6, 25.1, 22.6, 22.1, 21.1, 15.7. Anal. calcd for $C_{21}H_{28}N_2O_4S$: C, 62.35; H, 6.98; N, 6.92; S, 7.93. Found: C, 62.33; H, 6.66; N, 6.88; S, 7.92%.

3.4.2. (3a*S*,4*S*,6a*R*)-4-{(1*R*,2*S*,5*R*)-[2-Isopropyl-5-methylcyclohexyl]oxy}-3a-[(S_S)-phenylsulfinyl-3,3a,4,6a-tetrahydro-6*H*-furo[3,4-*c*]pyrazol-6-one, *syn*-4. Prepared by cycloaddition of diazomethane to **2**. It was isolated from the filtrate resulting from successive removals of the *anti*-**4** adduct, mp 108–110°C (white solid); $[\alpha]_D=+232.4$ (*c* 0.5, chloroform); IR (KBr): 1785, 1554, 1474, 1442, 1086, 1052. δ_H 7.60 (m, 5H), 5.88 (dd, 1H, *J* 2.1 and 1.0), 5.81 (s, 1H), 5.18 (dd, 1H, *J* 19.3 and 2.1), 4.85 (dd, 1H, *J* 19.3 and 1.0), 3.47 (dt, 1H, *J* 10.7 and 4.4), 2.20–0.70 (m, 18H). δ_C 164.9, 138.0, 133.4, 129.9, 125.0, 101.5, 92.5, 83.9, 78.4, 70.4, 47.8, 41.9, 33.8, 31.5, 25.7, 22.8, 21.9, 20.9, 16.0. Anal. calcd for $C_{21}H_{28}N_2O_4S$: C, 62.35; H, 6.98; N, 6.92; S, 7.93. Found: C, 62.44; H, 6.84; N, 7.08; S, 7.82.

3.4.3. (3a*R*,4*S*,6a*S*)-4-{(1*R*,2*S*,5*R*)-[2-Isopropyl-5-methylcyclohexyl]oxy}-3a-(phenylsulfonyl)-3,3a,4,6a-tetrahydro-6*H*-furo[3,4-*c*]pyrazol-6-one, *anti*-6. Prepared by oxidation of *anti*-**4** with *m*-CPBA. It was crystallized from dichloromethane–ethyl ether (yield 85%), mp 138–140°C (white solid); $[\alpha]_D=-132.0$ (*c* 1.0, chloroform). IR (Nujol): 1770, 1585, 1340, 1330, 1165. δ_H 7.87 (m, 2H), 7.72 (m, 1H), 7.58 (m, 2H), 6.17 (dd, 1H, *J* 1.9 and 0.8), 5.76 (dd, 1H, *J* 19.0 and 0.8), 5.39 (s, 1H), 4.77 (dd, 1H, *J* 19.0 and 1.9), 3.44 (dt, 1H, *J* 10.8 and 4.4), 2.20–0.70 (m, 18H). δ_C 163.4, 137.3, 134.9, 130.3, 129.0, 105.0, 94.9, 84.8, 83.4, 72.7, 48.3, 42.0, 33.8, 31.6, 24.6, 22.5, 21.9, 21.1, 15.7. Anal. calcd for $C_{21}H_{28}N_2O_5S$: C, 59.98; H, 6.71; N, 6.66; S, 7.62. Found: C, 59.96; H, 6.40; N, 6.60; S, 7.49%.

3.4.4. (3a*S*,4*S*,6a*R*)-4-{(1*R*,2*S*,5*R*)-[2-Isopropyl-5-methylcyclohexyl]oxy}-3a-(phenylsulfonyl)-3,3a,4,6a-tetrahydro-6*H*-furo[3,4-*c*]pyrazol-6-one, *syn*-6. Prepared by cycloaddition of diazomethane to **3**. It was isolated dissolving the crude reaction in toluene and further precipitation with hexane (yield 42%), mp 128–129°C (white solid); $[\alpha]_D=+212.5$ (*c* 1.0, chloroform). IR (KBr): 1784, 1580, 1561, 1447, 1310, 1288, 1160, 1140. δ_H 7.90 (m, 2H), 7.78 (m, 1H), 7.67 (m, 2H), 6.00 (dd, 1H, *J* 2.2 and 1.5), 5.86 (s, 1H), 5.45 (dd, 1H, *J* 18.8 and 2.2), 5.10 (dd, 1H, *J* 18.8 and 1.5), 3.39 (dt, 1H, *J* 10.8 and 4.4), 2.10–0.50 (m, 18H). δ_C 164.7, 135.6, 135.3, 130.2, 129.2, 101.3, 95.3, 83.7, 81.3, 73.4, 47.7, 41.9, 33.7, 31.4, 25.4, 22.6, 21.9, 20.9, 15.7. Anal. calcd for $C_{21}H_{28}N_2O_5S$: C, 59.98; H, 6.71; N, 6.66; S, 7.62. Found: C, 60.04; H, 6.44; N, 6.62; S, 7.60%.

3.4.5. (3a*R*,6*S*,6a*S*)- and (3a*S*,6*S*,6a*R*)-6-{(1*R*,2*S*,5*R*)-[2-Isopropyl-5-methylcyclohexyl]}-6a-(phenylsulfonyl)-3,3a,6,6a-tetrahydro-4*H*-furo[3,4-*c*]pyrazol-4-one, *syn*-7 and *anti*-7. Prepared by cycloaddition of diazomethane to **3**. Data deduced from the crude reaction mixture. δ_H *syn* 6.20 (s, 1H), 5.17 (dd, 1H, *J* 18.8 and 1.6), 4.45 (dd, 1H, *J* 18.8 and 8.6), 3.73 (dd, 1H, *J* 8.6 and 1.6). δ_H *anti* 5.94 (s, 1H), 5.02 (dd, 1H, *J* 19.6 and 4.8), 4.85 (dd, 1H, *J* 19.6 and 10.2), 3.64 (dd, 1H, *J* 10.2 and 4.8). The other signals were coincident with those of the other isomers.

3.4.6. (3*R*,3a*S*,6*S*,6a*R*)-6-{(1*R*,2*S*,5*R*)-[2-Isopropyl-5-methylcyclohexyl]oxy}-3-methyl-6a-[(S_S)-phenylsulfinyl)-3,3a,6,6a-tetrahydro-4*H*-furo[3,4-*c*]pyrazol-4-one, *anti*, *exo*-9. Prepared by cycloaddition of diazoethane to **2**. It was purified by flash chromatography (hexane–ethyl ether, 1:1) (yield 54%), mp 173–174°C (white solid). $[\alpha]_D=-115.2$ (*c* 0.25, chloroform). IR (KBr): 1777, 1580, 1443, 1342, 1318, 1191, 1127. δ_H 7.75 (m, 2H), 7.54 (m, 3H), 5.94 (s, 1H), 4.98 (dq, 1H, *J* 7.3 and 2.8), 3.76 (dt, 1H, *J* 10.5 and 4.4), 2.63 (m, 1H), 2.37 (d, 1H, *J* 2.8), 2.20–0.83 (m, 17 H), 1.10 (d, 3H, *J* 7.3). δ_C 172.4, 139.6, 132.7, 129.4, 127.0, 116.2, 103.9, 92.8, 84.7, 48.5, 44.5, 42.4, 33.9, 31.7, 25.2, 22.7, 22.1, 21.3, 17.4, 15.9. Anal. calcd for $C_{22}H_{30}N_2O_4S$: C, 63.13; H, 7.22; N, 6.69; S, 7.66. Found: C, 63.05; H, 6.98; N, 6.70; S, 7.79%.

3.4.7. (3*S*,3a*R*,6*S*,6a*S*)-6-{(1*R*,2*S*,5*R*)-[2-Isopropyl-5-methylcyclohexyl]oxy}-3-methyl-6a-[(S_S)-phenylsulfinyl)-3,3a,6,6a-tetrahydro-4*H*-furo[3,4-*c*]pyrazol-4-one, *syn*, *exo*-9. Prepared by cycloaddition of diazoethane to **2**. Data deduced from a 53:47 mixture of *syn*,*exo*-**9**/*anti*,*exo*-**9** adducts obtained by flash chromatography (hexane–ethyl ether, 1:1). δ_H 7.54 (m, 5H), 6.39 (s, 1H), 4.81 (qd, 1H, *J* 7.3 and 4.4), 3.65 (dt, 1H, *J* 10.9 and 4.4), 2.63 (d, 1H, *J* 4.4), 2.30 (m, 1H), 2.20–0.80 (m, 17H), 0.66 (d, 3H, *J* 7.3). δ_C 171.7, 136.8, 132.9, 129.2, 125.8, 116.8, 104.6, 89.9, 84.9, 47.8, 43.6, 41.9, 33.9, 31.6, 25.4, 23.0, 22.0, 20.9, 16.8, 16.1.

3.4.8. (3*S*,3a*S*,6*S*,6a*R*)-6-{(1*R*,2*S*,5*R*)-[2-Isopropyl-5-methylcyclohexyl]oxy}-3-methyl-6a-[(S_S)-phenylsulfinyl)-3,3a,6,6a-tetrahydro-4*H*-furo[3,4-*c*]pyrazol-4-one, *anti*, *endo*-9. Prepared by cycloaddition of diazoethane to **2**. Data deduced from a 14:86 mixture of *anti*,*endo*-**9**/*anti*,*exo*-**9** adducts obtained by flash chromatography (hexane–ethyl ether, 1:1). δ_H 6.17 (s, 1H), 3.84 (dt, 1H, *J* 4.4 and 10.6), 3.46 (m, 1H), 2.76 (d, 1H, *J* 8.8), 2.30–0.80 (m, 18H), 1.42 (d, 3H, *J* 7.6). δ_C 169.9, 139.0, 132.8, 129.3, 126.5, 114.7, 102.4, 89.2, 83.9, 48.5, 42.3, 41.8, 34.0, 31.6, 25.1, 22.6, 22.1, 21.3, 15.8, 14.2.

3.4.9. (3*R*,3a*R*,6*S*,6a*S*)-6-{(1*R*,2*S*,5*R*)-[2-Isopropyl-5-methylcyclohexyl]oxy}-3-methyl-6a-[(S_S)-phenylsulfinyl)-3,3a,6,6a-tetrahydro-4*H*-furo[3,4-*c*]pyrazol-4-one, *syn*, *endo*-9. Prepared by cycloaddition of diazoethane to **2**. Data deduced from a 32:37:31 mixture of *syn*,*endo*-**9**/

anti,*endo*-**9**/*anti*,*exo*-**9** obtained by flash chromatography (hexane–ethyl ether, 1:1). δ_H 6.33 (s, 1H), 3.72 (dc, 1H, *J* 9.7 and 7.7), 3.14 (d, 1H, *J* 9.7), 1.43 (d, 3H, *J* 7.4). The rest of the signals were coincident with those of the other isomers.

3.4.10. (3*S*,3a*R*,4*S*,6a*S*)-4-{(1*R*,2*S*,5*R*)-[2-Isopropyl-5-methylcyclohexyl]oxy}-3-methyl-3a-[(S_S)-phenylsulfinyl)-3,3a,4,6a-tetrahydro-6*H*-furo[3,4-c]pyrazol-6-one, 10. Prepared by cycloaddition of diazoethane to **2**. Data deduced from the crude reaction mixture. δ_H 5.56 (q, 1H, *J* 7.7), 5.55 (s, 1H), 54.53 (s, 1H), 1.60 (d, 3H, *J* 7.7). The rest of the signals were coincident with those of the other isomers.

3.4.11. (3*R*,3a*S*,6*S*,6a*R*)-6-{(1*R*,2*S*,5*R*)-[2-Isopropyl-5-methylcyclohexyl]oxy} - 3 - methyl - 6a - (phenylsulfonyl)-3,3a,6,6a-tetrahydro-4*H*-furo[3,4-*c*]pyrazol-4-one, *anti*, *exo*-11. Prepared by cycloaddition of diazoethane to **3**. It was purified by precipitation with hexane (yield 34%) from an ethereal solution of a mixture of *anti*,*exo*-**11** and *syn*,*exo*-**11**, obtained by flash chromatography (hexane–ethyl ether, 1:1), mp 153–154°C (white solid); $[\alpha]_D$ = +130.7 (*c* 0.5, chloroform). IR (KBr): 1781, 1584, 1551, 1447, 1347, 1174, 1086. δ_H 8.08 (m, 2H), 7,73 (m, 1H), 7.61 (m, 2H), 5.55 (s, 1H), 5.23 (qd, 1H, *J* 7.3 and 2.7), 3.51 (td, 1H, *J* 10.8 and 4.4), 3.37 (d, 1H, *J* 2.7), 1.85–0.60 (m, 18H), 1.58 (d, 3H, *J* 7.3). δ_C 172.0, 137.4, 134.8, 130.5, 128.9, 117.3, 101.7, 93.4, 81.0, 48.2, 45.5, 41.8, 33.8, 31.8, 24.7, 22.5, 22.0, 21.4, 17.9, 15.6. Anal. calcd for $C_{22}H_{30}N_2O_5S$: C, 60.81; H, 6.96; N, 6.45; S, 7.38. Found: C, 60.71; H, 7.31; N, 6.41; S, 7.31%.

3.4.12. (3*S*,3a*R*,6*S*,6a*S*)-6-{(1*R*,2*S*,5*R*)-[2-Isopropyl-5-methylcyclohexyl]oxy} - 3 - methyl - 6a - (phenylsulfonyl)-3,3a,6,6a-tetrahydro-4*H*-furo[3,4-*c*]pyrazol-4-one, *syn*, *exo*-11. Prepared by cycloaddition of diazoethane to **3**. Data deduced from a 65:35 mixture of *anti*,*endo*-**11**/*syn*,*exo*-**11** obtained by flash chromatography (hexane–ethyl ether, 1:1). δ_H 8.07 (m, 2H), 7.73 (m, 1H), 7.80 (m, 1H), 7.67 (m, 2H), 6.08 (s, 1H), 5.01 (dc, 1H, *J* 5.0 and 7.3), 3.27 (dt, 1H, *J* 10.7 and 4.4), 3.16 (d, 1H, *J* 5.0), 2.00–0.40 (m, 18H), 1.54 (d, 3H, *J* 7.3). δ_C 171.0, 135.6, 134.1, 129.6, 128.9, 116.1, 101.9, 90.8, 83.3, 47.5, 47.0, 41.8, 33.8, 31.4, 24.7, 22.7, 21.4, 20.9, 18.4, 15.7.

3.4.13. (3a*S*,3a*S*,6*S*,6a*R*)-6-{(1*R*,2*S*,5*R*)-[2-Isopropyl-5-methylcyclohexyl]oxy} - 3 - methyl - 6a - (phenylsulfonyl)-3,3a,6,6a-tetrahydro-4*H*-furo[3,4-*c*]pyrazol-4-one, *anti*, *endo*-11. Prepared by cycloaddition of diazoethane to **3**. Data deduced from a mixture of 85:15 *anti*,*endo*-**11**/*syn*,*exo*-**11** obtained by flash chromatography (hexane–ethyl ether, 1:1). δ_H 7.99 (m, 2H), 7.77–7.56 (m, 3H), 5.81 (s, 1H,), 4.70 (dq, 1H, *J* 8.6 and 7.6), 3.68 (d, 1H, *J* 8.6), 3.60 (td, 1H, *J* 10.7 and 4.4), 2.20–0.35 (m, 18H), 1.65 (d, 3H, *J* 7.6).

3.4.14. (3a*R*,3a*R*,6*S*,6a*S*)-6-{(1*R*,2*S*,5*R*)-[2-Isopropyl-5-methylcyclohexyl]oxy} - 3 - methyl - 6a - (phenylsulfonyl)-3,3a,6,6a-tetrahydro-4*H*-furo[3,4-*c*]pyrazol-4-one, *syn*, *endo*-11. Prepared by cycloaddition of diazoethane to **3**. Data deduced from a 57:32:11 mixture of *syn*,*endo*-**11**/*anti*,*endo*-**11**/*exo*,*anti*-**11** obtained by flash chromatography (hexane–ethyl ether, 1:1). δ_H 8.06 (m, 2H), 7.80 (m, 1H), 7.66 (m, 1H), 6.01 (s, 1H), 5.17 (dq, 1H, *J* 10.2 and 7.5), 3.65 (d, 1H, *J* 10.2); 3.29 (td, 1H, *J* 4.4 and 10.7), 2.20–0.35 (m, 18H) 1.50 (d, 3H, *J* 7.5).

3.4.15. (3a*R*,4*S*,6a*S*)-4-{(1*R*,2*S*,5*R*)-[2-Isopropyl-5-methylcyclohexyl]oxy}-3a-[(S_S)-(phenylsulfinyl)]-hexahydro-6*H*-furo[3,4-*c*]pyrazol-6-one, *anti*-5. Prepared by reaction of *anti*-**4** with aluminium amalgam (quantitative yield). Mp 137–138°C (white solid); $[\alpha]_D$ = +47.6 (*c* 0.25, chloroform). IR (KBr): 3313, 1795, 1584, 1084, 1053. δ_H 7.71 (m, 2H), 7.60 (m, 3H), 5.73 (s, 1H), 4.01 (s, 1H), 3.89 (d, 1H, *J* 13.9), 3.69 (dt, 1H, *J* 10.6 and 4.4), 3.11 (d, 1H, *J* 13.9), 2.49 (m, 1H), 2.23–0.83 (m, 17H). δ_C 173.1, 139.6, 132.6, 129.8, 125.4, 105.2, 83.9, 78.5, 65.1, 52.1, 48.4, 42.5, 34.0, 31.7, 25.1, 22.6, 22.1, 21.2, 15.7. Anal. calcd for $C_{21}H_{30}N_2O_4S$: C, 62.04; H, 7.44; N, 6.89; S, 7.89. Found: C, 61.79; H, 7.27; N, 6.93; S, 8.17%.

3.4.16. (3a*S*,4*S*,6a*R*)-4-{(1*R*,2*S*,5*R*)-[2-Isopropyl-5-methylcyclohexyl]oxy} - 3a - (phenylsulfonyl) - hexahydro-6*H*-furo[3,4-*c*]pyrazol-6-one, *syn*-8. Prepared by reaction of *syn*-**6** with aluminium amalgam and purified by column chromatography (hexane–ethyl acetate, 4:1) (yield 30%). Mp 122–123°C (white solid); $[\alpha]_D$ = +60.9 (*c* 0.25, chloroform). IR (KBr): 3326, 1784, 1582, 1445, 1240, 1082. δ_H 7.92 (m, 2H), 7.78 (m, 1H), 7.66 (m, 2H), 5.89 (s, 1H), 4.75 (s, 1H), 3.79 (d, 1H, *J* 12.1), 3.37 (dt, 1H, *J* 10.6 and 4.5), 3.36 (d, 1H, *J* 12.1), 2.09 (m, 1H), 1.65–0.43 (m, 17H). δ_C 172.1, 136.1, 135.2, 130.1, 129.2, 101.3, 82.9, 82.0, 68.1, 56.2, 47.9, 42.3, 33.7, 31.5, 25.3, 22.6, 22.0, 21.2, 15.7. Anal. calcd for $C_{21}H_{30}N_2O_5S$: C, 59.69; H, 7.16; N, 6.63; S, 7.59. Found: C, 59.27; H, 7.11; N, 6.50; S, 7.46%.

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11. The *syn* and *anti* approaches are defined with respect to the alkoxy group at C-5.
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13. The four diastereoisomers formed in these reactions correspond to *endo* and *exo* modes of addition of the dipole to each diastereotopic face of the dipolarophile. The *exo* mode yielded the adducts with the methyl group at the pyrazoline ring in a *trans* arrangement with respect to the furanone moiety and a *cis* arrangement with respect to the sulfinyl group, whereas the *endo* mode afforded the opposite relative stereochemistry.
14. The authors have deposited coordinates for adduct *anti*-**11*exo*** with the Cambridge Crystallographic Data Centre (deposition number CCDC 188287), the coordinates can be obtained, on request, from the Director Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2/EZ, UK.
15. The relationship between the magnitude of the $J_{3,6a}$ coupling constant and the *endo* and *exo* character of the adducts (lower value for the *exo* adducts) is not completely conclusive. In fact, there have been reported some cases indicating the opposite relationship. See for example Ref. 12a.
16. For a detailed discussion about the conformational preferences of β-oxygenated sulfoxides and sulfones, see: Alcudia, F.; Carretero, J. C.; García Ruano, J. L.; Martínez, M. C.; Rodríguez, J. H. *Tetrahedron* **1985**, *41*, 2419–2433 and references cited therein.