

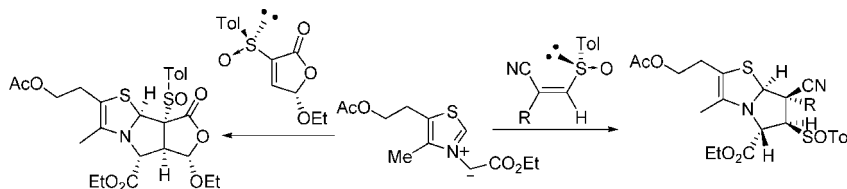
# Pyrrolo[2,1-*b*]thiazole Derivatives by Asymmetric 1,3-Dipolar Reactions of Thiazolium Azomethine Ylides to Activated Vinyl Sulfoxides

José Luis García Ruano,\* Alberto Fraile, M. Rosario Martín,\* Gema González, and Cristina Fajardo

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

jose Luis.garcia.ruano@uam.es

Received July 31, 2008



1,3-Dipolar reactions of thiazolium azomethine ylides to enantiopure cyclic and acyclic vinyl sulfoxides provide an efficient access to polyfunctionalized pyrrolo[2,1-*b*][1,3]thiazoles in a highly regio- and stereoselective manner. Regioselectivity can be inverted by modifying the position of the sulfinyl group at the double bond of the sulfinylfuranones. The sulfoxide is the main controller of the *endo* selectivity of these processes as well as of the  $\pi$ -facial selectivity in reactions of (*Z*)-3-*p*-tolylsulfinylacrylonitriles. In contrast, the  $\pi$ -facial selectivity in reactions of 5-alkoxy-3-*p*-tolylsulfinyl furan-2(5*H*)-ones is mainly controlled by the configuration at C-5, affording the *anti* adducts with respect to the alkoxy group as the major or exclusive adducts.

## Introduction

The interest in polyhydroderivatives of pyrrolo[2,1-*b*]thiazoles is related to the wide scope of their biological activities, allowing their use as hepatoprotective, hypoglycemic (antidiabetic), antibiotic, anticonvulsant, antiinflammatory, or antileukemic agents, bactericides, or as dopaminergic neurotransmitters in CNS in vivo and dipeptidyl peptidase IV (DPP-IV) inhibitors.<sup>1</sup>

There is a rich history regarding the preparation and importance of tetrahydropyrrolo[2,1-*b*]thiazol-5(6*H*)-one scaffolds. There are reports of solution-<sup>2</sup> and solid-phase<sup>3</sup> syntheses of derivatives of this bicyclic scaffold. The majority rely on the

formation of thiazolidine intermediate through the reaction of  $\beta$ -amino thiols (generally L-cysteine) with  $\gamma$ -formyl acid derivatives or their corresponding acetals<sup>3d</sup> in the presence of stannous chloride.

Additionally, polyhydropyrrolo[2,1-*b*]thiazoles, with no lactam moiety in their skeleton, have interesting pharmacological properties and have been successfully used as intermediates in the synthesis of pyrrolidines, such as racemic  $\alpha$ -allokainic<sup>4a</sup> and kainic acids<sup>4b</sup> or 2*S*,4*R*-4-methylpyrrolidine-2,4-dicarboxylate.<sup>5</sup> However, the antecedents of the asymmetric synthesis of polyhydropyrrolo[2,1-*b*]thiazoles are scarce. Katritzky<sup>6</sup> and Beaupere<sup>7</sup> obtained this system via a condensation reaction with L-cysteine ester and D-monosaccharides as chiral reagents,

(1) (a) Campbell, D. A.; Betancort, J. M.; Winn, D. T. US Patent US 2006009518, 2006. (b) Wagner, H.; Schoenafinger, K.; Jaehne, G.; Gaul, H.; Buning, C.; Tschank, G.; Werner, U. PCT Int. WO 2005012312, 2005; *Chem. Abstr.* **2005**, 142, 219272. (c) Abe, T.; Matsunaga, H.; Mihira, A.; Sato, C.; Ushiroguchi, H.; Sato, K.; Takasaki, T.; Venkatesan, A. M.; Mansour, T. S. US Pat. US 2004132708, 2004; *Chem. Abstr.* **2004**, 141, 550737. (d) Aicher, T. D.; Cheon, S. H.; Nadelson, J.; Simpson, W. R. J.; Houlihan, W. J. Eur. Pat. EP 702015, 1996; *Chem. Abstr.* **1996**, 124, 343285. (e) Suzuki, N.; Nakayama, A.; Saijo, T.; Hasegawa, M.; Yokohama, S. Japanese Patent 04145086, 1992; *Chem. Abstr.* **1992**, 117, 212487. (f) Tverdokhlebov, A. V. *Heterocycles* **2007**, 71, 761–798, and references cited therein.

(2) Qiu, W.; Gu, X.; Soloshonok, V. A.; Carducci, M. D.; Hruby, V. J. *Tetrahedron Lett.* **2001**, 42, 145–148.

(3) (a) Scott, W. L.; Martynnow, J. G.; Huffman, J. C.; O'Donnell, M. J. *J. Am. Chem. Soc.* **2007**, 129, 7077–7088, and references cited therein. (b) Nielsen, T. E.; Le Quement, S.; Meldal, M. Gu, X.; Ying, J.; Agnes, R. S.; Navratilova, E.; Davis, P.; Stahl, G.; Porreca, F.; Yamamura, H. I. *Org. Lett.* **2005**, 7, 3601–3604. (c) Hruby, V. J. *Org. Lett.* **2004**, 6, 3285–3288. (d) Cayley, A. N.; Cox, R. J.; Ménard-Moyon, C.; Schmidt, J. P.; Taylor, R. J. K. *Tetrahedron Lett.* **2007**, 48, 6556–6560.

(4) (a) Kraus, G. A.; Nagy, J. O. *Tetrahedron* **1985**, 41, 3537–3545. (b) Monn, J. A.; Valli, M. J. *J. Org. Chem.* **1994**, 59, 2773–2778.

(5) Esslinger, C. S.; Titus, J.; Koch, H. P.; Bridges, R. J.; Chamberlin, A. R. *Bioorg. Med. Chem.* **2002**, 10, 3509–3515.

(6) Katritzky, A. R.; Zhang, Y.; He, H.-Y. *Arkivoc* **2002**, 161, 170.

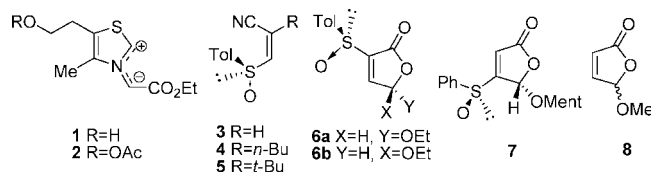


FIGURE 1. Dipoles and dipolarophiles studied.

respectively. Another reported method involves the ring contraction of 7,5-fused bicyclic thiazolidinelactams.<sup>8</sup>

Retrosynthetic analysis of polyhydropyrrolo[2,1-*b*]thiazoles shows the 1,3-dipolar addition of thiazolium ylides to alkenes as the most direct route for their preparation. However, the asymmetric addition of **1** (Figure 1) to 2-methylacrylate bearing an Evans oxazolidinone as chiral auxiliary is the only reported example.<sup>5,9,10</sup> Although enantioselective catalysis afforded good results in the synthesis of enantiomerically pure pyrrolidines using azomethine ylides generated from imino ester,<sup>11</sup> thiazolium ylides, because of their strongly delocalized structure, are not likely to join efficiently to the so far studied catalysts. Therefore, the use of chiral dipolarophiles for the asymmetric synthesis of polyhydropyrrolo[2,1-*b*]thiazoles maintains its interest.

Several years ago, we initiated a program focused on the applicability of vinyl sulfoxides as dipolarophiles in asymmetric 1,3-dipolar reactions. In this field, the excellent features of the arylsulfinylfuran-2(5*H*)-ones<sup>12</sup> and 3-*p*-tolylsulfinylacrylonitriles<sup>13</sup> as chiral dipolarophiles have been evidenced in their reactions with diazoalkanes, nitrones, nitrile oxides, and carbonyl ylides. Otherwise, reactions of *N*-metalated azomethine ylides with sulfinylacrylates<sup>14</sup> and 2-sulfinylcyclopentenone<sup>15</sup> also provided an excellent access to the asymmetric synthesis of pyrrolidine rings. These results, and those concerning the cycloaddition of 3-oxopyridinium betaines,<sup>16</sup> are so far the only

reported examples on asymmetric [3 + 2] cycloaddition of azomethine ylides to chiral vinyl sulfoxides.

The reported results prompted us to investigate the behavior of the arylsulfinylfuran-2(5*H*)-ones and 3-*p*-tolylsulfinylacrylonitriles as chiral dipolarophiles in their reactions with thiazolium ylides as a method for preparing tetrahydropyrrolo[2,1-*b*]thiazole scaffolds. In this paper, we report the results obtained in the reactions of thiazolium ylides **1**<sup>4b</sup> and **2** (Figure 1) with acyclic (**3**–**5**)<sup>17</sup> and cyclic (**6**<sup>18</sup> and **7**<sup>19</sup>) vinyl sulfoxides, which have provided a quick and efficient entry to a variety of optically pure functionalized pyrrolo[2,1-*b*]thiazoles. These studies have also improved our knowledge on the role of the sulfinyl group in asymmetric 1,3-dipolar reactions and widened the scope of vinyl sulfoxides as chiral dipolarophiles.

## Results and Discussion

Unstable ylides **1** and **2** were generated from the corresponding quaternary ammonium bromides with amine base in the presence of the dipolarophile. Initially we studied the behavior of these ylides with the acyclic sulfoxides. The reaction of sulfinylacrylonitrile **3** with ylide **1** afforded pyrrole **9** (Scheme 1), resulting from desulfinylation and further opening of the thiazole ring at the primary adduct.

However, the primary adducts could be isolated starting from ylide **2**, which reacted with **3** in a completely stereoselective and regioselective way, affording only compound **10** (Scheme 2) in almost quantitative yield. However, after chromatographic purification, the isolated yield was only 50% because it was not quite stable in solution due to its easy desulfinylation. Reaction of **2** with **4** also produced **11** as the only adduct but its lower reactivity, due to the higher steric hindrance, determined a conversion of 50% (the unreacted dipolarophile could be recovered). Compound **11** was less prone to desulfinylation than **10**, and therefore, it could be obtained in 39% isolated yield after purification (78% based on recovered starting material). The reaction of the most sterically hindered sulfinylacrylonitrile **5** with ylide **2** was not successful, although the unaltered dipolarophile could be recovered after long period of times (Scheme 2).

We decided to investigate the reactions of ylides **1** and **2** with cyclic dipolarophiles because of the presumably higher stability of the resulting adducts, which are less prone to desulfinylation. As a control experiment, initially we studied the reaction of 5-methoxyfuran-2(5*H*)-one (**8**) with ylide **2** under different conditions. It did not take place successfully (starting material and other not identifiable products were recovered from the reaction mixtures), which proves the moderate reactivity of the ylides derived from the thiazolium salts, which are not able to react with the nonactivated furanone. Fortunately, the incorporation of the sulfinyl group into the dipolarophile dramatically increases the reactivity, and therefore, the reaction of furanone **6a** with ylide **1** in acetonitrile proceeded at room temperature in 5 min, yielding the adduct *anti*-**12a-endo** only (Scheme 3). It is the result of the attack of the dipole, in its *s-trans* conformation (see Figure 2), to the opposite face to that occupied by the OEt group and *endo* mode approach. After

(7) Marek, D.; Wadouachi, A.; Uzan, R.; Beaupere, D.; Nowogrocki, G.; Laplace, G. *Tetrahedron Lett.* **1996**, *37*, 49–52.

(8) Agoston, K.; Geyer, A. *Tetrahedron Lett.* **2004**, *45*, 1895–1898.

(9) The antecedents of cycloaddition of thiazolium azomethine ylides to racemic olefinic dipolarophiles are also scarce. Polyhydropyrrolo[2,1-*b*]thiazoles are reported by Kraus and Tsuge in references 4a and 10, respectively. For a recent example of formation of aromatic systems, see: (a) Berry, C. R.; Zifcsak, C. A.; Hlasta, D. *Org. Lett.* **2007**, *9*, 4099–4102.

(10) Tsuge, O.; Kanemasa, S.; Takenaka, S. *Bull. Chem. Soc. Jpn.* **1985**, *58*, 31373157 a, nd 3320–3336.

(11) (a) Llamas, T.; Gomez Arrayás, R.; Carretero, J. C. *Org. Lett.* **2006**, *8*, 1795–1798. (b) Zeng, W.; Zhou, Y. *Tetrahedron Lett.* **2007**, *48*, 4619–4622. (c) Alemparte, C.; Blay, G.; Jørgensen, K. A. *Org. Lett.* **2005**, *7*, 4569–4572. (d) Nájera, C.; Retamosa, M. G.; Sansano, J. M. *Org. Lett.* **2007**, *9*, 4025–4028. (e) Saito, S.; Tsubogo, T.; Kobayashi, S. *J. Am. Chem. Soc.* **2007**, *129*, 5364–5365, and references cited therein.

(12) (a) García Ruano, J. L.; Fraile, A.; González, G.; Martín, M. R.; Clemente, F. R.; Gordillo, R. *J. Org. Chem.* **2003**, *68*, 6522–6534. (b) García Ruano, J. L.; Alonso, M.; Fraile, A.; Martín, M. R.; Peromingo, M. T.; Tito, A. *J. Org. Chem.* **2005**, *70*, 8942–8947. (c) García Ruano, J. L.; Bercial, F.; Fraile, A.; Martín, M. R. *Synlett* **2002**, *73*, 76. (d) García Ruano, J. L.; Fraile, A.; Martín Castro, A. M.; Martín, M. R. *J. Org. Chem.* **2005**, *70*, 8825–8834. (e) García Ruano, J. L.; Fraile, A.; Martín, M. R.; Núñez, A. *J. Org. Chem.* **2006**, *71*, 6536–6541. (f) García Ruano, J. L.; Bercial, F.; González, G.; Martín Castro, A. M.; Martín, M. R. *Tetrahedron: Asymmetry* **2002**, *13*, 1993–2002.

(13) García Ruano, J. L.; Alonso de Diego, S. A.; Blanco, D.; Martín Castro, A. M.; Martín, M. R.; Rodríguez Ramos, J. H. *Org. Lett.* **2001**, *3*, 3173–3176.

(14) García Ruano, J. L.; Tito, A.; Peromingo, M. T. *J. Org. Chem.* **2002**, *67*, 981–987.

(15) García Ruano, J. L.; Tito, A.; Peromingo, M. T. *J. Org. Chem.* **2003**, *68*, 10013–10019.

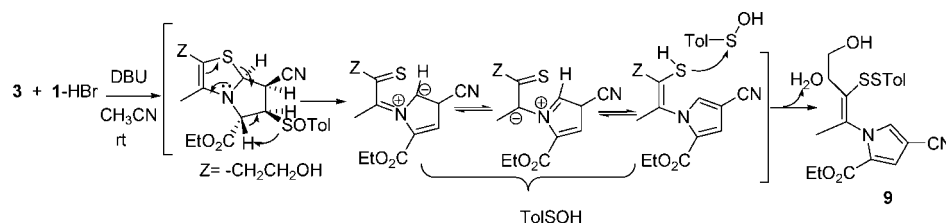
(16) (a) Takahashi, T.; Fujii, A.; Sugita, J.; Hagi, T.; Kitano, K.; Arai, Y.; Koizumi, T. *Tetrahedron: Asymmetry* **1991**, *2*, 1379–1390. (b) Prakash, K. R. C.; Trzcinska, M.; Johnson, K. M.; Kozikowski, A. P. *Bioorg. Med. Chem. Lett.* **2000**, *10*, 1443–1446. (c) Aggarwal, V. K.; Grainger, R. S.; Newton, G. K.; Spargo, P. L.; Hobson, A. D.; Adams, H. *Org. Biomol. Chem.* **2003**, *1*, 1884–1893, and references cited therein.

(17) García Ruano, J. L.; Esteban Gamboa, A.; Martín Castro, A. M.; Rodríguez, J. H.; López Solera, M. I. *J. Org. Chem.* **1998**, *63*, 3324–3332.

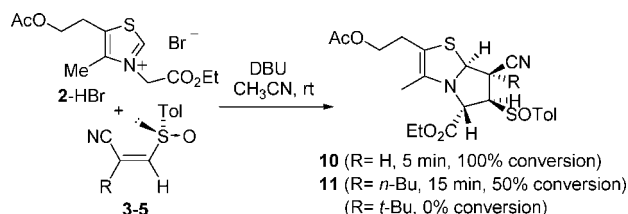
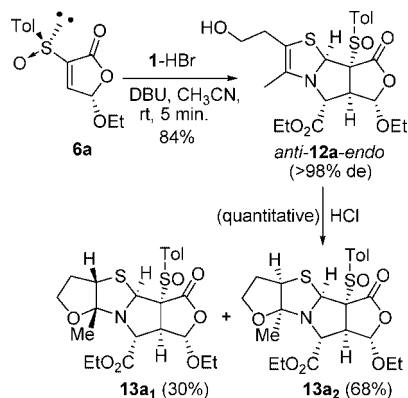
(18) Carretero, J. C.; García Ruano, J. L.; Yuste, F.; Lorente, A. *Tetrahedron: Asymmetry* **1993**, *4*, 177–180.

(19) García Ruano, J. L.; Bercial, F.; Fraile, A.; Martín Castro, A. M.; Martín, M. R. *Tetrahedron: Asymmetry* **2000**, *11*, 4737–4752.

## SCHEME 1. Reaction of Ylide 1 with Sulfinylacrylonitriles 3



## SCHEME 2. Reaction of Ylide 2 with Sulfinylacrylonitriles 3–5

SCHEME 3. Reaction of Thiazolium Ylide 1 with Sulfinylfuran-2(5*H*)-one 6a and Subsequent Cyclization

purification by filtration on Florisil, *anti*-12a-endo was isolated in 84% yield. Chromatographic purification sharply decreased the yield because of the partial cyclization of *anti*-12a-endo into a mixture of **13a<sub>1</sub>** and **13a<sub>2</sub>**, resulting from the attack of the OH to both faces of the double bond. When this reaction is provoked by silica gel, a mixture of both compounds was obtained in high yield (81%), which becomes quantitative by addition of HCl to a solution of *anti*-12a-endo in chloroform. After their chromatographic separation, **13a<sub>1</sub>** and **13a<sub>2</sub>** could be isolated in 30% and 68% yield, respectively.

Under the same conditions, furanone **6b** reacted with **1** affording an 86:14 mixture of *anti*-12b-endo and *syn*-12b-endo (Scheme 4). These two diastereoisomers result from the approach of the ylide to each face of the double bond at **6b** in their *endo*-mode, the major one being that resulting from the *anti* approach to the alkoxy group. Chromatographic separation of this mixture was not feasible due to their easy cyclization in contact with the silica gel to the corresponding tetracyclic compounds **13**. When a chloroform solution of the mixture of adducts was treated with a HCl solution, the cyclization took place in almost quantitative yield and afforded a mixture of four cyclized compounds, the major ones **13b<sub>1</sub>** and **13b<sub>2</sub>** (derived from *anti*-12b-endo) being isolated in 32% and 48% yields, respectively (Scheme 4).

As the primary adducts obtained in these reactions are prone to cyclization, we investigated the reactions of **6a** and **6b** with ylide **2**. The results (Scheme 5) were similar to those obtained

from **1**. Only one adduct, *anti*-14a-endo, was obtained from furanone **6a** in 78% isolated yield (after chromatographic separation), whereas a 75:25 mixture of two diastereoisomers, *anti*-14b-endo and *syn*-14b-endo, which could not be separated, was obtained from furanone **6b**.

As all these reactions evolved in a completely regioselective manner, the preparation of the adducts with the opposite regiochemistry became an important challenge in order to broaden the structural diversity of the pyrrolo[2,1-*b*]thiazole derivatives. With this aim, we studied the reaction of menthyloxyfuranone **7**, bearing the sulfinyl group at C-4, with ylide **2**. Complex mixtures were obtained under conditions identical to those employed for sulfinylfuranones **6**. The use of different bases, such as Et<sub>3</sub>N or TMP, did not improve the results. The adducts could be obtained eventually when thiazolium ylide **2** was generated before adding 4-sulfinylfuranone, using a 1:1.6:1.4 ratio of **7**:2-HBr/TMP in acetonitrile at room temperature. Under these conditions, we could identify in the <sup>1</sup>H NMR spectrum of the reaction crude a 93:7 mixture of two diastereoisomers, *anti*-15-endo and *syn*-15-endo (Scheme 6), which could be purified but were not separated by chromatography. The major diastereoisomer was isolated in its diastereomerically pure form by precipitation from the mixture with AcOEt–hexane (39%), and its structure was unequivocally determined by X-ray analysis.<sup>20</sup> This result gives evidence that the sulfinyl group is mainly responsible for the regiochemistry of these reactions, and it can be controlled by choosing the position where the sulfinyl group is located at the dipolarophile.

Once the influence of the sulfur function on the regioselectivity was known, we also studied the reaction of sulfone **7**<sup>19</sup> with ylide **2**. A 71:18:7:4 mixture of four adducts was obtained (Scheme 6). Despite the lower stereoselectivity control exerted by the sulfonyl group, the two major adducts could be purified and identified as *anti*-15'-endo (61% isolated yield) and *syn*-15'-endo (16% isolated yield).

Structural assignment of compounds **10**–**15** was made by NMR experiments. The configurations of the pyrrolothiazoles **12a,b**, **13**, **14a,b**, and **15** were assigned by assuming that the configurations at C-5 of the starting furanones **6a**, **6b**, **7**, and **7** remained unaltered in the course of these reactions and that the ylides reacted in their *anti* conformation,<sup>4b,10</sup> which was confirmed by X-ray analyses of the adducts obtained from furanones **6** and **7** with isoquinolinium (unpublished results) or thiazolium azomethine ylide, respectively. Stereochemical results can be rationalized by assuming that dipoles **1** and **2** always adopt the *anti* conformation (Figure 2) in order to avoid the steric repulsion Me/CO<sub>2</sub>Et which destabilizes the *syn* rotamer.

Reactions with sulfinylacrylonitriles **3** and **4** evolved in a completely  $\pi$ -facial and *endo* selective manner affording **10** and

(20) Crystallographic data (excluding structure factors) for *anti*-15-endo have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 695820. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44(0)-1223-366033 or e-mail: deposit@ccdc.cam.ac.uk].



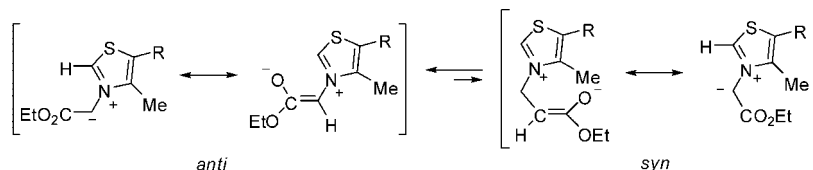
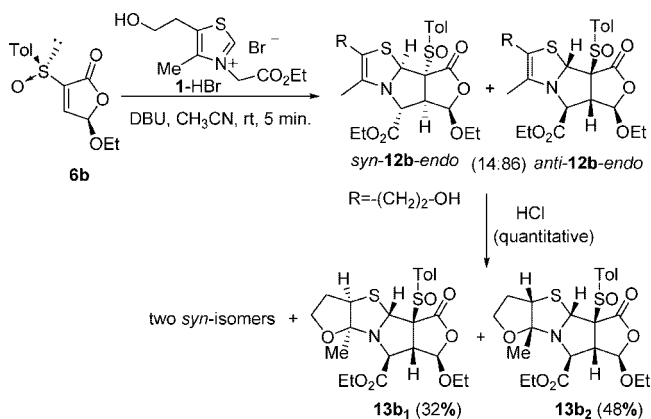


FIGURE 2. Preferred stereochemistry for dipoles **1** and **2**.

**SCHEME 4. Reaction of Thiazolium Ylide **1** with Sulfynylfuran-2(5*H*)-one **6b** and Subsequent Cyclization**



**11**, respectively, as the only adducts. These results were explained on the assumption of a complete shift of the conformational equilibrium at dipolarophiles toward the rotamer that minimizes the dipolar repulsion between the S–O and C–N bonds (Figure 3). The orientation of the tolyl group determines a large difference in the steric hindrance of the two diastereotopic faces (the bottom face is the sterically disfavored), which results in the complete control of the  $\pi$ -facial selectivity. Moreover, the electrostatic repulsion of the sulfinyl oxygen and the ester group at the *exo* approach justifies the high *endo* selectivity observed in these reactions (Figure 3).

The results obtained from sulfinyl furanones cannot be explained so easily. The major or exclusive formation of the *anti* adducts (with respect to the OEt group) indicates that the influence of the configuration at C-5 is larger than that of the sulfur one on the  $\pi$ -facial selectivity control. This is easily understood taking into account the rigidity of C-5 and the conformational flexibility around the C–S bond. The fact that evolution of **6a** is completely  $\pi$ -facial selective, whereas **6b** affords a mixture of two isomers resulting from the attack to opposite faces, can be explained by assuming that the more reactive conformation around the C–S bond is that exhibiting the *p*-tolyl group in an *anti*-relationship with respect to the carbonyl oxygen (**A** in Figure 4).<sup>21</sup> It would orientate the sulfinyl oxygen to the face which displays the OEt group in **6a** but to the opposite one in **6b**. In the first case the orientation of both chiral centers would be reinforced, thus explaining its complete facial selectivity, whereas in **6b** the orientation favored for C-5 and S would be different and therefore its evolution would be less stereoselective (Figure 4). The orientation proposed for the *p*-tolyl group would also account for the complete *endo* character

of these reactions because of its strong steric interactions with the dipole in the *exo*-approaches (Figure 4). The justification that the reactive conformation in these reactions is **A** (with the *p*-tolyl group in *anti* relationship with respect to the carbonyl oxygen) can be the electrostatic repulsion between the sulfinyl oxygen and the negative end of the dipole, which would be larger when this latter attacks the dipolarophile at its conformation **B** (lower distance).

The  $\pi$ -facial and *endo* selectivities observed in reactions of compound **7** can be understood with a similar reasoning and assuming that most stable conformation of **7** (depicted in Scheme 6) is the most reactive.

In summary, we have studied the usefulness of different activated vinyl sulfoxides as dipolarophiles in the highly stereoselective synthesis of a variety of pyrrolo[2,1-*b*]thiazole derivatives. The sulfinyl group dramatically increased the dipolarophilic reactivity of the double bonds and had a crucial role on the control of the regioselectivity and the stereoselectivity ( $\pi$ -facial and *endo*-selectivity) of these processes.

## Experimental Section

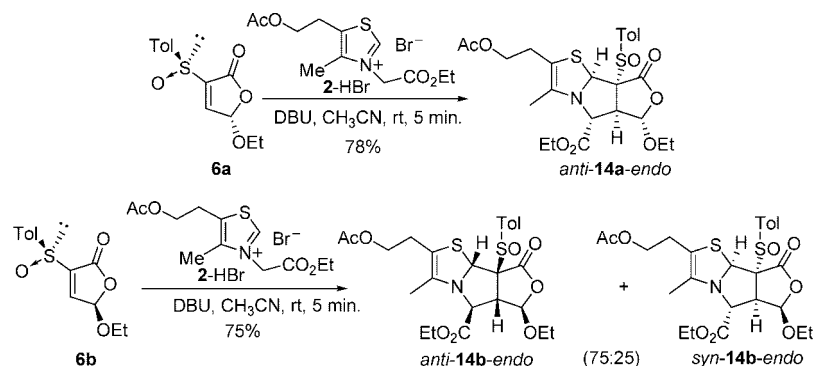
### Reaction of (Z)-3-*p*-Tolylsulfinylacrylonitriles **3–5** with Thiazolium Ylide.

**General Procedure.** To a stirred suspension of the corresponding sulfinylacrylonitrile (0.16 mmol) and the corresponding salt (0.22 mmol) in dry acetonitrile (3 mL), under argon at room temperature, was added DBU (0.19 mmol). After the time indicated in each case, the solvent was evaporated in vacuo and the residue was dissolved in dichloromethane and washed with water and brine. The aqueous layers were extracted with dichloromethane several times. The organic layers were dried (Na<sub>2</sub>SO<sub>4</sub>), filtered, and concentrated in vacuo. The reaction time and the purification method are indicated in each case.

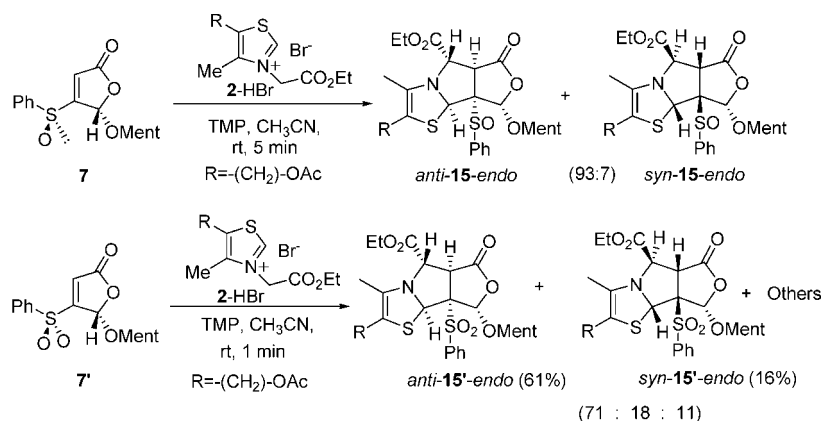
**Ethyl 4-Cyano-1-[4-hydroxy-1-methyl-2-[(4-methylphenyl)-disulfanyl]but-1-en-1-yl]-1*H*-pyrrole-2-carboxylate (**9**).** Compound **9** was obtained as the major product following the general procedure from (Z)-3-[(*R*)-*p*-tolylsulfinyl]propenenitrile (**3**) and the thiazolium salt **1**–HBr after 5 min of reaction. It was purified by flash column chromatography (AcOEt–hexane, 1:3): yield 21%; IR (neat) 3528, 2233, 1710, 1635, 1595, 1261, 1074 cm<sup>−1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  7.27 and 7.20 (AA'BB' system, 4H), 7.13 (d, 1H, *J* = 1.5 Hz), 6.08 (d, 1H, *J* = 1.5 Hz), 4.25 (t, 2H, *J* = 7.1 Hz), 3.86 (m, 2H), 2.93 (m, 2H), 2.41 (s, 3H), 2.17 (s, 3H), 1.32 (t, 3H, *J* = 7.1 Hz); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz)  $\delta$  159.4 (CO), 139.5 (C), 137.4 (C), 134.0 (C), 132.7 (C), 132.0 (CH), 130.1 (CH), 123.8 (C), 119.8 (CH), 114.9 (CN), 94.1 (C), 61.3 (CH<sub>2</sub>), 60.9 (CH<sub>2</sub>), 33.9 (CH<sub>2</sub>), 21.8 (CH<sub>3</sub>), 21.2 (CH<sub>3</sub>), 14.2 (CH<sub>3</sub>); MS (FAB+) 403 (M + H, 31), 385 (12), 279 (32), 247 (100), 138 (19). By treatment of alcohol with acetic anhydride acetyl derivative **9**–Ac was obtained: IR (neat) 2232, 1740, 1719, 1639, 1548, 1259 cm<sup>−1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  7.27 and 7.18 (AA'BB' system, 4H), 7.11 (d, 1H, *J* = 1.8 Hz), 6.21 (d, 1H, *J* = 1.8 Hz), 4.27 (m, 2H), 4.19 (q, 2H, *J* = 7.2 Hz), 3.02 (m, 2H), 2.39 (s, 3H), 2.15 (s, 3H), 2.10 (s, 3H), 1.30 (t, 3H, *J* = 7.2 Hz); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz)  $\delta$  171.0 (C), 158.6 (C), 139.3 (C), 137.5 (C), 132.7 (CH), 132.69 (C), 132.0 (C), 131.4 (CH), 130.1 (CH), 124.3 (C), 119.6 (CH), 115.0 (CN), 93.9 (C), 61.7 (CH<sub>2</sub>), 60.8 (CH<sub>2</sub>), 29.6 (CH<sub>2</sub>), 21.3 (CH<sub>3</sub>), 21.2 (CH<sub>3</sub>), 21.0 (CH<sub>3</sub>), 12.2 (CH<sub>3</sub>).

(21) Nevertheless, the electrostatic repulsion between the sulfinyl and carbonyl oxygens suggests for **6a** and **6b** that rotamers **B** must be the most stable ones (it has been supported by theoretical calculations in compounds of similar structure). The reason justifying that the more reactive conformation with ylides is **A** (with the *p*-tolyl group in *anti* relationship with respect to the carbonyl oxygen) can be the electrostatic repulsion between the sulfinyl oxygen and the negative end of the dipole, which would be larger when the latter attacks to the dipolarophile at its conformation **B**.

## SCHEME 5. Reaction of Thiazolium Ylide 2 with Sulfinylfuran-2(5H)-ones 6



## SCHEME 6. Cycloaddition of Ylide 2 to 4-Phenylsulfinylfuranone 7 and 4-Phenylsulfonylfuranone 7'



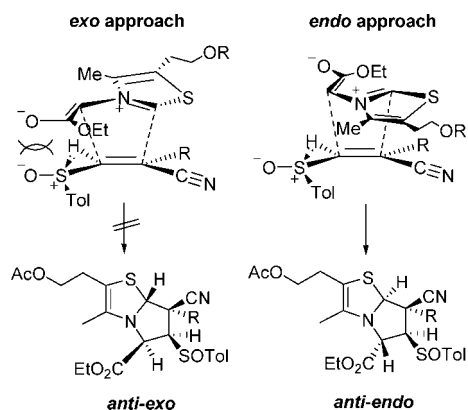
Ethyl [5*S*,6*R*,7*S*,7*aS*,(*S*)*R*]-2-[2-(Acetyloxy)ethyl]-7-cyano-3-methyl-6-(*p*-tolylsulfinyl)-5,6,7,7*a*-tetrahydropyrrolo[2,1-*b*][1,3]-thiazole-5-carboxylate (**10**). Compound **10** was obtained as the sole compound following the general procedure from (Z)-3-[(*R*)-*p*-tolylsulfinyl]propenenitrile (**3**) and the thiazolium salt 2-HBr after 5 min of reaction. It was purified by flash column chromatography (AcOEt–hexane, 1:3): yield 48%; white solid; mp (Et<sub>2</sub>O–hexane) 104–105 °C; [α]<sub>D</sub> +197.4 (c 0.5, CHCl<sub>3</sub>); IR (KBr) 2241, 1734, 1296, 1084, 1053 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz) δ 7.65 and 7.34 (AA'BB' system, 4H), 5.21 (d, 1H, *J* = 5.6 Hz), 4.91 (d, 1H, *J* = 5.6 Hz), 4.14 (t, 2H, *J* = 6.6 Hz), 4.08 (m, 2H), 3.84 (dd, 1H, *J* = 7.6 and 5.7 Hz), 3.33 (dd, 1H, *J* = 7.6 and 5.8 Hz), 2.57 (m, 2H), 2.41 (s, 3H), 2.05 (s, 3H), 1.94 (s, 3H), 1.20 (t, 3H, *J* = 7.1 Hz); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) δ 171.0 (C), 170.3 (C), 143.0 (C), 139.5 (C), 133.3 (C); 130.3 (CH), 124.6 (CH), 115.1 (CN), 104.1 (C), 70.1 (CH), 65.2 (CH), 62.6 (CH<sub>2</sub>), 62.2 (CH<sub>2</sub>), 60.9 (CH), 39.9 (CH), 27.0 (CH<sub>2</sub>), 21.5 (CH<sub>3</sub>), 21.0 (CH<sub>3</sub>), 13.9 (CH<sub>3</sub>), 12.4 (CH<sub>3</sub>). Anal. Calcd for C<sub>22</sub>H<sub>26</sub>N<sub>2</sub>O<sub>5</sub>S<sub>2</sub>: C, 57.12; H, 5.67; N, 6.06; S, 13.86. Found: C, 56.99; H, 5.50; N, 6.07; S, 14.12.

Ethyl [5*S*,6*R*,7*S*,7*aS*,(*S*)*R*]-2-[2-(Acetyloxy)ethyl]-7-butyl-7-cyano-3-methyl-6-(*p*-tolylsulfinyl)-5,6,7,7*a*-tetrahydropyrrolo[2,1-*b*][1,3]thiazole-5-carboxylate (**11**). Following the general procedure from (Z)-2-*n*-butyl-3-[(*R*)-*p*-tolylsulfinyl]propenenitrile (**4**) and the thiazolium salt 2-HBr, compound **11** was obtained as the sole isomer along with starting material in a 50:50 ratio after 15 min of reaction. It was purified by flash column chromatography (AcOEt–hexane, 1:6): yield 39%; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz) δ 7.52 and 7.31 (AA'BB' system, 4H), 5.00 (d, 1H, *J* = 5.5 Hz), 4.78 (s, 1H), 4.13 (t, 2H, *J* = 6.6 Hz), 3.92 (m, 2H), 3.39 (d, 1H, *J* = 5.5 Hz), 2.54 (m, 2H), 2.40 (s, 3H), 2.04 (s, 3H), 1.94 (s, 3H), 1.70–1.20 (m, 6H), 1.10 (t, 3H, *J* = 7.1 Hz), 0.90 (t, 3H, *J* = 7.1 Hz); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) δ 171.0 (C), 170.5 (C), 142.4 (C), 139.0 (C), 133.4 (C), 130.1 (CH), 124.2 (CH), 117.3 (CN), 102.7 (C), 76.5 (CH), 71.1 (CH), 62.6 (CH<sub>2</sub>), 61.9 (CH<sub>2</sub>), 58.3 (CH), 53.0 (C), 36.7 (CH<sub>2</sub>), 27.4 (CH<sub>2</sub>), 27.1 (CH<sub>2</sub>), 22.6 (CH<sub>2</sub>), 21.4 (CH<sub>3</sub>), 21.0 (CH<sub>3</sub>), 13.8 (CH<sub>3</sub>), 13.6 (CH<sub>3</sub>), 12.0 (CH<sub>3</sub>).

## Reaction of Furanones with Thiazolium Ylides.

**General Procedure.** To a stirred suspension of furanone (0.56 mmol) and azolium salt (0.68 mmol) in dry acetonitrile (15 mL), under argon at room temperature, was added DBU (0.68 mmol). After the time indicated in each case, the solvent was evaporated in vacuo and the residue was dissolved in dichloromethane and washed with water and brine. The aqueous layers were extracted with dichloromethane several times. The organic layers were dried (Na<sub>2</sub>SO<sub>4</sub>), filtered, and concentrated in vacuo. The reaction time and the purification method are indicated in each case.

Ethyl [5*R*,5*aR*,6*S*,8*aS*,8*bS*,(*S*)*S*]-6-Ethoxy-2-(2-hydroxyethyl)-3-methyl-8*a*-*p*-tolylsulfinyl-8-oxo-5*a*,6,8*a*,8*b*-tetrahydro-5*H*,8*H*-furo[3',4':3,4]pyrrolo[2,1-*b*][1,3]thiazole-5-carboxylate (*anti*-12*a*-endo). Compound *anti*-12*a*-endo was obtained as the sole compound following the general procedure from [5*S*,(*S*)*S*]-5-ethoxy-3-*p*-tolylsulfinylfuran-2(5*H*)-one (**6a**) and thiazolium salt 1-HBr, after 5 min of reaction. It was purified by flash column chromatography (acetone–hexane, 1:2) using Florisil as the stationary phase: yield

FIGURE 3.  $\pi$ -Facial and *endo*-selectivities in reactions of **3** and **4**.

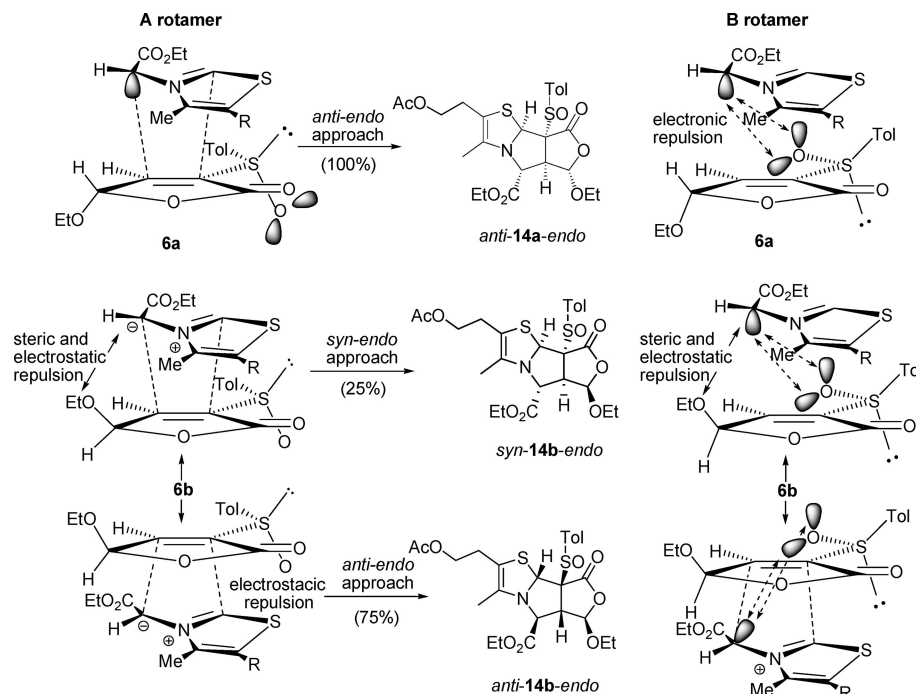


FIGURE 4. Rationalization of the  $\pi$ -facial and *endo*-selectivities of reactions of **6a** and **6b**.

84%; white solid; mp 117–119 °C dec;  $[\alpha]_D^{25} = +17.4$  (c 0.5, acetone); IR (KBr) 3692–3138, 3549, 1755, 1737, 1492, 1080, 1052  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (acetone- $d_6$ , 300 MHz)  $\delta$  7.66 and 7.43 (AA'BB' system, 4H), 5.64 (d, 1H,  $J = 1.8$  Hz), 5.29 (s, 1H), 4.89 (d, 1H,  $J = 2.2$  Hz), 4.18 (m, 2H), 3.75 (m, 2H), 3.60 (t, 1H,  $J = 2.0$  Hz), 3.41 (m, 2H), 3.22 (t, 1H,  $J = 6.0$  Hz), 2.44 (s, 3H), 2.21 (m, 2H), 1.74 (s, 3H), 1.29 (t, 3H,  $J = 7.1$  Hz), 1.21 (t, 3H,  $J = 7.1$  Hz);  $^{13}\text{C}$  NMR (acetone- $d_6$ , 75 MHz)  $\delta$  170.1 (C), 169.1 (C), 143.8 (C), 136.0 (C), 133.4 (C), 130.4 (CH), 127.2 (CH), 107.2 (C), 106.2 (CH), 75.7 (C), 72.6 (CH), 67.4 (CH), 66.2 (CH<sub>2</sub>), 62.2 (CH<sub>2</sub>), 61.3 (CH<sub>2</sub>), 53.9 (CH), 31.9 (CH<sub>2</sub>), 21.5 (CH<sub>3</sub>), 15.2 (CH<sub>3</sub>), 14.5 (CH<sub>3</sub>), 12.1 (CH<sub>3</sub>). Anal. Calcd for  $\text{C}_{23}\text{H}_{29}\text{NO}_7\text{S}_2$ : C, 55.74; H, 5.90; N, 2.83; S, 12.94. Found: C, 55.75; H, 5.85; N, 2.77; S, 13.19.

**Ethyl 6-Ethoxy-2-(2-hydroxyethyl)-3-methyl-8a-p-tolylsulfonfyl-8-oxo-5a,6,8a,8b-tetrahydro-5H,8H-furo[3',4':3,4]pyrrolo[2,1-b][1,3]thiazole-5-carboxylates (12b-endo).** Compound **12b-endo** was obtained as a mixture of diastereoisomers *anti*-**12b-endo** and *syn*-**12b-endo** in 86:14 ratio from [5*R*,(*S*)]-5-ethoxy-3-*p*-tolylsulfonfylfuran-2(5*H*)-one (**6b**) and thiazolium salt with free OH **1**, after 5 min. It could not be purified by flash column chromatography. The spectroscopic data were measured from the NMR spectra of the crude mixture: colorless oil; IR (neat) 3711–3150, 1755, 1700, 1647, 1624, 1492, 1083, 1053  $\text{cm}^{-1}$ .

**[5*S*,5*aS*,6*R*,8*aR*,8*bR*,(*S*)]-*anti*-**12b-endo**:**  $^1\text{H}$  NMR (acetone- $d_6$ , 300 MHz)  $\delta$  7.46 and 7.39 (AA'BB' system, 4H), 5.59 (s, 1H), 5.36 (d, 1H,  $J = 2.1$  Hz), 4.94 (s, 1H), 4.23 (m, 2H), 3.54 (m, 2H), 3.31 (m, 3H), 2.41 (s, 3H), 2.34 (m, 2H), 1.78 (s, 3H), 1.32 (t, 3H,  $J = 7.1$  Hz), 0.82 (t, 3H,  $J = 7.1$  Hz);  $^{13}\text{C}$  NMR (acetone- $d_6$ , 75 MHz)  $\delta$  169.8 (C), 169.1 (C), 143.6 (C), 137.1 (C), 133.6 (C), 130.5 (CH), 126.5 (CH), 106.7 (CH), 106.4 (C), 82.4 (C), 74.9 (CH), 67.7 (CH), 65.6 (CH<sub>2</sub>), 62.2 (CH<sub>2</sub>), 61.4 (CH<sub>2</sub>), 50.6 (CH), 31.9 (CH<sub>2</sub>), 21.4 (CH<sub>3</sub>), 15.0 (CH<sub>3</sub>), 14.5 (CH<sub>3</sub>), 12.1 (CH<sub>3</sub>).

**[5*R*,5*aR*,6*R*,8*aS*,8*bS*,(*S*)]-*syn*-**12b-endo**:**  $^1\text{H}$  NMR (acetone- $d_6$ , 300 MHz)  $\delta$  7.66 (m, 2H), 5.68 (d, 1H,  $J = 7.1$  Hz), 5.24 (s, 1H), 5.00 (d, 1H,  $J = 2.3$  Hz), 4.05 (m, 2H), 2.44 (s, 3H), 1.70 (s, 3H), 1.23 (t, 3H,  $J = 7.2$  Hz), 1.09 (t, 3H,  $J = 7.0$  Hz).

**Ethyl [5*R*,5*aR*,6*S*,8*aS*,8*bS*,(*S*)]-6-Ethoxy-2-[(2-acetoxy)ethyl]-3-methyl-8a-p-tolylsulfonfyl-8-oxo-5a,6,8a,8b-tetrahydro-5H,8H-furo[3',4':3,4]pyrrolo[2,1-b][1,3]thiazole-5-carboxylate (*anti*-**14a-endo**).** Compound *anti*-**14a-endo** was obtained as the sole compound

following the general procedure from [5*S*,(*S*)]-5-ethoxy-3-*p*-tolylsulfonfylfuran-2(5*H*)-one (**6a**) and thiazolium salt **2**–HBr after 5 min of reaction. It was purified by flash column chromatography (acetone–hexane, 1:3): yield 78%; white solid; mp 127–129 °C dec;  $[\alpha]_D^{25} = +7.2$  (c 0.75,  $\text{CHCl}_3$ ); IR (KBr) 1769, 1736, 1658, 1117, 1055  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  7.67 and 7.35 (AA'BB' system, 4H), 5.43 (s, 1H), 5.37 (d, 1H,  $J = 1.4$  Hz), 4.47 (d, 1H,  $J = 2.5$  Hz), 4.30 (m, 2H), 3.93 (t, 2H,  $J = 6.6$  Hz), 3.84 (m, 1H), 3.62 (m, 2H), 2.44 (s, 3H), 2.34 (t, 2H,  $J = 6.6$  Hz), 1.98 (s, 3H), 1.70 (s, 3H), 1.37 (t, 3H,  $J = 7.1$  Hz), 1.25 (t, 3H,  $J = 7.1$  Hz);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz)  $\delta$  170.8 (C), 169.3 (C), 167.5 (C), 143.1 (C), 134.2 (C), 132.1 (C), 129.7 (CH), 126.3 (CH), 106.7 (C), 104.9 (CH), 74.0 (C), 71.7 (CH), 66.9 (CH), 65.7 (CH<sub>2</sub>), 62.4 (CH<sub>2</sub>), 62.3 (CH<sub>2</sub>), 53.2 (CH), 26.9 (CH<sub>2</sub>), 21.6 (CH<sub>3</sub>), 20.9 (CH<sub>3</sub>), 14.8 (CH<sub>3</sub>), 14.1 (CH<sub>3</sub>), 12.2 (CH<sub>3</sub>). Anal. Calcd for  $\text{C}_{25}\text{H}_{31}\text{NO}_8\text{S}_2$ : C, 55.85; H, 5.81; N, 2.61; S, 11.93. Found: C, 55.85; H, 5.67; N, 2.52; S, 12.29.

**Ethyl 6-Ethoxy-2-[(2-acetoxy)ethyl]-3-methyl-8a-p-tolylsulfonfyl-8-oxo-5a,6,8a,8b-tetrahydro-5H,8H-furo[3',4':3,4]pyrrolo[2,1-b][1,3]thiazole-5-carboxylate (14b-endo).** Compound **14b-endo** was obtained as a mixture of diastereoisomers *anti*-**14b-endo** and *syn*-**14b-endo** in 75:25 ratio from [5*R*,(*S*)]-5-ethoxy-3-*p*-tolylsulfonfylfuran-2(5*H*)-one (**6b**) and thiazolium salt **2**–HBr after 5 min. They were purified by flash column chromatography (acetone–hexane, 1:3), but they could not be separated. Their spectroscopic data were measured from the NMR spectra of a 75:25 diastereoisomeric mixture: overall yield 75%; IR (neat) 1758, 1737, 1650, 1597, 1083, 1054  $\text{cm}^{-1}$ .

**[5*S*,5*aS*,6*R*,8*aR*,8*bR*,(*S*)]-*anti*-**14b-endo**:**  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  7.49 and 7.28 (AA'BB' system, 4H), 5.75 (s, 1H), 4.99 (d, 1H,  $J = 2.2$  Hz), 4.50 (d, 1H,  $J = 1.6$  Hz), 4.32 (m, 2H), 4.06 (m, 2H), 3.31 (dd, 1H,  $J = 2.2$  and 1.6 Hz), 3.27 (m, 2H), 2.48 (m, 2H), 2.38 (s, 3H), 2.01 (s, 3H), 1.73 (s, 3H), 1.38 (t, 3H,  $J = 7.1$  Hz), 0.83 (t, 3H,  $J = 7.1$  Hz);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz)  $\delta$  170.6 (C), 168.8 (C), 167.7 (C), 142.5 (C), 135.1 (C), 132.5 (C), 129.5 (CH), 125.6 (CH), 106.0 (C), 105.7 (CH), 81.4 (C), 74.1 (CH), 67.2 (CH), 65.0 (CH<sub>2</sub>), 62.2 (CH<sub>2</sub>), 62.1 (CH<sub>2</sub>), 49.4 (CH), 26.8 (CH<sub>2</sub>), 21.2 (CH<sub>3</sub>), 20.7 (CH<sub>3</sub>), 14.3 (CH<sub>3</sub>), 14.0 (CH<sub>3</sub>), 12.0 (CH<sub>3</sub>).

**[5*R*,5*aR*,6*R*,8*aS*,8*bS*,(*S*)]-*syn*-**14b-endo**:**  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  7.61 and 7.35 (AA'BB' system, 4H), 5.43 (d, 1H,  $J = 7.2$  Hz), 5.26 (s, 1H), 5.00 (d, 1H,  $J = 2.0$  Hz), 4.17 (q, 2H,  $J =$



7.1 Hz), 3.96 (m, 2H), 3.87 (m, 1H), 3.78 (dd, 1H,  $J = 7.2$  and 2.0 Hz), 3.69 (m, 1H), 2.43 (s, 3H), 1.99 (s, 3H), 1.71 (s, 3H), 1.30 (t, 3H,  $J = 7.2$  Hz), 1.25 (t, 3H,  $J = 7.1$  Hz).

**Ethyl [8S,(S)S]-2-[2-(Acetyloxy)ethyl]-3-methyl-8-menthyloxy-8a-(phenylsulfonyl)-6-oxo-5a,6,8a,8b-tetrahydro-5H,8H-furo[3',4':3,4]pyrrolo[2,1-b][1,3]thiazole-5-carboxylate (15).** To a stirred solution of (*S,S*)-4-phenylsulfonylfuranone (**7**) (0.55 mmol) in dry acetonitrile (8 mL), under argon at room temperature, was added quickly a solution of ylide **2** (0.8 mmol) in dry acetonitrile (4 mL), freshly prepared by addition of TMP (0.8 mmol) to a suspension of thiazolium salt **2-HBr** (0.9 mmol) in dry acetonitrile (4 mL). After 5 min, dichloromethane was added to the reaction mixture, and it was washed with water. The aqueous layers were extracted with dichloromethane several times. The organic layers were dried ( $\text{Na}_2\text{SO}_4$ ), filtered, and concentrated in vacuo. The  $^1\text{H}$  NMR spectrum shows a mixture of diastereoisomers *anti*-**15-endo** and *syn*-**15-endo** in 93:7 ratio, along with the starting material **7** and other compounds. Diastereoisomers **15** were purified by flash column chromatography (AcOEt–hexane, 1:3).

**[5S,5aR,8S,8aR,8bR,(S)S]-anti-15-endo.** Compound *anti*-**15-endo** was obtained as the major cycloadduct. It was isolated by precipitation of a mixture of isomers *anti*-**15-endo** and *syn*-**15-endo** (86:14) from AcOEt–hexane: yield 39%; mp (AcOEt–hexane) 102–103 °C;  $[\alpha]_{\text{D}}^{20} -50.4$  ( $c$  0.5,  $\text{CHCl}_3$ ); IR (KBr) 1776, 1754, 1726, 1443, 1383, 1311, 1253, 1121, 1043  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  7.83 (m, 2H), 7.53 (m, 3H), 6.04 (s, 1H), 5.97 (s, 1H), 4.55 (d, 1H,  $J = 1.7$  Hz), 4.29–4.07 (m, 4H), 3.63 (dt, 1H,  $J = 10.8$  and 4.1 Hz), 3.53 (d, 1H,  $J = 1.7$  Hz), 2.66 (m, 1H), 2.45 (m, 2H), 2.14 (m, 2H), 2.06 (s, 3H), 1.76–0.80 (m, 15 H), 1.67 (s, 3H), 1.34 (t, 3H,  $J = 7.2$  Hz);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz)  $\delta$  172.8 (C), 170.8 (C), 168.6 (C), 140.9 (C), 133.5 (C); 131.9 (CH), 129.1 (CH), 126.8 (CH), 106.4 (CH), 103.6 (C), 85.0 (CH), 79.4 (C), 71.0 (CH), 65.7 (CH), 62.5 ( $\text{CH}_2$ ), 62.4 ( $\text{CH}_2$ ), 49.1 (CH), 48.5 (CH), 42.6 ( $\text{CH}_2$ ), 34.0 ( $\text{CH}_2$ ), 31.5 (CH), 27.2 ( $\text{CH}_2$ ), 25.0 (CH), 22.6 ( $\text{CH}_2$ ), 22.1 ( $\text{CH}_3$ ), 21.2 ( $\text{CH}_3$ ), 20.9 ( $\text{CH}_3$ ), 16.0 ( $\text{CH}_3$ ), 14.2 ( $\text{CH}_3$ ), 11.6 ( $\text{CH}_3$ ). Anal. Calcd for  $\text{C}_{32}\text{H}_{43}\text{NO}_8\text{S}_2$ : C, 60.64; H, 6.84; N, 2.21; S, 10.12. Found: C, 60.32; H, 6.74; N, 2.19; S, 9.98.

**[5R,5aS,8S,8aS,8bS,(S)S]-syn-15-endo.** Compound *syn*-**15-endo** was obtained as the minor cycloadduct. It could not be isolated diastereoisomerically pure. The spectroscopic parameters were obtained from the spectrum of a 25:75 mixture of *anti*-**15-endo** and *syn*-**15-endo**:  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  7.79 (m, 2H), 7.57 (m, 3H), 5.88 (s, 1H), 5.82 (s, 1H), 4.27–4.08 (m, 4H), 4.00 (d, 1H,  $J = 3.6$  Hz), 3.72 (d, 1H,  $J = 3.6$  Hz), 3.57 (td, 1H,  $J = 10.5$  and 4.0 Hz), 2.72–0.75 (m, 20H), 2.05 (s, 3H), 1.73 (s, 3H), 1.30 (t, 3H,  $J = 7.1$  Hz);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz)  $\delta$  171.9 (C), 170.8 (C), 170.7 (C), 138.2 (C), 136.3 (C), 132.6 (CH), 129.3 (CH), 126.3 (CH), 121.6 (C), 102.2 (CH), 84.1 (CH), 78.0 (C), 76.2 (CH), 67.4 (CH), 63.1 ( $\text{CH}_2$ ), 62.0 ( $\text{CH}_2$ ), 49.5 (CH), 47.9 (CH), 42.0 ( $\text{CH}_2$ ), 34.0 ( $\text{CH}_2$ ), 31.6 (CH), 26.8 ( $\text{CH}_2$ ), 25.1 (CH), 22.8 ( $\text{CH}_2$ ), 22.1 ( $\text{CH}_3$ ), 21.1 ( $\text{CH}_3$ ), 20.8 ( $\text{CH}_3$ ), 16.1 ( $\text{CH}_3$ ), 14.0 ( $\text{CH}_3$ ), 13.9 ( $\text{CH}_3$ ).

**Ethyl [8S,(S)S]-2-[2-(Acetyloxy)ethyl]-3-methyl-8-menthyloxy-8a-(phenylsulfonyl)-6-oxo-5a,6,8a,8b-tetrahydro-5H,8H-furo[3',4':3,4]pyrrolo[2,1-b][1,3]thiazole-5-carboxylates (15').** The compounds were obtained from dipole **2** and [(*S,S*)-5-(*l*)-menthyloxy-4-phenylsulfonylfuran-2(5H)-one (**7'**) following the procedure used

with the corresponding sulfoxide. After 1 min at room temperature, complete transformation of sulfone was observed by TLC. The spectroscopic signals corresponding to adducts *anti*-**15'-endo** and *syn*-**15'-endo** and those of other two possible adducts were observed in a ratio of 71:18:7:4 in the  $^1\text{H}$  NMR spectrum of the crude reaction mixture. The products *anti*-**15'-endo** and *syn*-**15'-endo** were isolated by column chromatography using hexane–ethyl acetate (4:1) as the eluent.

**anti-15'-endo (major):** 61% isolated yield; white solid; mp 89–90 °C (recrystallized from diethyl ether–hexane);  $[\alpha]_{\text{D}}^{20} -34.5$  ( $c$  0.5,  $\text{CHCl}_3$ ); IR (neat) 1781, 1737, 1656, 1585, 1449, 1370, 1223, 1147  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  7.88 (m, 2H), 7.66 (m, 1H), 7.53 (m, 2H), 6.33 (s, 1H), 6.04 (s, 1H), 4.88 (s, 1H), 4.35 (q, 2H,  $J = 7.1$  Hz), 4.23 (s, 1H), 4.06 (m, 2H), 3.40 (dt, 1H,  $J = 10.8$  and 4.3 Hz), 2.54 (m, 1H), 2.42 (m, 1H), 2.16 (m, 1H), 2.03 (s, 3H), 1.72–0.54 (m, 17H), 1.68 (s, 3H), 1.39 (t, 3H,  $J = 7.1$  Hz);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz)  $\delta$  172.9 (C), 170.9 (C), 168.6 (C), 139.0 (C), 134.1 (CH), 133.1 (C); 130.7 (CH), 128.5 (CH), 104.1 (CH), 104.0 (C), 82.3 (CH), 80.8 (CH), 73.6 (CH), 66.2 (CH), 62.8 ( $\text{CH}_2$ ), 62.2 ( $\text{CH}_2$ ), 50.9 (CH), 48.5 (CH), 42.2 ( $\text{CH}_2$ ), 34.0 ( $\text{CH}_2$ ), 31.7 (CH), 26.9 ( $\text{CH}_2$ ), 24.3 (CH), 22.6 ( $\text{CH}_2$ ), 22.0 ( $\text{CH}_3$ ), 21.3 ( $\text{CH}_3$ ), 20.9 ( $\text{CH}_3$ ), 15.8 ( $\text{CH}_3$ ), 14.1 ( $\text{CH}_3$ ), 11.6 ( $\text{CH}_3$ ). Anal. Calcd for  $\text{C}_{32}\text{H}_{43}\text{NO}_8\text{S}_2$ : C, 59.15; H, 6.67; N, 2.16; S, 9.87. Found: C, 59.25; H, 6.69; N, 2.51; S, 9.61.

**syn-15'-endo (minor):** 16%;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  7.98 (m, 2H), 7.75 (m, 1H), 7.60 (m, 2H), 6.14 (s, 1H), 5.82 (s, 1H), 4.31–4.05 (m, 6H), 3.55 (dt, 1H,  $J = 10.6$  and 4.4 Hz), 2.67–0.78 (m, 20H), 2.03 (s, 3H), 1.74 (s, 3H), 1.31 (t, 3H,  $J = 7.1$  Hz);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz)  $\delta$  171.0 (C), 170.8 (C), 170.2 (C), 135.9 (C), 135.1 (CH), 134.9 (C), 130.5 (CH), 129.3 (CH), 119.3 (C), 101.7 (CH), 83.8 (CH), 81.3 (C), 75.5 (CH), 67.3 (CH), 62.9 ( $\text{CH}_2$ ), 62.1 ( $\text{CH}_2$ ), 52.3 (CH), 47.9 (CH), 41.8 ( $\text{CH}_2$ ), 33.9 ( $\text{CH}_2$ ), 31.6 (CH), 26.7 ( $\text{CH}_2$ ), 24.8 (CH), 22.7 ( $\text{CH}_2$ ), 22.1 ( $\text{CH}_3$ ), 21.2 ( $\text{CH}_3$ ), 20.9 ( $\text{CH}_3$ ), 16.0 ( $\text{CH}_3$ ), 14.0 ( $\text{CH}_3$ ), 13.8 ( $\text{CH}_3$ );  $^1\text{H}$  NMR ( $\text{C}_6\text{D}_6$ , 300 MHz)  $\delta$  7.93 (m, 2H), 6.91 (m, 3H), 6.33 (s, 1H), 5.99 (s, 1H), 4.54 (d, 1H,  $J = 3.4$  Hz), 4.29 (d, 1H,  $J = 3.4$  Hz), 3.86 (m, 2H), 3.48 (dt, 1H,  $J = 10.6$  and 4.5 Hz), 2.60–0.60 (m, 20H), 1.68 (s, 3H), 1.55 (s, 3H), 0.92 (t, 3H,  $J = 7.1$ );  $^{13}\text{C}$  NMR ( $\text{C}_6\text{D}_6$ , 75 MHz)  $\delta$  171.1 (C), 170.5 (C), 170.3 (C), 136.7 (C), 136.3 (C), 135.0 (CH), 131.1 (CH), 129.3 (CH), 121.2 (C), 102.2 (CH), 84.4 (CH), 82.2 (C), 77.1 (CH), 68.3 (CH), 63.0 ( $\text{CH}_2$ ), 62.1 ( $\text{CH}_2$ ), 53.5 (CH), 48.8 (CH), 42.6 ( $\text{CH}_2$ ), 34.5 ( $\text{CH}_2$ ), 32.0 (CH), 27.3 ( $\text{CH}_2$ ), 25.5 (CH), 23.3 ( $\text{CH}_2$ ), 22.6 ( $\text{CH}_3$ ), 21.9 ( $\text{CH}_3$ ), 20.8 ( $\text{CH}_3$ ), 16.7 ( $\text{CH}_3$ ), 14.3 ( $\text{CH}_3$ ).

**Acknowledgment.** We thank the Spanish Government (DGICYT, Grant No. CTQ2006-06741/BQU) and Comunidad Autónoma de Madrid (CCG07-UAM/PPQ-1849) for financial support.

**Supporting Information Available:** Experimental procedures and spectroscopic data for compounds **2-HBr** and **13a<sub>1</sub>–13b<sub>2</sub>**, NMR spectra of all new compounds, and crystallographic data for compound *anti*-**15-endo** (CIF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

JO801705D