Asymmetric 1,3-Dipolar Cycloaddition of N-Metalated Azomethine Ylides to Methyl (*S*)-2-(*p*-Tolylsulfinyl)acrylate. Synthesis of Optically Pure 2,4,5-Trisubstituted 2,5-Dihydro-1*H*-pyrroles†

José Luis García Ruano,* Amelia Tito,* and M. Teresa Peromingo

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

joseluis.garcia.ruano@uam.es

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The first 1,3-dipolar reaction of azomethine ylides with optically pure vinyl sulfoxide are reported. The presence of the sulfinyl group increase the reactivity of the acrylate moiety as a dipolarophile, and the reactions evolve with complete regio- and endo-selectivities. Nevertheless, mixtures of the two diastereoisomers **4** and **5** (75−88% de) resulting from the anti dipole/s-cis dipolarophile and syn dipole/s-trans dipolarophile approaches, respectively, are obtained. The stereoselectivity can be controlled by using THF or MeCN as solvents or by changing the reaction temperature in MeCN. After separation of the cycloadducts, optically pure 2,5-dihydro-1*H*-pyrroles are easily obtained by pyrolytic desulfinylation.

Introduction

The importance of substituted pyrrolidines in the chemical synthesis of pharmacologically or biologically interesting molecules is well recognized.[1] The 1,3-dipolar cycloaddition of azomethine ylides to α,β-unsaturated carbonyl compounds is one of the most useful methods for the preparation of these molecules[2] because of their usually high degree of regioselectivity and stereoselectivity.[3] These reactions have been intensively investigated by Grigg[4] and Kanemasa[5] in their racemic version. Dipoles are usually obtained by deprotonation of iminoesters with NEt_3 or DBU in the presence of a silver or lithium salt. The chiral version of this process has been developed in the last years[1b] mainly using optically pure acrylates as dipolarophiles.[4b,6−8]

The good results obtained by us in asymmetric Diels−Alder reaction starting from optically pure vinyl sulfoxides[9] with the sulfinyl group controlling the π-facial selectivity had prompted us to study the [3 + 2] cycloaddition reactions of these substrates with 1,3-dipoles. In this sense we have reported the behavior of some sulfinyl ethylenes with diazoalkanes[10] and nitrile oxides.[11] The described results indicated a very efficient control of the stereoselectivity as well as a substantial increase in the reactivity, but the easy desulfinylation of the resulting adducts restricted the scope of the reaction. On this basis we reasoned that reactions of N-metalated azomethine ylides with sulfinyl acrylates supporting the chiral information at sulfur could become a new entry to the synthesis of highly substituted pyrrolidines, which constitute the main building blocks of many alkaloids and pharmacologically active compounds.[12] If one bears in mind that the dipolarophilic features (reactivity, regioselectivity, and stereoselectivity) of menthyl acrylates were very difficult to be improved, this work initially

† Dedicated to the memory of the late Dr. María Victoria Martín (IQO, CSIC).

* To whom correspondence should be addressed.

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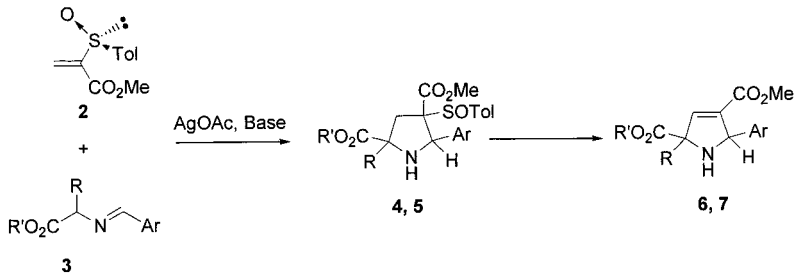
Scheme 1

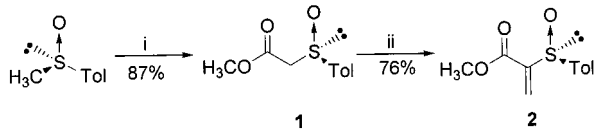


aimed at checking the influence of the sulfinyl group in the course of the cycloadditions with azomethine ylides (to our knowledge, this is the first report concerning reactions of these dipoles with optically pure vinyl sulfoxides[13]), as well as taking advantage of the easy desulfinylation of the adducts in order to synthesize pyrrolines. Nevertheless, the obtained results revealed a stereochemical behavior of the used dipolarophiles highly dependent on the reaction conditions, which can be used for synthetic purposes. In this paper we report the results obtained in reactions of methyl 2-(*p*-tolylsulfinyl)acrylate (**2**) with N-metalated azomethine ylides derived from glycine and alanine **3** and the conversion of the resulting adducts **4** and **5** in optically pure 2,4,5-trisubstituted 2,5-dihydro-1*H*-pyrroles **6** and **7** (Scheme 1).

Results and Discussion

The synthesis of methyl (*S*)-2-(*p*-tolylsulfinyl)acrylate (**2**) was achieved as depicted in Scheme 2 by using optically pure methyl (*R*)-2-(*p*-tolylsulfinyl)acetate (**1**) [ee ≥ 97% was established by ^{1}H NMR with Eu(tfc)$_3$] as the starting material. Compound **1** was readily prepared by

Scheme 2[a]



[a] Key: (i) (a) LHMDS (2 equiv), −78 °C, THF, 0.5 h, (b) $ClCO_2Me$ (1 equiv), −78 °C, THF, 3 h; (ii) (c) HCHO (3 equiv), Me_2NH (3 equiv), MeCN, rt, 48 h, (d) MeI (5 equiv), $CaCO_3$ (3 equiv), MeCN, rt, 90 min.

deprotonation of (*R*)-methyl *p*-tolyl sulfoxide with Li(HMDS) (2 equiv) in THF and further reaction at −78 °C with methyl chloroformate.[14] The Mannich reaction of compound **1** with CH_2O/Me_2NH and further in situ nitrogen quaternization furnished pure olefin **2**.[15]

The results obtained in the 1,3-dipolar cycloadditions of vinyl sulfoxide **2** with the iminoesters **3a**−**d** are depicted in Table 1. All these reactions yielded a mixture of only two adducts, **4** and **5**, which could be easily separated by flash chromatography. In some experiences we could isolate small amounts of the pyrroline **7** resulting from desulfinylation of **5** (see later). Polymerization of the sulfoxide as well as hydrolysis of the dipoles contribute to reduce the isolated yields, which ranged between 50 and 75%.

The reaction of **3a** with the sulfoxide was initially conducted under the reaction conditions reported by Kanemasa[5a] (LiBr/NEt_3 at room temperature) for the reaction of **3a** with methyl acrylate, but only traces of **4a** could be detected because polymerization and decomposition products were predominant in the reaction mixture (entry 1). Better results were obtained under the reactions conditions described in entry 2 [AgOAc (catalyst, 0.075)/DBU (0.6) in THF, 43% yield], which afforded a 65/35 mixture of the cycloadducts **4a** and **5a** in moderate overall isolated yield.[16] If one starts from naphthyl iminoester **3b,** a similar **4b** and **5b** mixture was obtained; however, the crystallization of these adducts is much easier (entries 6 and 7), which suggests that the use of the naphthyl residue at the dipole is much more convenient despite that it does not improve the stereoselectivity of these reactions. In the latter reactions, small amounts of the pyrroline **7b** could also be isolated, as a result of the spontaneous desulfinylation of **5b** (see later). The yields strongly decreased when the reactions were performed at temperatures lower than 0 °C (entries 14 and 15). The best results for R = H were obtained under the conditions reported by Pätzel[8b]—AgOAc/DBU (molar ratio 0.15/1.2) in THF—with combined isolated yields higher than 70% at room temperature or reflux (entries 8 and 10). The expected increase of the stereoselectivity when the temperature decreased was observed, the best result having been obtained at 0 °C (74% de, entry 9).

To know the influence of the 2-*p*-tolylsulfinyl group in the dipolarophilic reactivity of the acrylate **2**, the reaction of methyl acrylate with the iminoester **3b** under the conditions described in entries 8 and 11 has been studied. This reaction requires ca. 48 h to afford the corresponding cis adduct in 75 and 25% yields, respectively. The comparison of these results with those indicated in Table 1 (entries 8 and 11) evidences that the sulfinyl group significantly increases the dipolarophilic reactivity. A

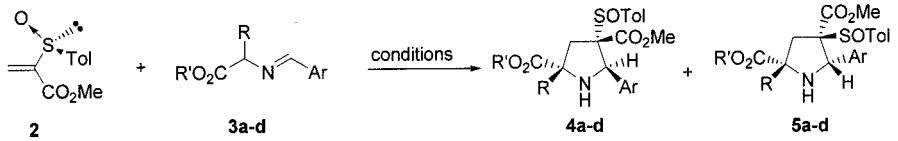
(13) (a) The experiences near to us are the 1,3 DC of (*R*)-*p*-tolyl vinyl sulfoxide with 1-methyl-3-oxidopyridinum, which gave three of the four possible diastereomers (Takahashi, T.; Kitano, K.; Hagi, T.; Nihonmatsu, H.; Koizumi, T. *Chem. Lett.* **1989**, 597), and in the racemic form the case of the vinyl sulfoxide activated by a trifluoromethyl group which undergoes the 1,3 DC with *N*-benzylazomethine ylide (Plancquaert, M. A.; Redon, M.; Janousek, Z.; Viehe, H. G. *Tetrahedron* **1996**, *52*, 4383).

(14) Compound **1** had been previously prepared by methanolysis of the corresponding *tert*-butyl ester (Hiroi, K.; Umemura, M.; Fujisawa, A. *Chem. Pharm. Bull.* **1993**, *41*, 666) or by enzymatic resolution of (±)-**1** (Ohta, H.; Kato, Y.; Tsuchihashi, G. *Chem. Lett.* **1986**, 217). The synthesis of (*R*)-**1** by reaction of the methyl acetate enolate with (*R*)-menthyl sulfinate, according to the procedure used to prepare other α-sulfinyl esters (see ref 21b), was unsuccessful due to the predominant formation of methyl acetoacetate.

(15) The synthesis of compound **2** had been previously described via organoselenium derivatives in 93% ee (Arai, Y.; Kuwayama, S.; Takeuchi, Y.; Koizuni, T. *Tetrahedron Lett.* **1985**, *26*, 6205). Both the yield and the optical purity of the product are improved by our procedure which additionally avoids the use of the highly toxic selenyl halide.

(16) In the absence of the silver salt, these reactions evolve with yields lower than 30% affording 1:1 mixtures of **4a** and **5a**.

Table 1. Asymmetric 1,3 Dipolar Reaction of N-Metalated Azomethine Ylides 3a−d with Chiral Vinyl Sulfoxide 2



2 **3a-d** **4a-d** **5a-d**

		iminoester			conditions				product ratio[a,b]		
entry	no.	Ar	R	R′	salt/base (equiv)	solvent	*T* (°C)	*t* (h)	**4**	**5**	**7**
1	**3a**	Ph	H	Me	LiBr/Et_3N (1.5/1.2)	THF	rt	1.0	100 (3)		
2	**3a**	Ph	H	Me	AgOAc/DBU (0.075/0.6)	THF	rt	0.2	65 (28)	35 (15)	
3	**3a**	Ph	H	Me	AgOAc/DBU (0.15/1.2)	THF	0	0.2	72 (32)	28 (13)	
4	**3a**	Ph	H	Me	AgOAc/DBU (1.5/1.0)	MeCN	0	0.65	27 (13)	73 (36)	
5	**3a**	Ph	H	Me	AgOAc/DBU (1.5/1.0)	MeCN	reflux	0.6	70 (34)	30 (14)	
6	**3b**	Nph	H	Me	AgOAc/DBU (0.075/0.6)	THF	rt	0.3	64 (35)	33 (19)	
7	**3b**	Nph	H	Me	AgOAc/DBU (0.075/0.6)	THF	0	3	70 (40)	25 (14)	5 (3)
8	**3b**	Nph	H	Me	AgOAc/DBU (0.15/1.2)	THF	rt	0.25	72 (56)	28 (21)	
9	**3b**	Nph	H	Me	AgOAc/DBU (0.15/1.2)	THF	0	0.5	87 (50)	13 (8)	
10	**3b**	Nph	H	Me	AgOAc/DBU (0.15/1.2)	THF	reflux	inst	62 (46)	38 (28)	
11	**3b**	Nph	H	Me	AgOAc/DBU (1.5/1.0)	MeCN	rt	0.5	19 (12)	81 (51)	
12	**3b**	Nph	H	Me	AgOAc/DBU (1.5/1.0)	MeCN	reflux	inst	90 (51)	10 (6)	
13	**3c**	Nph	Me	Me	AgOAc/DBU (0.075/0.6)	THF	0	3.0	72 (43)	28 (16)	
14	**3c**	Nph	Me	Me	AgOAc/DBU (0.075/0.6)	THF	−20	2.5	75 ((19)	25 (6)	
15	**3c**	Nph	Me	Me	AgOAc/DBU (0.075/0.6)	THF	−40	3.5	68 (18)	32 (9)	
16	**3c**	Nph	Me	Me	AgOAc/DBU (1.0/0.6)	THF	0	1.0	75 (39)	25 (13)	
17	**3c**	Nph	Me	Me	AgOAc/DBU (0.15/1.2)	THF	rt	0.5	90 (47)	10 (5)	
18	**3c**	Nph	Me	Me	AgOAc/DBU (0.15/1.2)	THF	0	1.0	80 (39)	20 (10)	
19	**3c**	Nph	Me	Me	AgOAc/DBU (0.15/1.2)	THF	reflux	inst	78 (41)	22 (12)	
20	**3d**	Nph	Me	Et	AgOAc/DBU (0.15/1.2)	THF	0	0.5	83 (44)	17 (9)	
21	**3d**	Nph	Me	Et	AgOAc/DBU (1.0/0.6)	THF	rt	inst	73 (38)	23 (14)	4
22	**3d**	Nph	Me	Et	AgOAc/DBU (0.075/0.6)	MeCN	rt	1	42 (25)	58 (34)	
23	**3d**	Nph	Me	Et	AgOAc/DBU (0.075/0.6)	MeCN	0	1.0	32 (20)	64 (42)	4
24	**3d**	Nph	Me	Et	AgOAc/DBU (1.5/1.0)	MeCN	rt	0.5	20 (12)	80 (49)	
25	**3d**	Nph	Me	Et	AgOAc/DBU (1.5/1.0)	MeCN	0	0.7	25 (15)	75 (44)	
26	**3d**	Nph	Me	Et	AgOAc/Et3N (1.5/1.0)	MeCN	rt	0.4	18 (11)	80 (48)	2
27	**3d**	Nph	Me	Et	AgOAc/DBU (1.5/1.0)	MeCN	reflux	inst	94 (50)	6 (3)	

[a] Determined by ^1H NMR from the reaction crude. [b] Isolated yield in parentheses (%).

similar conclusion can be drawn by comparison of the reaction time of entry 11 with that described for the menthyl acrylate,[17] which requires 2 h under the same conditions.

The use of α-alkyl-substituted iminoesters **3c,d** as dipoles afforded quite similar results, indicating that the presence of the methyl group instead of the hydrogen atom scarcely modifies the reactivity and stereoselectivity of the dipoles in these reactions. Thus, reaction of **3c** with **2** under AgOAc/DBU in THF affords mixtures of **4c** and **5c** similar to those obtained from **3b** under the same conditions (compare entries 7 and 13). In this case we have checked that the polymerization processes are favored when reaction temperature decreased and, therefore, the isolated yields of the adducts decreased. On the contrary, the stereoselectivity was not substantially affected by changes in the temperature (entries 13−15). The use of stoichiometric amounts of AgOAc slightly reduced the reaction times but scarcely affected either the stereoselectivity or the yield (compare entries 13 and 16). Once again, the use of the conditions reported by Pätzel[8b] [AgOAc/DBU (0.15/1.2)] improved the stereoselectivity (entries 17 and 18), which was the highest at room temperature (80% de, entry 17). The use of ethyl ester **3d** as the dipole instead of the corresponding methyl one **3c** merely solved the problem derived from the identification by ^1H NMR of the two carbomethoxy groups in the adducts **4c** and **5c**, but it had not any influence in the reaction results (compare entries 18 and 20).

When the reactions of **3d** with **2** were carried out in MeCN instead of THF as the solvent, a complete inversion of the stereoselectivity was observed,[18] and mixtures of **4d** and **5d**, the latter being the major product, were obtained (entries 22−26). The stereoselectivity increased as the temperature decreased (compare entries 22 and 23) but mainly when the AgOAc was used in higher than stoichiometric amounts (entries 24 and 25), even in the case that Et_3N instead of DBU was used as the base (entry 26). This change in the stereoselectivity promoted by the solvent had not been observed in reactions using menthyl esters as dipolarophiles,[6c] which suggests that the sulfinyl group must play some role in this behavior.

Finally, when the reaction of **3d** with **2** was conducted in refluxing MeCN (entry 27), an inversion of the stereoselectivity was also observed and the adduct **4d** was obtained as the major one with 88% de, higher than those obtained in THF at any temperature. Reactions of **2** with **3a,b** were also studied in MeCN. At rt (room temperature) or 0 °C, the stereoselectivity was the opposite to that observed in THF (entries 4 and 11), whereas under reflux of MeCN the adduct obtained as the major one was the same as in THF (entries 5 and 12), the highest de having been obtained on starting from **3b** (80%, entry 12).

The main synthetic conclusion that can be withdrawn from these results is the fact that the use of compound **2** as a dipolarophile allows the synthesis of the adducts **4** or **5** as the major ones by changing the solvent (THF or

(17) Barr, D. A.; Dorrity, M. J.; Grigg, R.; Hargreaves, S.; Malone, J. F.; Montgomery, J.; Redpth, J.; Stevenson, P.; Thornton-Pett, M. *Tetrahedron* **1995**, *51*, 273.

(18) The use of $PhCH_3$ as the solvent afforded results similar to those obtained in THF.

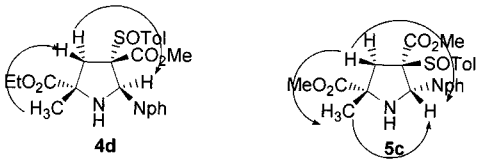


Figure 1.

MeCN) or the temperature (when MeCN was used as the solvent). This is a clear advantage of alkyl 2-(*p*-tolylsulfinyl)acrylates with respect to menthyl acrylates as dipolarophiles, as the latter are only suitable to obtain one kind of adducts.

The relative stereochemistry of the substituents Ar and CO_2R' was assigned trans for compounds **4** and cis for compounds **5** on the basis of NOESY experiments (Figure 1). The absolute configuration was unequivocally assigned by single-crystal X-ray analysis[19] of **4d** and **5c** (Supporting Information). The homochiral integrity of the adducts **4c,d** (≥99% ee) was established by chiral HPLC.[20] Under the same HPLC conditions, decomposition of the adducts **5** was observed, thus precluding to establish their ee's in this step (see later). Racemic compounds required for these studies were prepared by reaction of the racemic vinyl sulfoxide (±)-**2** with the corresponding iminoesters **3**.

Once the absolute configuration of the cycloadducts **4** and **5** had been unequivocally assigned, we could conclude that all the reactions were completely regioselectively (only one regioisomer was detected) and endoselectively controlled by the ester group (Ar and CO_2Me at C-4 are in a cis arrangement in both adducts). The change of the solvent determines the inversion of the π-facial selectivity at dipolarophile and, simultaneously, the syn → anti isomerization of the dipole. The fact that the favored approach of the dipole takes place from a different face of the dipolarophile depending on the solvent used (THF or MeCN) could be explained by taking into account the relative polarity of both solvents (higher for MeCN) and their different abilities to become associated with the metal (higher for THF). Thus, conformation **A** (Figure 2), exhibiting the highest dipolar moment, must be relatively stabilized in the more polar solvent (MeCN). This preference will be stronger as a consequence of the weak association of the metal with both oxygen atoms at vinyl sulfoxide. In THF, such a weak association will be less important due to the higher ability of the solvent to stabilize the metal. In addition, the low polarity of this solvent determines the conformational shift toward the rotamer with the sulfinyl oxygen in an *s*-cis arrangement (**B** in Figure 2) to minimize the electrostatic repulsion between the oxygens.[21] At this conformation, the metal must be associated only with the sulfinyl oxygen, the most basic center at the dipolarophile. As we can see in Figure 2, the less hindered face is different for both conformations, which would explain that the π-facial selectivity was the opposite in THF and CH_3CN. Additionally, the configuration at C-4 of the major adduct obtained in each case (**4** in THF and **5** in MeCN) is that predicted from this stereochemical model.

Taking into account that the cis arrangement of the substituents at C-2 and C-5 for the adducts **5**, obtained as the major ones in MeCN at room temperature, is coincident with that observed in reactions of menthyl acrylate with several N-metalated azomethine ylides, which evolved with high endo and diastereofacial selectivities (de's up to 95%), the formation of **5** could be explained by assuming the endo approach of the dipoles **3**, which adopt the syn structure in MeCN (it was proposed to explain the evolution of the reactions with menthyl acrylate[6c]), to the less hindered face of the sulfoxide **2** in conformation **A** (Figure 2), which is favored in this solvent. As both moieties are stabilized with the metal, it is not surprising that the best conditions for these reactions require the use of more than 1 equiv of AgOAc.

The trans relationship between the aryl and CO_2Me (at C-2) groups in cycloadducts **4**, favored in THF, can only be explained by assuming that the dipoles **3** will adopt an anti stereochemistry before reacting with the sulfoxide. Despite the large number of papers concerning reactions of N-metalated azomethine ylides, this is the first case where it is observed that the change in solvent modifies the stereoselectivity.[22] Therefore, we propose this change must be related to the nature of the used dipolarophile. The equilibrium between the syn and anti arrangements of the dipole must be shifted toward the latter, mainly due to the formation of a weakly chelated species. All the reactions of menthyl acrylates usually evolve through the syn dipoles thus yielding adducts with the aromatic and the ester at C-2 in a cis arrangement. The nucleophilic ability of the sulfinyl oxygen, higher in THF than in MeCN due to the most efficient solvation of the latter, must be able to break the weak chelation of the syn dipole, allowing its equilibration with the anti dipole, which would be the most reactive one due to the partial association of the metal with the sulfinyl oxygen at the dipolarophile and the carbonyl oxygen at the dipole (Figure 2).[23]

The retro-1,3-dipolar cycloaddition[24] could account for the change observed in the π-facial selectivity when reactions are conducted in refluxing MeCN. To check this proposal, we have dissolved diastereomerically pure adduct **5b** in MeCN and refluxed the solution for 10 min in the presence of AgOAc/DBU (1.5/1.0 equiv). As a result, a 83:17 mixture of **4b**/**5b** was isolated, which is similar to that obtained under the conditions described in the entry 12 (Table 1). An almost identical result was

(19) The authors have deposited atomic coordinates for **4d** and **5c** with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, U.K.

(20) Chiral HPLC was performed on a Chiralcel OD column (Daicel) eluting with 90:10 hexane/2-propanol and a flow rate of 0.5 mL/min.

(21) (a) Tietze, L. F.; Schuffenhauer, A.; Schreiner, P. R. *J. Am. Chem. Soc.* **1998**, *120*, 7952. (b) Alonso, I.; Carretero, J. C.; García Ruano, J. L. *J. Org. Chem.* **1993**, *58*, 3231 and references therein.

(22) The formation of the adducts resulting from the evolution of syn and anti dipoles has been reported for N-metalated azomethine ylides derived from aliphatic aldehydes[6a] as well as in reactions conducted in refluxing toluene.[5a]

(23) Other alternative explanations, such as those involving a nonconcerted mechanism but a Michael type reaction followed by the intramolecular attack of the anionic intermediate to the C=N bond (proposed in reactions of nitroalkenes with N-metalated azomethine ylides (Ayerbe, M.; Arrieta, A.; Cossío, F. P. *J. Org. Chem.* **1998**, *63*, 1795), have also been considered to explain the stereochemistry of the adduct **4**. Nevertheless, the formation of the intermediate Michael products was not observed by NMR, which allows us to discard this evolution. However, this is not unexpected taking into account that the ionic structure of such intermediates should not be favored in low-polarity solvents, such as THF, which is the solvent where the formation of **4** is predominant.

(24) (a) Szöllösy, Á.; Yischer, T.; Kádas, I.; Töke, L.; Tóth, G. *Tetrahedron* **1999**, *55*, 7279. (b) Tsuge, O.; Kanemasa, S.; Takenaka, S. *Bull. Chem. Soc. Jpn.* **1985**, *58*, 3137.

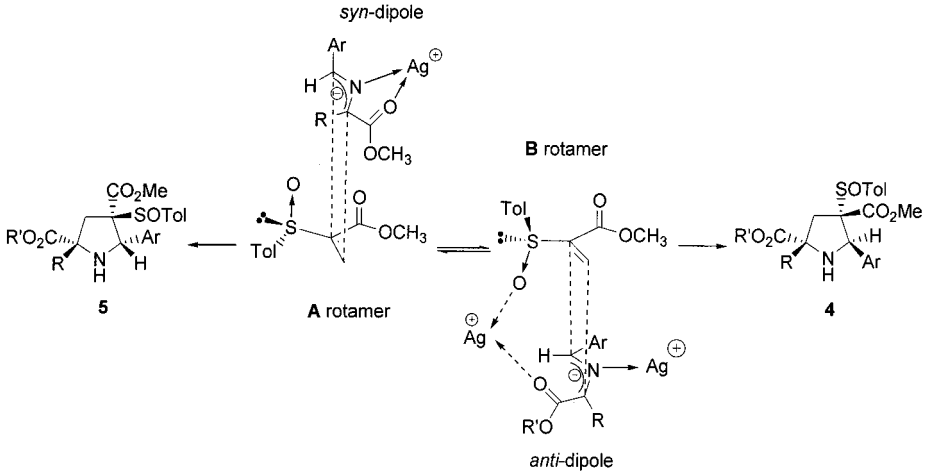
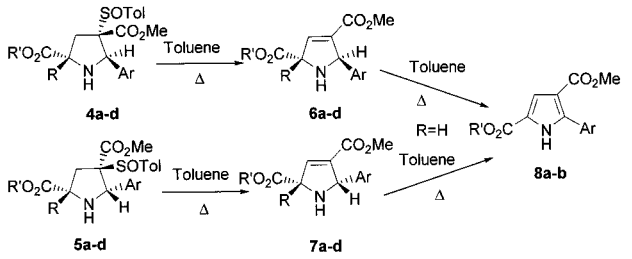


Figure 2.

obtained starting from diastereomerically pure **5c**. When the same test was performed from **5c** in THF at room temperature, we observed the formation of a quite small amount of **4c** (less than 15%) after 1 h. It suggests that cycloreversion is much more difficult in THF and is not significant to explain the results observed under the conditions collected in Table 1.

Finally, we have studied the conversion of the diasteromerically pure sulfinylpyrrolidines **4** and **5** into their corresponding 2,5-dihydro-1*H*-pyrroles derivatives by pyrolytic desulfinylation. This transformation was readily made by heating **4** or **5** in refluxing toluene. The obtained results are indicated in Table 2.

Table 2. Desulfinylation of Pyrrolidines 4 and 5



entry	starting compound	reaction time (h)	products (isolated yield, %)
1	**4c**	3	**6c** (86)
2	**4d**	3	**6d** (89)
3	**4a**	2.5	**6a** (73)
4	**4b**	2.5	**6b** (77)
5	**4a**	3	**6a** (68) + **8a** (17)
6	**4b**	3	**6b** (74) + **8b** (18)
7	**5c**	2	**7c** (91)
8	**5d**	2	**7d** (92)
9	**5a**	1.5	**7a** (81)
10	**5b**	1.5	**7b** (86)
11	**5a**	2	**7a** (73) + **8a** (18)
12	**5b**	2	**7b** (76) + **8b** (19)

As we can see, an almost complete desulfinylation is observed in ca. 3 h, affording **6** and **7,** respectively, in high yields. The pyrrolidines **5** require shorter reaction times to be transformed into **7** as it could be demonstrated by studying the evolution of an equimolecular mixture of **4c** + **5c**. After 1 h, **5c** had been transformed into **7c** in 67% whereas **4c** affords **6c** only in 19%. Moreover, the reaction was completed after 2 h for **5c** into **7c**, whereas only 39% of **4c** had been transformed into **6c**. This conclusion, which can be rationalized taking into account the higher steric congestion of the adducts **5** with three groups at cis arrangement, would account for the fact that only pyrrolines **7** were detected in the reactions mixtures obtained in some cycloadditions (see Table 1). The regioselectivity of the desulfinylation is complete, with exclusive formation of the 2,5-dihydropyrrole instead of the most conjugated 4,5-dihydroderivative, which could be a consequence of the stereochemical requirements of the syn-pyrolytic elimination, because of the eclipsing interactions of the groups Ar and CO_2-Me which unstabilize the TS affording 4,5-dihydropyrroles. The homochirality of the pyrrolines **7c,d** has been confirmed by chiral HPLC.[25]

As a conclusion, we can state that the 2-(*p*-tolylsulfinyl)acrylates exhibit very good features as chiral dipolarophiles. Compound **2** exhibits a higher reactivity with N-metalated azomethine ylides than its corresponding acrylates. On the other hand, the presence of the sulfinyl group completely controls the regio- and endo- selectivities. Moreover, these reactions yield easily separable mixtures of diastereoisomers resulting from the approaches of the syn dipole to the less hindered face of the sulfoxide in its s-trans conformation and the anti dipole to the less hindered face of the sulfoxide in its s-cis conformation. As this facial stereoselectivity can be efficiently controlled by the solvent (THF or MeCN) or by increasing the temperature (in MeCN), it can be advantageously used to prepare pyrrolidines with both trans and cis arrangements at the C-2 and C-5 positions. Moreover, the easy and completely regioselective desulfinylation of the resulting pyrrolidines allows the synthesis of optically pure 2,5-1*H*-pyrroles in high yields The use of these compounds as precursors of Kainic acid derivatives[26] is currently under study in our laboratory.

Experimental Section

General Methods. All moisture-sensitive reactions were performed in flame-dried glassware equipped with rubber septa under a positive pressure of argon. THF and diethyl ether were distilled from sodium−benzophenone under argon and CH_2Cl_2 over P_2O_5. Flash chromatography was carried out

(25) Chiral HPLC was performed on a Chiralcel OD column (Daicel) eluting with 99:1 hexane/2-propano1 and a flow rate of 0.1 mL/min.

(26) Rubio, A.; Ezquerra, J.; Escribano, A.; Ramuiñán, M. J.; Vaquero, J. J. *Tetrahedron Lett.* **1998**, *39*, 2171.

with silica gel Merck 60 (230−400 mesh ASTM). HPLC analysis were performed on a Chiralcel OD (Daicel) column. NMR spectra were determined in $CDCl_3$ solution at 200.1 and 50.3 MHz for ^1H and ^{13}C NMR, respectively.

Methyl (+)-(*R*)-(p-Tolylsulfinyl)acetate (1). To a solution of HMDS (39 mmol) in THF (150 mL) at −78 °C under argon was added *n*-butyllithium (1.98 M in hexane, 19.7 mL, 39 mmol), which was then diluted in THF (30 mL). The mixture was stirred at −78 °C for 30 min, and a solution of (+)-(*R*)-methyl *p*-tolyl sulfoxide[27] (39 mmol) in THF (30 mL) was added. After the mixture had been stirred at −78 °C for 30 min, methyl chloroformate (19 mmol) was added and the reaction mixture was further stirred at −78 °C for 3 h. When the reaction was completed (checked by TLC ethyl acetate−hexane, 1:2) 300 mL of saturated aqueous ammonium chloride was added. The organic layer was diluted with ethyl acetate (3 × 100 mL) and was added to 10% aqueous HCl (2 × 50 mL). The combined organic extracts were washed with saturated aqueous NaCl, dried over anhydrous $MgSO_4$, filtered, and evaporated in vacuo to yield a light yellow oil, which was purified by column chromatography (ethyl acetate−hexane, 1:2) to give the methyl ester **1** (3.59 g, 87% yield) (ee ≥ 97%, Eu(tfc$_3$) 0.4 equiv): $[\alpha]^{25}_D$ +193 (*c* 1.75, MeOH) (lit.[14] $[\alpha]^{25}_D$ +193 (*c* 1.75, MeOH)); ^1H NMR δ 7.49 and 7.26 (AA′BB′ system, 4H, Tol), 3.76 (d, 1H, J = 13.4, CH−SO), 3.62 (s, 3H, CO_2Me), 3.6 (d, 1H, J = 13.4, CH−SO), 2.33 (s, 3H, CH_3−Tol); ^{13}C NMR δ 164.9, 141.9, 139.4, 129.7, 123.7, 61.0, 52.2, 21.0.

Methyl (+)-(*S*)-2-(p-Tolylsulfinyl)acrylate (2). A solution of methyl (+)-(*R*)-(*p*-tolylsulfinyl)acetate (17 mmol) in MeCN (70 mL) was stirred at room temperature. Dimethylamine 40% solution in water (51 mmol) and formaldehyde 37% solution in water (51 mmol) were added to the above solution. The reaction mixture was stirred at room temperature for 2 days. When the reaction was completed (checked by TLC ethyl acetate−hexane, 1:4), 400 mL of water was added and the organic layer was diluted with dichloromethane (3 × 100 mL) and extracted. The organic layers were combined, dried over anhydrous $MgSO_4$, filtered, and evaporated in vacuo to yield a light yellow oil. To this oil was added MeCN (70 mL), which was then stirred at room temperature. Methyl iodide (85 mmol, 5 equiv) and calcium carbonate (51 mmol, 3 equiv) were added to the above solution, and the reaction mixture was further stirred for 90 min. When the reaction was completed (checked by TLC ethyl acetate−hexane, 1:4), 400 mL of water was added and the crude product was extracted with dichloromethane (3 × 100 mL). The organic layers were combined, dried over anhydrous $MgSO_4$, filtered, and evaporated in vacuo to yield a yellow oil, which was purified by column chromatography (ethyl acetate−hexane, 1:4) to give the methyl (+)-(*S*)-2-(*p*-tolylsulfinyl)acrylate (2.6 g, 76% yield): $[\alpha]^{20}_D$ +262 (*c* 0.68, $CHCl_3$) (ee ≥ 97%, Eu(tfc)$_3$ 0.4 equiv) (lit.[15] $[\alpha]^{20}_D$ +263 (*c* 0.68, $CHCl_3$)); IR ($CHCl_3$) 1720, 1450 cm^{-1}; ^1H NMR δ 7.64 and 7.30 (AA′BB′ system 4H, Tol), 6.89 (s, 1H, CH), 6.80 (s, 1H, CH), 3.74 (s, 3H, CO_2Me), 2.41 (s, 3H, CH_3−Tol); ^{13}C NMR δ 162.2, 147.3, 142.3, 139.7, 129.8, 128.1, 125.9, 52.2, 21.4.

Preparation of Imine 3a. Imine from benzaldehyde and the methyl ester of the amino acid glycine as it hydrochloride salt was prepared according to the literature procedure[5a] heating to reflux 21 h and without further distillation.

Preparation of Imines 3b−d. Imines from 2-naphthaldehyde and the ester of the corresponding amino acid glycine[4] or alanine[6b] as its hydrochloride salt were prepared according to literature procedures increasing the reactions times to 4 days.

Asymmetric 1,3-Dipolar Cycloaddition Reactions.

General Procedure. A solution of iminoester (1 equiv) in MeCN and AgOAc (1.5 equiv) was stirred for 10 min, and DBU (1 equiv) was added to the above solution. The reaction mixture was stirred for 10 min before the addition of the methyl (+)-(*S*)-2-(*p*-tolylsulfinyl)acrylate (1 equiv) in MeCN. When the reaction was completed (checked by TLC ethyl acetate−hexane, 1:2), saturated aqueous ammonium chloride was added. The products were extracted with diethyl ether. The combined organic extracts were washed with saturated aqueous NaCl, filtered, dried over anhydrous $MgSO_4$, and evaporated. The yellow oil was purified by flash column chromatography (ethyl acetate−hexane, 1:5) to give a mixture of cycloadducts **4** and **5**.

Dimethyl (−)-(2*S*,4*S*,5*R*,*S*$_S$)-5-Phenyl-4-(*p*-tolylsulfinyl)-pyrrolidine-2,4-dicarboxylate (4a): yellow oil; $[\alpha]^{20}_D$ −22 (*c* 0.2, $CHCl_3$); IR ($CHCl_3$) 3490, 1720 cm^{-1}; ^1H NMR δ 7.46−7.19 (m, 4H Tol and 5H, Ph), 4.95 (s, 1H, CH−Ph), 4.15 (dd, 1H, J = 8.7, J = 6.3, CH−CO_2Me), 3.79 (s, 3H, CO_2Me), 3.20 (s, 3H, CO_2Me), 2.66 (dd, 1H, J = 13.8, J = 6.3, CH), 2.37 (dd, 1H, J = 13.8, J = 8.7, CH), 2.33 (s, 3H, CH_3Tol); ^{13}C NMR δ 174.5, 168.0, 142.2, 138.2, 136.9, 129.6, 128.3, 128.2, 127.3, 125.4, 80.2, 66.4, 57.7, 52.4, 51.6, 28.3, 21.3; MS (FAB) *m*/*z*: 402 (MH^+). Anal. Calcd for $C_{21}H_{23}NO_5S$: C, 62.82; H, 5.77; N, 3.49; S, 7.99. Found: C, 62.68; H, 5.82; N, 3.51; S, 8.11.

Dimethyl (−)-(2*S*,4*R*,5*S*,*S*$_S$)-5-Phenyl-4-(*p*-tolylsulfinyl)-pyrrolidine-2,4-dicarboxylate (5a): yellow oil; $[\alpha]^{20}_D$ −28 (*c* 0.2, $CHCl_3$); IR ($CHCl_3$) 3340, 1730 cm^{-1}; ^1H NMR δ 7.43−7.19 (m, 4H, Tol and 5H, Ph), 4.91 (s, 1H, CH−Ph), 4.03 (dd, 1H, J = 10, J = 6.3, CH−CO_2Me), 3.72 (s, 3H, CO_2Me), 3.18 (s, 3H, CO_2Me), 2.87 (dd, 1H, J = 14, J = 10, CH), 2.33 (s, 3H, CH_3Tol), 2.22 (dd, 1H, J = 14, J = 6.3, CH); ^{13}C NMR δ 173.3, 168.2, 142.2, 137.0, 136.8, 129.6, 128.4, 127.0, 125.4, 79.5, 68.2, 58.5, 52.2, 51.6, 29.8, 21.3; MS (FAB) *m*/*z* 402 (MH^+). Anal. Calcd for $C_{21}H_{23}NO_5S$: C, 62.82; H, 5.77; N, 3.49; S, 7.99. Found: C, 62.78; H, 5.72; N, 3.62; S, 7.72.

Dimethyl (−)-(2*S*,4*S*,5*R*,*S*$_S$)-5-(2-Naphthyl)-4-(*p*-tolylsulfinyl)pyrrolidine-2,4-dicarboxylate (4b): yellow needles (ether−hexane), mp 112−114 °C; $[\alpha]^{20}_D$ −21 (*c* 0.2, $CHCl_3$); IR ($CHCl_3$) 3510, 1734 cm^{-1}; ^1H NMR δ 7.98−7.40 (m, 7H, Nph), 7.38 and 7.22 (AA′BB′ system, 4H, Tol), 5.15 (s, 1H, CH−Nph), 4.25 (dd, 1H, J = 8.7, J = 6.5, CH−CO_2Me), 3.84 (s, 3H, CO_2-Me), 3.13 (s, 3H, CO_2Me), 2.75 (dd, 1H, J = 14, J = 6.5, CH), 2.44 (dd, 1H, J = 14, J = 8.7, CH), 2.36 (s, 3H, CH_3Tol); ^{13}C NMR δ 174.5, 168.0, 142.2, 136.8, 135.5, 133.3, 133.1, 129.6, 128.0, 127.9, 127.7, 126.5, 126.1, 126.0, 125.4, 125.1, 80.3, 66.5, 57.7, 52.5, 51.6, 28.3, 21.3; MS (FAB) *m*/*z* 452.2 (MH^+). Anal. Calcd for $C_{25}H_{25}NO_5S$: C, 65.50; H, 5.58; N, 3.10; S, 7.10. Found: C, 65.82; H, 5.46; N, 2.98; S, 7.24.

Dimethyl (−)-(2*S*,4*R*,5*S*,*S*$_S$)-5-(2-Naphthyl)-4-(*p*-tolylsulfinyl)pyrrolidine-2,4-dicarboxylate (5b): yellow needles (ether−hexane), mp 95−96 °C; $[\alpha]^{20}_D$ −35 (*c* 0.2, $CHCl_3$); IR ($CHCl_3$) 3550, 1737 cm^{-1}; ^1H NMR δ 7.93−7.44 (m, 7H, Nph), 7.42 and 7.20 (AA′BB′ system 4H, Tol), 5.10 (s, 1H, CH−Nph), 4.12 (dd, 1H, J = 10, J = 6, $CHCO_2Me$), 3.77 (s, 3H, CO_2Me), 3.10 (s, 3H, CO_2Me), 2.95 (dd, 1H, J = 14, J = 10, CH), 2.34 (s, 3H, CH_3Tol), 2.30 (dd, 1H, J = 14, J = 6, CH); ^{13}C NMR δ 173.3, 168.3, 142.3, 137.0, 134.2, 133.4, 133.2, 129.8, 128.2, 128.0, 127.7, 126.4, 126.3, 125.5, 124.8, 124.6, 79.7, 68.4, 58.5, 52.3, 51.8, 29.8, 21.3; MS (FAB) *m*/*z* 452.2 (MH^+). Anal. Calcd for $C_{25}H_{25}NO_5S$: C, 65.50; H, 5.58; N, 3.10; S, 7.10. Found: C, 65.35; H, 5.62; N, 2.99; S, 7.14.

Dimethyl (−)-(2*S*,4*S*,5*R*,*S*$_S$)-2-Methyl-5-(2-naphthyl)-4-(*p*-tolylsulfinyl)pyrrolidine-2,4-dicarboxylate (4c): yellow needles (ether−hexane), mp 120 °C; $[\alpha]^{20}_D$ −42 (*c* 0.2, $CHCl_3$) (ee ≥ 99%, HPLC); IR ($CHCl_3$) 3450, 1720 cm^{-1}; ^1H NMR δ 8.06−7.44 (m, 7H, Nph), 7.40 and 7.25 (AA′BB′ system, 4H, Tol), 5.05 (s, 1H, CH−Nph), 3.87 (s, 3H, CO_2Me), 3.04 (s, 3H, CO_2Me), 3.12 (d, 1H, J = 14, CH), 2.27 (d, 1H, J = 14, CH), 2.37 (s, 3H, CH_3−Tol), 1.59 (s, 3H, CH_3); ^{13}C NMR δ 177.2, 168.2,142.1, 136.9, 135.5, 133.3, 133.1, 129.5, 127.9, 127.6, 127.5, 126.4, 126.0, 125.9, 125.4, 125.3, 81.0, 68.0, 63.9, 61.9, 52.6, 36.1, 27.9, 21.3, 14.1; MS (FAB) *m*/*z* 466 (MH^+). Anal. Calcd for $C_{26}H_{27}NO_5S$: C, 67.08; H, 5.85; N, 3.01; S, 6.89. Found: C, 66.99; H, 5.75; N, 2.93; S, 7.02.

Dimethyl (−)-(2*S*,4*R*,5*S*,*S*$_S$)-2-Methyl-5-(2-naphthyl)-4-(*p*-tolylsulfinyl)pyrrolidine-2,4-dicarboxylate (5c): yellow needles (ether−hexane), mp 110−112 °C; $[\alpha]^{20}_D$ −57 (*c* 0.2, $CHCl_3$); IR ($CHCl_3$) 3440, 173 cm^{-1}; ^1H NMR δ 8.06−7.44 (m, 7H, Nph), 7.40 and 7.25 (AA′BB′ system, 4H, Tol), 5.11 (s, 1H, CH−Nph), 3.80 (s, 3H, CO_2Me), 3.18 (s, 3H, CO_2Me), 2.65 (d, 1H, J = 14, CH), 2.46 (d, 1H, J = 14, CH), 2.37 (s, 3H, CH_3−

(27) Carreño, M. C.; García Ruano, J. L.; Martín, A. M.; Pedregal, C.; Rodriguez, J. H.; Rubio, A.; Sánchez, J.; Solladiè, G. *J. Org. Chem.* **1990**, *55*, 2120.

Tol), 1.63 (s, 3H, CH_3); ^{13}C NMR δ 177.0, 168.0, 142.3, 137.3, 136.5, 133.3, 133.1, 129.4, 127.8, 127.8, 127.6, 126.5, 126.3, 126.0, 125.1, 125.0, 81.0, 67.0, 64.0, 52.7, 51.1, 34.2, 21.33; MS (FAB) *m/z* 466 (MH^+). Anal. Calcd for $C_{26}H_{27}NO_5S$: C, 67.08; H, 5.85; N, 3.01; S, 6.89. Found: C, 67.06; H, 6.13; N, 2.84; S, 7.37.

2-Ethyl 4-Methyl (−)-(2*S*,4*S*,5*R*,*S*$_S$)-2-Methyl-5-(2-naphthyl)-4-(*p*-tolylsulfinyl)pyrrolidine-2,4-dicarboxylate (4d): yellow needles (ether−hexane), mp 127−129 °C; $[\alpha]^{20}_D$ −36 (*c* 0.2, $CHCl_3$) (ee ≥ 99%, HPLC); IR ($CHCl_3$) 3440, 1730 cm^{-1}; ^{1}H NMR δ 8.06−7.44 (m, 7H, Nph), 7.40 and 7.25 (AA′BB′ system, 4H, Tol), 5.14 (s, 1H, CH−Nph), 4.24 (q, 2H, CH_2–O, *J* = 7.0), 3.55 (d, 1H, *J* = 14, CH), 3.20 (s, 3H, CO_2Me), 2.66 (d, 1H, *J* = 14, CH), 2.37 (s, 3H, CH_3−Tol), 1.67 (s, 3H, CH_3), 1.38 (t, 3H, CH_3–CH_2, *J* = 7.0); ^{13}C NMR δ 177.0, 168.0, 142.0, 137.1, 135.4, 133.3, 133.1, 129.5, 127.9, 127.6, 127.5, 126.4, 126.0, 125.9, 125.4, 125.3, 81.3, 67.0, 64.0, 61.6, 51.5, 34.1, 26.7, 21.3, 14.3; MS (FAB) *m/z* 480.2 (MH^+). Anal. Calcd for $C_{27}H_{29}NO_5S$: C, 67.62; H, 6.09; N, 2.92; S, 6.69. Found: C, 67.65; H, 5.93; N, 3.04; S, 6.51.

2-Ethyl 4-Methyl (−)-(2*S*,4*R*,5*S*,*S*$_S$)-2-Methyl-5-(2-naphthyl)-4-(*p*-tolylsulfinyl)pyrrolidine-2,4-dicarboxylate (5d): yellow needles (ether−hexane), mp 115−116 °C; $[\alpha]^{20}_D$ −47 (*c* 0.2, $CHCl_3$); IR ($CHCl_3$) 3438, 1742 cm^{-1}; ^{1}H NMR δ 8.06−7.44 (m, 7H, Nph), 7.40 and 7.25 (AA′BB′ system, 4H, Tol), 5.10 (s, 1H, CH−Nph), 4.30 (q, 2H, CH_2–O, *J* = 7.0), 3.20 (s, 3H, CO_2Me), 2.72 (d, 1H, *J* = 14, CH), 2.46 (d, 1H, *J* = 14, CH), 2.37 (s, 3H, CH_3−Tol), 1.67 (s, 3H, CH_3), 1.42 (t, 3H, CH_3–CH_2, *J* = 7.0 Hz); ^{13}C NMR δ 177.6, 168.5, 142.5, 137.5, 136.8, 133.9, 133.4, 130.4, 128.2, 127.5, 127.2, 126.4, 126.1, 125.9, 125.2, 125.0, 81.5, 68.7, 63.8, 61.9, 51.6, 36.1, 30.12, 21.3, 14.1; MS (FAB) *m/z* 480.2 (MH^+). Anal. Calcd for $C_{27}H_{29}NO_5S$: C, 67.62; H, 6.09; N, 2.92; S, 6.69. Found: C, 67.58; H, 6.12; N, 3.11; S, 6.80.

Desulfinylation of Products 4 or 5 (6 or 7). A solution of **4** or **5** in toluene was refluxed for the time indicated in Table 2. The solvent was evaporated in vacuo, and the residue was purified by column chromatography (ethyl acetate−hexane, 1:5) to give **6** or **7**.

Dimethyl (−)-(2*S*,5*R*)-5-Phenyl-2,5-dihydro-1*H*-pyrrole-2,4-dicarboxylate (6a): yellow oil; $[\alpha]^{20}_D$ −12 (*c* 0.2, $CHCl_3$); IR ($CHCl_3$) 3482, 1751 cm^{-1}; ^{1}H NMR δ 7.58−7.34 (m, 5 H, Ph), 6.78 (dd, 1H, *J* = 2.2, *J* = 1.7, CH═C), 6.05 (dd, 1H, *J* = 5, *J* = 1.7, CH−Ph), 5.5 (dd, 1H, CH, *J* = 5, *J* = 2.2), 3.67 (s, 3H, CO_2Me), 3.56 (s, 3H, CO_2Me); ^{13}C NMR δ 177.3, 165.2, 137.2, 128.3, 128.1, 126.8, 125.2, 124.5, 65.0, 63.6, 55.5; MS (EI) *m/z* 261.1 (M^+). Anal. Calcd for $C_{14}H_{15}NO_4$: C, 64.36; H, 5.79; N, 5.36. Found: C, 64.29; H, 5.85; N, 5.34.

Dimethyl (−)-(2*S*,5*R*)-5-(2-Naphthyl)-2,5-dihydro-1*H*-pyrrole-2,4-dicarboxylate (6b): yellow oil; $[\alpha]^{20}_D$ −10 (*c* 0.2, $CHCl_3$); IR ($CHCl_3$) 3550, 1742 cm^{-1}; ^{1}H NMR δ 7.55−7.36 (m, 11 H, Nph), 6.75 (dd, 1H, *J* = 2.2, *J* = 1.7, CH═C), 6.09 (dd, 1H, *J* = 5.0, *J* = 1.7, CH−Nph), 5.60 (dd, 1H, CH, *J* = 5, *J* = 2.2), 3.71 (s, 3H, CO_2Me), 3.57 (s, 3H, CO_2Me); ^{13}C NMR δ 179.2, 170.4, 135.1, 133.4, 131.7, 131.5, 127.9, 127.4, 127.0, 126.1, 125.5, 124.2, 129.9, 125.1, 64.9, 63.4, 61.1; MS (EI) *m/z* 311.2 (M^+). Anal. Calcd for $C_{18}H_{17}NO_4$: C, 69.44; H, 5.50; N, 4.50. Found: C, 69.50; H, 5.59; N, 4.53.

Dimethyl (−)-(2*S*,5*R*)-2-Methyl-5-(2-naphthyl)-2,5-dihydro-1*H*-pyrrole-2,4-dicarboxylate (6c): yellow needles (ether−hexane), mp 120−122 °C; $[\alpha]^{20}_D$ −31 (*c* 0.2, $CHCl_3$); IR ($CHCl_3$) 3462, 1742 cm^{-1}; ^{1}H NMR δ 7.85−7.36 (m, 11 H, Nph), 6.85 (d, 1H, *J* = 2.4, CH═C), 5.54 (d, 1H, *J* = 2.4, CH−Nph), 3.79 (s, 3H, CO_2Me), 3.57 (s, 3H, CO_2Me), 1.68 (s, 3H, CH_3); ^{13}C NMR δ 179.5, 163.5, 142.3, 140.0, 137.6, 133.3, 133.0, 128.3, 127.9, 127.6, 126.7, 125.9, 125.8, 125.3,129.3, 72.0, 68.0, 52.8, 51.6, 26.7; MS (EI) *m/z* 325.2 (M^+). Anal. Calcd for $C_{19}H_{19}NO_4$: C, 70.40; H, 5.89; N, 4.31. Found: C, 70.48; H, 5.85; N, 4.45.

2-Ethyl 4-Methyl (−)-(2*S*,5*R*)-2-Methyl-5-(2-naphthyl)-2,5-dihydro-1*H*-pyrrole-2,4-dicarboxylate (6d): yellow oil; $[\alpha]^{20}_D$ −21 (*c* 0.2, $CHCl_3$); IR ($CHCl_3$) 3452, 1734 cm^{-1}; ^{1}H NMR δ 7.82−7.36 (m, 11 H, Nph), 6.84 (d, 1H, *J* = 2.4, CH═C), 5.53 (d, 1H, *J* = 2.4, CH−Nph), 4.31 (q, 2H, *J* = 7.0, CH_2–O), 3.68 (s, 3H, CO_2Me), 1.59 (s, 3H, CH_3), 1.33 (t, 3H, *J* = 7.0, CH_3–CH_2); ^{13}C NMR δ 178.2, 169.5, 142.5, 141.2, 137.4, 134.3, 133.4, 128.5, 127.6, 127.1, 126.3, 125.7, 125.4 125.0, 65.8, 64.1, 61.7, 50.2, 29.6, 14.3; MS (EI) *m/z* 339.3 (M^+). Anal. Calcd for $C_{20}H_{21}NO_4$: C, 70.78; H, 6.24; N, 4.13. Found: C, 70.80; H, 6.20; N, 4.21.

Dimethyl (−)-(2*S*,5*S*)-5-Phenyl-2,5-dihydro-1*H*-pyrrole-2,4-dicarboxylate (7a): yellow oil; $[\alpha]^{20}_D$ −15 (*c* 0.2, $CHCl_3$); IR ($CHCl_3$) 3350, 1730 cm^{-1}; ^{1}H NMR δ 7.55−7.36 (m, 5 H, Ph), 6.82 (dd, 1H, *J* = 2.4, *J* = 1.7, CH═C), 6.12 (dd, 1H, *J* = 5, *J* = 1.7, CH−Ph), 5.57 (dd, 1H, CH, *J* = 5, *J* = 2.4), 3.68 (s, 3H, CO_2Me), 3.58 (s, 3H, CO_2Me); ^{13}C NMR δ 179.1, 169.1, 137.2, 128.3, 128.1, 126.8, 128.5, 126.4, 124.2, 65.0, 63.6, 55.5; MS (EI) *m/z* 261.1 (M^+). Anal. Calcd for $C_{14}H_{15}NO_4$: C, 64.36; H, 5.79; N, 5.36. Found: C, 64.48; H, 5.65; N, 5.42.

Dimethyl (−)-(2*S*,5*S*)-5-(2-Naphthyl)-2,5-dihydro-1*H*-pyrrole-2,4-dicarboxylate (7b): yellow oil; $[\alpha]^{20}_D$ −12 (*c* 0.2, $CHCl_3$); IR ($CHCl_3$) 3540, 1740 cm^{-1}; ^{1}H NMR δ 7.55−7.36 (m, 11 H, Nph), 6.79 (dd, 1H, *J* = 2.4, *J* = 1.7, CH═C), 6.15 (dd, 1H, *J* = 5, *J* = 1.7, CH−Nph), 5.63 (dd, 1H, *J* = 5, *J* = 2.4, CH), 3.68 (s, 3H, CO_2Me), 3.58 (s, 3H, CO_2Me); ^{13}C NMR δ 178.1, 169.0, 135.2, 133.2, 131.2, 131.1, 128.2, 127.3, 127.1, 126.5, 125.7, 124.3, 129.5, 125.3, 65.6, 63.8, 61.2; MS (EI) *m/z* 311.2 (M^+). Anal. Calcd for $C_{18}H_{17}NO_4$: C, 69.44; H, 5.50; N, 4.50. Found: C, 69.58; H, 5.75; N, 4.45.

Dimethyl (−)-(2*S*,5*S*)-2-Methyl-5-(2-naphthyl)-2,5-dihydro-1*H*-pyrrole-2,4-dicarboxylate (7c): yellow needles (ether−hexane), mp 102−104 °C; $[\alpha]^{20}_D$ −34 (*c* 0.2, $CHCl_3$) (ee ≥ 99%, HPLC); IR ($CHCl_3$) 3448, 1730 cm^{-1}; ^{1}H NMR δ 7.85−7.36 (m, 11 H, Nph), 6.96 (d, 1H, *J* = 2.43, CH═C), 5.41 (d, 1H, *J* = 2.43, CH−Nph), 3.78 (s, 3H, CO_2Me), 3.58 (s, 3H, CO_2-Me), 1.53 (s, 3H, CH_3); ^{13}C NMR δ 180.0, 169.0, 137.2, 136.5, 133.3, 129.3,128.5, 127.6, 125.9, 124.7, 123.0, 123.5, 66.0, 64.2, 60.4, 49.8, 29.6, 14.3; MS (EI) *m/z* 325.3 (M^+). Anal. Calcd for $C_{19}H_{19}NO_4$: C, 70.40; H, 5.89; N, 4.31. Found: C, 70.51; H, 5.82; N, 4.51.

2-Ethyl 4-Methyl (−)-(2*S*,5*S*)-2-Methyl-5-(2-naphthyl)-2,5-dihydro-1*H*-pyrrole-2,4-dicarboxylate (7d): yellow oil; $[\alpha]^{20}_D$ −25 (*c* 0.2, $CHCl_3$) (ee ≥ 99%, HPLC); IR ($CHCl_3$) 3451, 1762 cm^{-1}; ^{1}H NMR δ 7.82−7.36 (m, 11 H, Nph), 6.96 (d, 1H, *J* = 2.4, CH═C), 5.43 (d, 1H, *J* = 2.4, CH−Nph), 4.26 (q, 2H, *J* = 7.0, CH_2–O), 3.67 (s, 3H, CO_2Me), 1.58 (s, 3H, CH_3), 1.33 (t, 3H, *J* = 7.0, CH_3–CH_2); ^{13}C NMR δ 180.0, 169.0, 142.7, 140.2, 137.7, 133.3, 133.1, 128.1, 127.6, 127.4, 126.5, 125.9, 125.6 125.3, 65.0, 63.6, 61.5, 49.8, 29.6, 14.3; MS (EI) *m/z* 339.3 (M^+). Anal. Calcd for $C_{20}H_{21}NO_4$: C, 70.78; H, 6.24; N, 4.13. Found: C, 70.81; H, 6.26; N, 4.22.

Dimethyl 5-(2-Phenyl)-1*H*-pyrrole-2,4-dicarboxylate (8a): yellow oil; IR ($CHCl_3$) 3512, 1721 cm^{-1}; ^{1}H NMR δ 9.35 (s, 1H, NH), 8.10 (s, 1H, CH−Ar), 7.92−7.40 (m, 5H, Ph), 3.90 (s, 3H, CO_2Me), 3.78 (s, 3H, CO_2Me); ^{13}C NMR δ 171.3, 159.9, 135.5, 129, 128.5, 127.2, 123, 122, 115, 110, 61.2, 55; MS (EI) *m/z* 259.3 (M^+). Anal. Calcd for $C_{14}H_{13}NO_4$: C, 64.86; H, 5.05; N, 5.40. Found: C, 64.52; H, 4.87; N, 5.28.

Dimethyl 5-(2-Naphthyl)-1*H*-pyrrole-2,4-dicarboxylate (8b): yellow oil; IR ($CHCl_3$) 3542, 1734 cm^{-1}; ^{1}H NMR δ 9.54 (s, 1H, NH), 8.36 (s, 1H, CH−Ar), 8.14−7.20 (m, 7H, Nph), 3.84 (s, 3H, CO_2Me), 3.77 (s, 3H, CO_2Me); ^{13}C NMR δ 178.3, 157.2, 134.1, 133.9, 133.6, 128.5, 128.0, 126.5, 125.9, 124.4, 125.0, 123.4, 116.4, 112.1, 61.3, 57.2; MS (EI) *m/z* 309.3 (M^+). Anal. Calcd for $C_{18}H_{15}NO_4$: C, 69.89; H, 4.89; N, 4.53. Found: C, 70.15; H, 4.75; N, 4.59.

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Supporting Information Available: X-ray diagrams and tables of data for compounds **4d** and **5c**. This material is available free of charge via the Internet at http://pubs.acs.org.

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