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Stereoselective Addition of α-Sulfinyl Carbanions to *N*-*p*-tolylsulfinylketimines: Synthesis of Optically Pure 1,2,2′-Trialkyl-2-aminoethanols

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The reactions of lithium carbanions derived from both enantiomers of methyl (**1**) and ethyl *p*-tolyl sulfoxide (**2**) with (*S*)-*N*-arylsulfinylketimines **3** and **4** took place in a highly stereoselective manner and good isolated yields. The configuration of the carbon bonded to nitrogen relies exclusively on the *N*-sulfinylimine configuration. When ethyl *p*-tolyl sulfoxide (**2**) is use as nucleophile, two chiral centers are created simultaneously, where the configuration of the carbon bonded to the sulfur is mainly controlled by **2**. The asymmetric induction increases with the temperature, being total at room temperature in the case of the matched pair of reactants. A non-oxidative Pummerer reaction on the obtained aminosulfoxides allows a straightforward synthesis of optically pure 1,2-ethanolamines with one or two chiral centers, including amino alcohols with a bulky quaternary carbon bonded to the amine group.

Introduction

The importance of the amine function in drugs, together with the increasing awareness on the importance of the chirality on their biological activity, make the asymmetric synthesis of amines an active area of research. Among the recent methods developed for this task, the nucleophilic addition of organometallic reagents to the C=N double bonds of aldimines[1] constitutes one of the most attractive approaches. The corresponding reactions with ketimines, affording optically pure α,α-disubstituted alkylamines, has been much less explored, probably due to the lower reactivity of these electrophiles and their propensity to enolization.[2] Moreover, the diastereoselectivity of the process may be compromised by the facile *E*,*Z* isomerization of these compounds. In this regard, it is worth mentioning that Grignard additions to ketimines derived from (*S*)-phenylglycinol containing 2-heteroalkyl[3] or α-methoxyalkyl[4] residues have been achieved with good stereoselectivities, owing to the ability of heteroatoms to form chelated species with magnesium and thus precluding the *E*,*Z* isomerization.

Moderate reactivity and stereoselectivity associated with the use of enantiopure aldimines can be substantially improved by using enantiopure *N*-sulfinylimines.[5] The stereoselectivity of these reactions is usually high, as it has been evidenced by several contributions from the groups of Davis[6] and Ellman.[7] Despite the scarcity of precedents concerning nucleophilic additions to *N*-sulfinylketimines,[8] the efficiency of the *N*-sulfinyl group in stereoselectivity control has been clearly demonstrated when the reactions are conducted in the presence of Me_3-Al.[8] However, to the best of our knowledge, none of the studied reactions involved the use of nucleophilic prochiral carbons or α-oxygenated carbanions for the simultaneous creation of two chiral centers and the formation of amino alcohols with the nitrogen bonded to a quaternary chiral carbon, respectively. In this sense, the use of the α-sulfinyl carbanions has been shown to be one of the most

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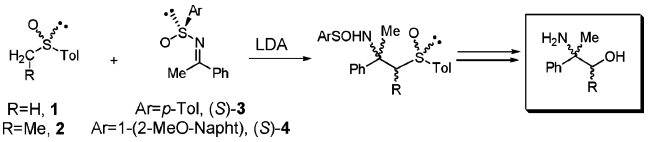
SCHEME 1. Synthesis of Amino Alcohols



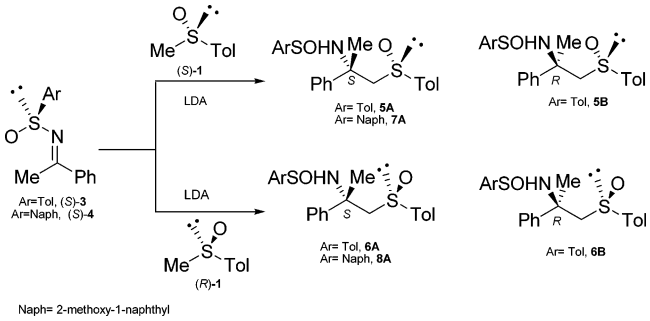
efficient methods to control the stereoselectivity of the nucleophilic additions to *N*-sulfinylaldimines resulting in the simultaneous creation of two chiral centers.[9] The resulting *β*-aminosulfoxides were transformed in a completely stereoselective manner into *β*-amino alcohols using a non-oxidative Pummerer reaction.[10] The potential interest of 2-aminoethanols as ligands[11] with the amine group bonded to a bulkier quaternary carbon prompted us to investigate the reaction of α-sulfinyl carbanions with *N*-sulfinylketimines and further transformation of the resulting aminosulfoxides into the corresponding *β*-amino alcohols (Scheme 1). Herein we report the results obtained in the reactions of (*R*)- and (*S*)-methyl and -ethyl *p*-tolyl sulfoxides, **1** and **2**, with (*S*)-*N*-[(*E*)-1-phenylethylidene]-*p*-toluenesulfinamide (**3**) and (*S*)-*N*-[(*E*)-1-phenylethylidene]-2-methoxy-1-naphthalenesulfinamide (**4**). Studies concerning the non-oxidative Pummerer reaction on the obtained *β*-aminosulfoxides, leading to the synthesis of optically pure 1,2,2′-trialkyl-2-aminoethanols, are also reported.

Results and Discussion

Methyl and ethyl *p*-tolyl sulfoxides, **1** and **2**, were prepared in both configurations by reaction of methyl and ethylmagnesium bromides with (*R*) and (*S*)-menthyl *p*-toluenesulfinates using the conditions reported by Solladié.[12] (*S*)-*N*-[(*E*)-1-phenylethylidene]-*p*-toluenesulfinamide (**3**)[13] and (*S*)-*N*-[(*E*)-1-phenylethylidene]-2-methoxy-1-naphthalenesulfinamide (**4**) were prepared according to the procedure reported by Davis.[14] The condensation of α-sulfinyl cabanions of (*R*)-**1** and (*S*)-**1** on the *N*-sulfinylketimines **3** and **4** afforded the desired products with good yields and diastereoselectivities, Table 1.

The reactivity of both ketimines is clearly lower than that of the previously studied aldimines[9] as the reactions usually require 24 h for completion. There is not a significant difference in reactivity for *N*-sulfinylketimines **3** and **4**. Reactions of **3** with both enantiomers of **1** at −78 °C afford mixtures of amino sulfoxides **5A** and **5B**, starting from (*S*)-**1**, or **6A** and **6B**, starting from (*R*)-**1**, in combined yields higher than 80% (entries 1 and 5). The diastereoselectivity from (*R*)-**1** (80% de, entry 5) is slightly higher than from (*S*)-**1** (60% de, entry 1). Under similar conditions, **4** evolves in a completely stereoselective manner with both enantiomers yielding **7A** from (*S*)-**1** (entry 3) and **8A** from (*R*)-**1** (entry 7) with excellent yields. At 0 °C, yields are in general moderate, around 65% (entries 2, 4, 6, and 8), but in some cases stereoselectivities are higher (compare entries 1 and 5 with 2 and 6 respectively). From the results in Table 1, it can thus be concluded that the reactions of ketimine **3** with both sulfoxides at 0 °C are completely stereoselective affording compounds **5A** (entry 2) and **6A** (entry 6) as single diastereomers (de > 98%, estimated by ^{1}H NMR on the reaction crudes).

TABLE 1. Addition of (*S*)-1 and (*R*)-1 to *N*-Sulfinylketimines 3 and 4



entry	imine	sulfoxide	*T* (°C)	yield[a] (%)	diastereomeric ratio[b]	de (%)
1	**3**	(*S*)-**1**	−78	82	**5A** (80)/**5B** (20)	60
2	**3**	(*S*)-**1**	0	67	**5A**	>98
3	**4**	(*S*)-**1**	−78	82	**7A**	>98
4	**4**	(*S*)-**1**	0	65	**7A**	>98
5	**3**	(*R*)-**1**	−78	85	**6A** (90)/**6B** (10)	80
6	**3**	(*R*)-**1**	0	65	**6A**	>98
7	**4**	(*R*)-**1**	−78	83	**8A**	>98
8	**4**	(*R*)-**1**	0	67	**8A**	>98

[a] Combined isolated yields. [b] Determined by ^{1}H NMR on the crude product.

Next, we focused our studies on the reactions of *N*-sulfinylketimines **3** and **4** with both enantiomers of the ethyl *p*-tolyl sulfoxide, (*R*)-**2** and (*S*)-**2**. As before, the condensation of the α-sulfinyl carbanions on *N*-sulfinylketimines **3** and **4** afforded the corresponding compounds **12**−**14**, with good yields and variable diastereoselectivities, Table 2. As expected from a steric point of view, the reactivity of the ethyl sulfoxide **2** is slightly lower than that of the methyl sulfoxide **1**, deduced from the longer reaction times, around 30 h required with both enantiomers. In all reactions, only two of the four possible diastereomeric 2-sulfinyl-1-propylamines are formed, which suggests that they evolve with a complete control of the stereoselectivity in one of the two newly created chiral centers.

Taking into account that the addition of methyl *p*-tolyl sulfoxide **1** evolves with almost complete control of the stereoselectivity at the iminic center, the same behavior can be anticipated for the bulkier ethyl *p*-tolyl sulfoxide **2**. Therefore, the isomers **A** and **B** should be epimers at

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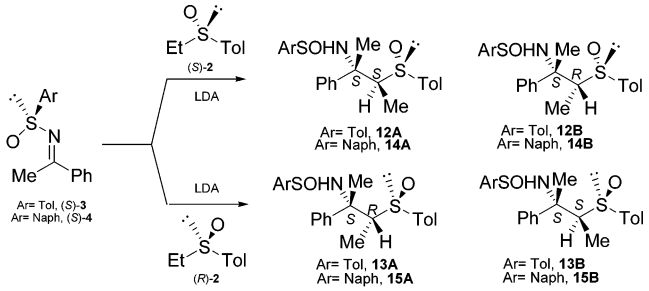
TABLE 2. Addition of (*S*)-2 and (*R*)-2 to *N*-Sulfinylketimines 3 and 4



Naph= 2-methoxy-1-naphthyl

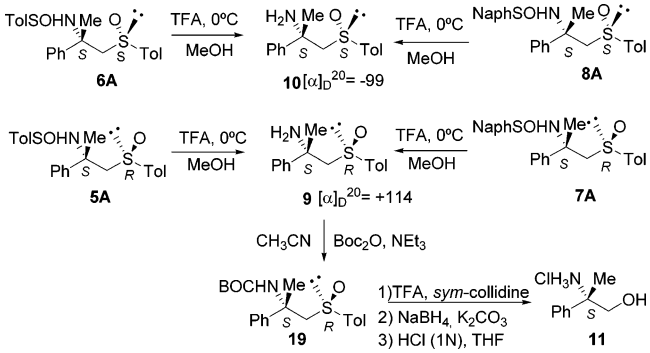
entry	imine	sulfoxide	*T* (°C)	yield[a] ((%)	diastereomeric ratio[b]	de (%) at C(2)
1	**3**	(*S*)-**2**	−78	77	**12A** (15)/**12B** (85)	70
2	**3**	(*S*)-**2**	0	73	**12A** (10)/**12B** (90)	80
3	**3**	(*S*)-**2**	0−10	75	**12A** (3)/**12B** (97)	94
4	**3**	(*S*)-**2**	rt	80	**12B**	>98
5	**4**	(*S*)-**2**	−78	79	**14A** (5)/**14B** (95)	90
6	**4**	(*S*)-**2**	0	62	**14A** (30)/**14B** (70)	40
7	**3**	(*R*)-**2**	−78	75	**13A** (40)/**13B** (60)	20
8	**3**	(*R*)-**2**	0	70	**13A** (23)/**13B** (77)	54
9	**4**	(*R*)-**2**	−78	85	**15A** (48)/**15B** (52)	4
10	**4**	(*R*)-**2**	0	72	**15A** (30)/**15B** (70)	40

[a] Combined isolated yields. [b] Determined by ^{1}H NMR on the crude product.

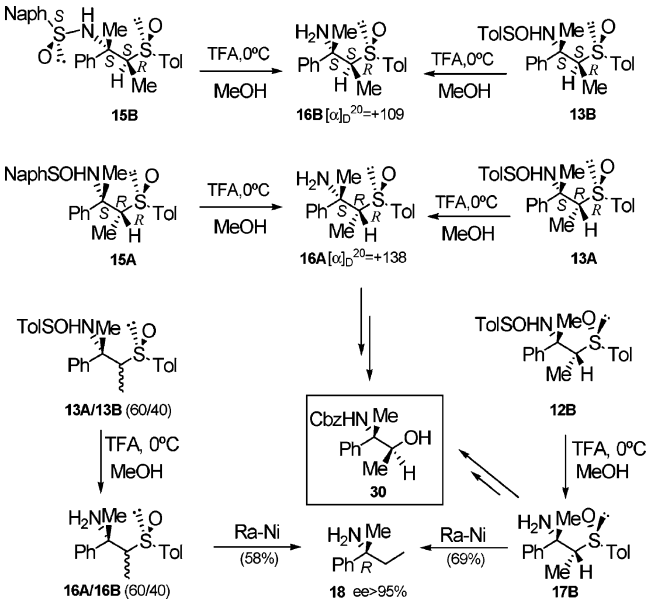
C(2), which was later confirmed (see configurational assignment). The magnitude and the sense of the changes in diastereoselectivity are dependent on the configuration of the sulfoxide and the structure of the *N*-sulfinylketimine. The de for the reactions of ketimine **3** with (*S*)-**2** is higher by increasing the temperature (entries 1−4). At room temperature, **12B** was obtained in 80% isolated yield as a single diastereoisomer (entry 4). Reactions of **3** with (*R*)-**2** are less stereoselective (compare entries 1 and 2 with 7 and 8 respectively). As in the previous case, the increase of the temperature improves the stereoselectivity (entries 7 and 8). Nevertheless, in this case the total control of the diastereoselectivity has not been possible because above 0 °C, the formation of byproducts is quite important.[15] The behavior of the naphthyl derivative **4** seems to be anomalous. At 0 °C it shows lower stereoselectivity than the *p*-tolyl derivative **3** in reactions with both ethyl sulfoxides, (*R*)-**2** (compare entries 8 and 10) and (*S*)-**2** (compare entries 2 and 6). The same behavior is observed in reactions of **3** and **4** with (*R*)-**2** at −78 °C (entries 7 and 9) and with (*S*)-**2** (compare entries 1 and 5). However, the de becomes higher by increasing the temperature in reactions of **4** with (*R*)-**2** (entries 9 and 10) but lower in those with (*S*)-**2** (entries 5 and 6) (vide infra).

Configurational Assignment. The configurational assignment of compounds **5**−**8** was made by chemical correlation (Scheme 2). Compounds **5A** and **7A** were transformed into the same aminosulfoxide **9** by hydrolysis of the N−S bond, which means that both compounds only differed in the sulfinyl residue at nitrogen. The same is true for **6A** and **8A**; both converted into **10** (Scheme 2). As compounds **9** and **10** are diastereomers (NMR) and

SCHEME 2. Chemical Correlation of Compounds 5−8



SCHEME 3. Chemical Correlation of Compounds 12-15



have a different configuration at sulfur (it only depends on the starting sulfoxide), their configuration at carbon bonded to the amine group must be identical. Absolute stereochemistry was established as (*S*) by chemical correlation of **9** with (*S*)-**11**[16] via a nonoxidative Pummerer reaction.[10] It also allowed us to assign as (*S*) the configuration of **5A**−**8A**, precursors of **9** and **10**. Thus, **B** isomers have an (*R*) configuration at the chiral carbon.

The configurational assignment of compounds **12**−**15** was accomplished as follows. The absolute configuration of compound **15B** (Scheme 3) was unambiguously established by X-ray analysis.[17] It has the (*S*) configuration at its two chiral carbons and a configuration at its two chiral sulfur identical to those of the starting products (*R*)-**2** and (*S*)-**4**.

Compounds **15B** and **13B** were hydrolyzed into the same compound **16B** (Scheme 3). Compounds **13A** and **15A** were analogously correlated by conversion into **16A**. Compounds **16A** and **16B** are diastereomers (NMR)

(15) At 45 °C we could measure a 65% de from the NMR spectra on the crude product, but the proportion of amino sulfoxides in the mixture was lower than 60%.

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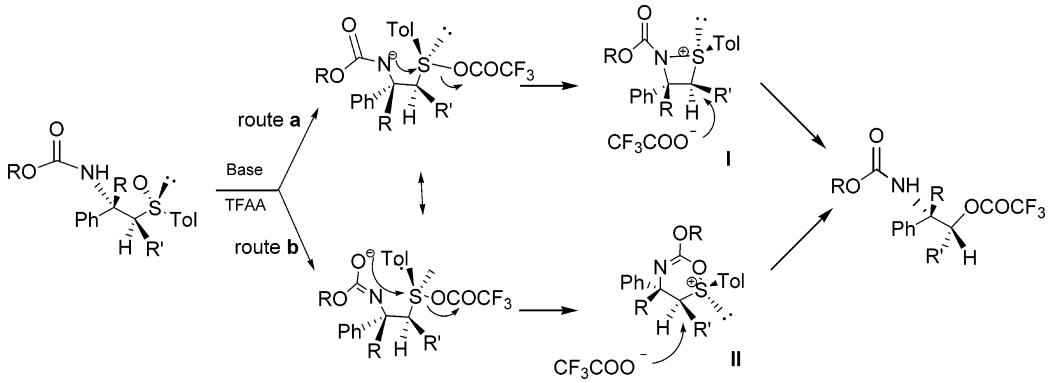
(17) The authors have deposited atomic coordinates for **15B** with the Cambridge Crystallographic Data Centre (Deposit No. 218989). The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, U.K.

SCHEME 4. Possible Pathways for the Non-Oxidative Pummerer Reactions



indicating they only differ in the configuration of one or two of the chiral carbons. A 60/40 mixture of **16A** and **16B** (obtained by hydrolysis of the 60/40 mixture of **13A** and **13B** from conditions of the entry 7, Table 2) was desulfinylated with Ra−Ni into the amine (*R*)-**18** with a very high optical purity (>95% ee, based on specific rotation[18]). This indicates that **16A** and **16B** have the same configuration at the benzylic position. As the (2*S*,3*S*,S*R*) configuration had been unequivocally assigned to **16B** (vide supra), the configuration (2*S*,3*R*,S*R*) must be assigned to **16A** (Scheme 4).

The configurational assignment of compounds **12** and **14** indicated in Table 2 is based on the assumption that the stereochemical evolution of the reactions of **3** and **4** with (*S*)-**2** and (*R*)-**2** must be similar. To confirm this assignment, compound **12B** was also correlated with the amine (*R*)-**18** (see Scheme 3), thus determining its configuration at the benzylic carbon as (*S*). Compounds **16A** and **17B** were transformed into the same amino alcohol **30,** with (*S***)** configuration at the hydroxylic carbon, under the conditions of the non-oxidative Pummerer reaction conditions (see synthesis of the amino alcohols), thus confirming they both have the *R* configuration in the carbon bonded to the sulfinyl group.

Mechanistic Considerations. From the results shown in Tables 1 and 2 it is evident that the configuration at the carbon bonded to nitrogen is completely controlled by the sulfur configuration at the sulfinyl ketimine, regardless of the configuration of the sulfinyl group at the nucleophile. The six-membered TS proposed by Ellman[8c] involving the association of the lithium to the sulfinyl oxygen and the nucleophilic carbon satisfactorily accounts for the experimental results. The chair like TS **B**, avoiding the 1,3-diaxial interaction between the aromatic residue at the *N*-arylsulfinyl group and the methyl group of the ketimine present in TS **A** (Figure 1), must be highly favored. This can explain the almost complete stereoselective evolution of the (*S*)-*N*-arylsulfinylimines **3** and **4** into amines with (*S*) configuration at the carbon bonded to nitrogen. The de observed in these reactions is higher than that found by Ellman in reactions of RMgX and RLi reagents with *N*-*tert*-butanesulfinylketimines in the absence of Me_3Al,[8c] probably due to the association of the lithium to the C-sulfinyl oxygen (vide infra). The small variations observed in the stereoselectivity with variable temperature and nature of the

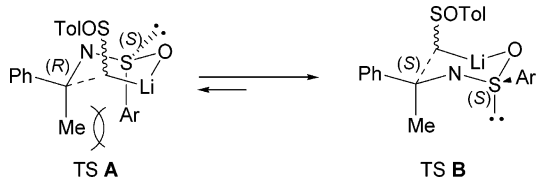


FIGURE 1. Transition states accounting for the stereoselectivity at the carbon bonded to nitrogen.

aromatic residue are difficult to explain (entries 1 and 5, Table 1), but the *E*/*Z* isomerization of the imine[2] and the association of the 2-methoxynaphthyl residue to the lithium may play some role.

Results shown in Table 2 indicate that the configuration at the carbon bonded to the sulfur atom is mainly controlled by that of the nucleophile. Thus, (*R*)-**2** mainly induces the (*S*) configuration whereas (*S*)-**2** gives the (*R*) configuration. This control is much more efficient starting from (*S*)-**2** (the reaction becomes completely stereoselective) and increases for both enantiomers when the temperature becomes higher. To explain these results we propose the stereochemical course indicated in Figure 2. On the basis that only TS **B** (Figure 1) can be involved, we assume that the structure of the attacking carbon at the TS of the nucleophilic addition could be described like a trigonal bipyramid with the apical positions occupied by the bulkier substituents (C=N and SOTol). Four possible transition states can be postulated (Figure 2). TS-$\mathbf{II}_{S}$ and TS-$\mathbf{II}_{R}$ have the C-sulfinyl oxygen associated to the lithium atom whereas such association does not exist for the corresponding TS-$\mathbf{I}_{S}$ and TS-$\mathbf{I}_{R}$. In the two latter cases, free rotation around the C−S bond is possible and the S−O bond will arrange anti with respect to the C−Li bond in order to minimize the electrostatic interactions. Moreover, the methyl group joined to C−Li will adopt the less hindered anti relationship with respect to the bulkier phenyl. Thus, the methyl group adopts a pseudoaxial arrangement in TS-$\mathbf{I}_{R}$ (derived from (*R*)-**2**), but a more stable pseudoequatorial position in TS-$\mathbf{I}_{S}$.

When the C-sulfinyl oxygen is associated with the lithium, the relative stability of the TS's is related to the steric interactions of the substituents at the four-membered ring, which necessarily adopt an eclipsed arrangement. Thus, the preferred configuration of the carbanion is the one that avoids the Tol/Me interaction. From Figure 2 it is easily deduced that TS-$\mathbf{II}_{S}$ is now less stable than TS-$\mathbf{II}_{R}$, due to the relative orientation of the methyl group in the chair like conformation. If we assume

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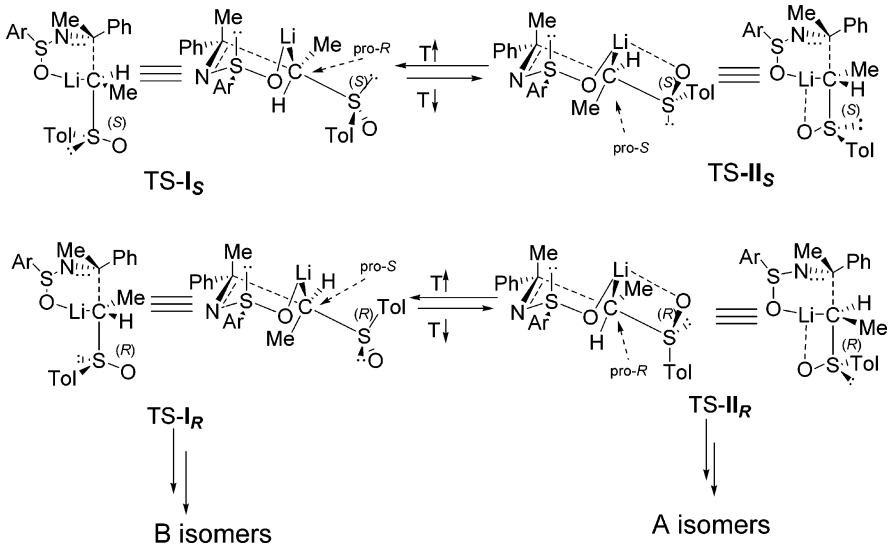


FIGURE 2. Stereochemical model accounting for the results in Tables 1 and 2.

the equilibration of the two possible transition states for each enantiomer (TS-**I** and TS-**II**) the experimental results can be satisfactorily explained. The equilibrium must be shifted toward TS-**I,** thus explaining the higher proportion of compounds **B** obtained in all the reactions shown in Table 2. Nevertheless the shifting toward TS-$\mathbf{I}_S$ must be higher than for TS-$\mathbf{I}_R$. An increase of the temperature would weak even more the association of the sulfinyl group to the lithium atoms, thus provoking the shift of the equilibrium toward TS-**I**, which would increase the proportion of the **B** isomers.

Synthesis of the Amino Alcohols. Once we obtained the amino sulfoxides, our last synthetic step was their conversion into the 1,2-ethanolamines containing two chiral centers, with the nitrogen bonded to a quaternary chiral carbon. This was made by using the conditions of the non-oxidative Pummerer reaction reported by Zanda et al.[10] because it is the best of the few reactions allowing the stereoselective substitution of sulfinyl by a hydroxyl group. Within this study we have also investigated some mechanistic aspects, mainly related to the nature of the intermediate species involved in the reaction. According to the stereochemical evolution suggested by Zanda, a highly strained thia-azacyclobutane ring would be involved as an intermediate[10] (**I** in Scheme 4). The presence of a quaternary carbon in our substrates suggested these intermediates would be strongly destabilized (they will always exhibit some Me/Me or Ph/Me eclipsed interaction), hindering progression of the reaction. As a second possibility the carbamoyl oxygen, instead of the nitrogen, can act as nucleophile, forming a more stable six membered intermediate (**II** in Scheme 4). This duality of intermediates was also considered by Zanda et al.[10b] in the case of substrates also containing quaternary carbons, but **II** was discarded on the basis that products having the Ar−S residue attached to the carbamic oxygen have never been observed or detected. They support the formation of the intermediates **I** on some NMR signals presumably corresponding to the four-membered intermediate.

Taking into account that this non-oxidative Pummerer reaction is very significant in the chemistry of chiral sulfoxides, we decided to study some aspects of the reaction on our substrates. We first explored the behavior of the *N*-*p*-tolylsulfinylamine **12B** in reaction with TFAA and *sym*-collidine, followed by hydrolysis with K_2CO_3. Unfortunately, only complex mixtures were formed under these conditions.[19] Thus, as a previous step to study the nonoxidative Pummerer reaction, we first hydrolyzed the N−S bond and then transformed the free amines into the corresponding carbamates.

The hydrolysis of the N−S bonds was conducted with TFA/MeOH at 0 °C in almost quantitative yields. The free amines **9**, **16A**, **16B** and **17B** were selected to continue this study.[20] Compounds **9** and **16B** were initially treated in acetonitrile with $(BOC)_2O$ in the presence of Et_3N to obtain the corresponding protected amines. The expected carbamates **19** and **20** were obtained in moderate chemical yields (45% and 43%, respectively). Compound **21**, resulting from a new attack of the amine to **19**, was also obtained in 40% yield (Scheme 5). On the other hand, compound **22** was unexpectedly obtained in similar yield in the reaction from **16B.** To improve the yield in carbamate we modified the reaction conditions[21] by changing the solvent (THF, CH_2Cl_2), the base (DMAP), the concentration, and the order in the addition of the reagents. However, under all these conditions, a high proportion of the ureas was always obtained. We were also unsuccessful in converting **21** and **22** into **19** and **20**, respectively, by hydrolysis under different conditions.

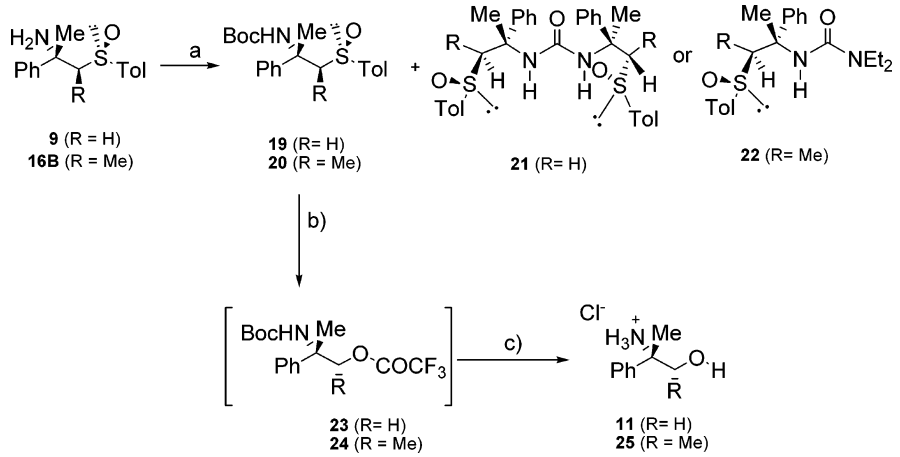
Before making additional efforts to solve this problem, we investigated the behavior of **19** and **20** under the Pummerer conditions. Fortunately, the results were satisfactory and the acyloxycarbamates **23** and **24** were exclusively obtained and then hydrolyzed into the cor-

(19) Their NMR spectra suggested that the sulfoxides had been reduced into thioethers and the N−S bond partially hydrolyzed. These results are similar to those previously obtained from the adducts resulting from reactions of *N*-sulfinyl aldimines (ref 9).

(20) Diastereoisomers **16A** and **16B** differ in the configuration at sulfinylated carbon, whereas **17B** and **16A** have different sulfur configuration, which allows to have information about the influence of all the chiral centers.

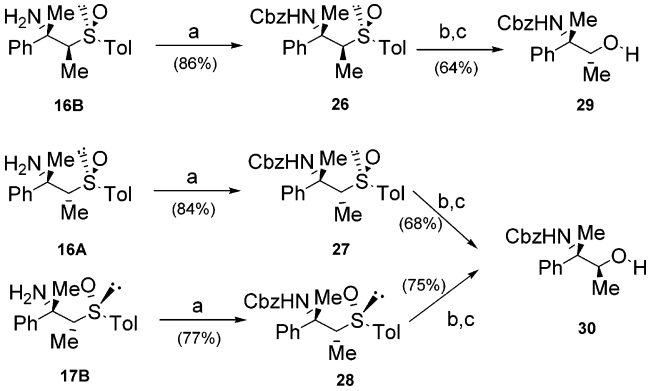
(21) Basel, Y.; Hassner, A. *J. Org. Chem*. **2000**, *65*, 6368.

SCHEME 5. Conversion of Amino Sulfoxides into Amino Alcohols via Boc Derivatives[a]



[a] Key: (a) BOC_2O, Et_3N, CH_3CN; (b) TFAA, *sym*-collidine, CH_3CN; (c) HCl (1 N), THF.

SCHEME 6. Conversion of the Amino Sulfoxides into Amino Alcohols via Cbz Derivatives[a]



[a] Key: (a) ClCOOBn, NaH, THF; (b) TFAA, *sym*-collidine, CH_3CN; (c) $NaBH_4$, K_2CO_3.

responding amino alcohol **11** (80% yield) and **25** (70% yield), respectively. The comparison of the specific rotation of compound **11** with that reported in the literature for (*S*)-2-amino-2-phenylpropanol[16] revealed its identity as well as suggested a high optical purity for compound **11**.

To avoid the formation of ureas **21** and **22** as byproducts (Scheme 5) and therefore improve the yield of the carbamates, we decided increase the reactivity of the electrophilic reagent by using benzyloxycarbonyl chloride/NaH instead of $(BOC)_2O/Et_3N$. Under these conditions, compounds **16A**, **16B**, and **17B** were transformed into their corresponding benzylcarbamates (**26**−**28**, Scheme 6) in isolated yields ranging between 77 and 86%, and the formation of the ureas was not observed. Finally, compounds **26**−**28** were treated with TFAA (4 equiv) and *sym*-collidine (5 equiv) in acetonitrile. The reaction of **28** was almost instantaneous at 0 °C, but **26** and **27** remained unaltered after several hours under these conditions. At room temperature, both compounds evolved satisfactorily into the corresponding alcohols, and **27** required less time than **26** (15 and 20 min, respectively). The resulting crudes were treated in situ with $NaBH_4$ and K_2CO_3. The *N*-benzyloxycarbonyl ethanolamines **29** and **30** were obtained in 64% and 68−75% isolated yield, respectively (Scheme 6).

We checked the enantiopurity of the alcohols **29** and **30** from the ^{1}H NMR spectra of their Mosher esters[22] (ee > 98%). These spectra confirmed the (*R*) configuration for alcohol **29** and (*S*) for alcohol **30**, in agreement with the expected inversion of the configuration of these nonoxidative Pummerer reactions.

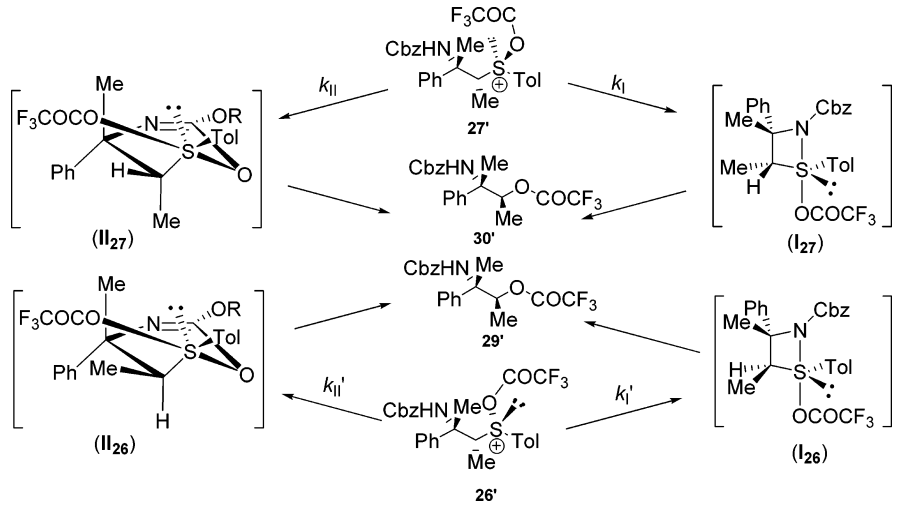
We performed an NMR study of the Pummerer reactions of **27**, similar to that made by Zanda et al.[10b] but changing the order in the addition of the reagents. First we recorded the NMR spectrum of **27** in the presence of 5 equiv of TFAA (see the Supporting Information). The instantaneous formation of the acyloxysulfonium salt **27′** was detected. The $\Delta\delta$ values ($\delta_{27} - \delta_{27'}$) for the CH−$CH_3$ grouping are 2.03 ppm (CH) and 1.01 ppm (CH_3), respectively. The salt remained unaltered until the base was added. The addition of *sym*-collidine effects the immediate appearance of the signals which correspond to the final trifluoroacetate **30′**. No other signals could be observed during the time of the experiment. We have done two experiments by adding 2.0 and 4.0 equiv of *sym*-collidine. The reaction rate, which can be followed by NMR, is dependent on the base concentration.

From this study we can conclude that the only observed signals are those corresponding to the acyloxy sulfonium salt **27′** and the trifluoracetoxy derivative **30′**. Taking into account that the observed $\Delta\delta$ values (vide supra) are similar to those reported by Zanda,[10b] we believe that the signals that he assigned as the four membered σ-sulfuranes are those corresponding to sulfonium salts.

Concerning the structures of the intermediates involved in these processes, the fact that reaction of **27** requires a shorter time than **26** (15 and 20 min, respectively) to be transformed into its corresponding trifluoroacetate, cannot be explained by assuming as intermediates the four membered σ-sulfuranes, $\mathbf{I_{27}}$ and $\mathbf{I_{26}}$. From Scheme 7 it can be deduced that $\mathbf{I_{27}}$ must be clearly less stable than $\mathbf{I_{26}}$, which is not consistent with the observed relative rates. By contrast, the relative stability of $\mathbf{II_{27}}$ and $\mathbf{II_{26}}$ (the first being slightly more stable,[23] Scheme 7) accounts for the experimental results. Zanda et al. face a similar problem[10c] because the substrate evolving more slowly is a precursor of the most stable four-membered

(22) Ohtani, I.; Kusumi, T.; Kashman, Y.; Kakisawa, H. *J. Am. Chem. Soc.* **1991**, *113*, 4092.

SCHEME 7. Possible Intermediates in the Nonoxidative Pummerer Reaction



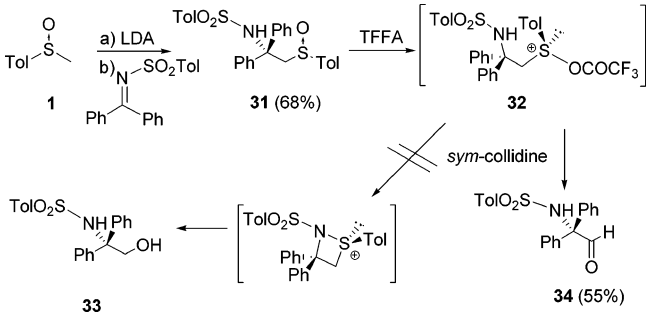
σ-sulfurane. They explain this by assuming the very quick formation of the intermediates, followed by their slow evolution (rate-determining step) into the rearranged trifluoroacetates (the most stable sulfurane would evolve more slowly). However, the increase of the reaction rate when the concentration of *sym*-collidine becomes higher (see above) and the fact that no signals attributable to σ-sulfuranes can be observed suggest the reaction of the acyloxysulfonium salt with the base as the rate-determining step.[24]

Conclusions

From the results obtained in reactions of sulfoxides **1** and **2** with the *N*-sulfinyl imines **3** and **4**, we can conclude that α-sulfinyl carbanions are able to add to the *N*-sulfinylketimines in a highly stereoselective way. It allows the efficient synthesis of the diastereomerically pure β-aminosulfoxides. These compounds can be transformed into optically pure 1,2,2′-trialkyl-2-aminoethanols by a non-oxidative Pummerer reaction with TFAA and *sym*-collidine. The six-membered σ-sulfuranes appear as the most probable intermediates for these latter reactions.

(23) Their relative stability must not be too much different, because the destabilization induced in $\mathbf{II}_{27}$ by the axial arrangement of the Me group, must be compensated by the $(Me/Me)_{gauche}$ interaction in $\mathbf{II}_{26}$. If we take into account that $\mathbf{II}_{26}$ will be additionally destabilized by the Me/$OCOCF_3$ interaction, presumably small due to the long S−O bond (see Scheme 7), the observed slightly lower reactivity of **27** is not surprising.

(24) To check the possible evolution through the four membered σ-sulfurane intermediates, we have prepared the *N*-sulfonyl aminosulfoxide **31**, unable to form the six membered σ-sulfuranes, by reaction of the *N*-sulfonylimine derived from benzophenone with racemic methyl *p*-tolyl sulfoxide in the presence of LDA. The reaction of **31** with TFAA (5 equiv) and *sym*-collidine (4 equiv) under the same experimental conditions used for carbamates did not evolve into the amino alcohol derivative **33** but yielded the aldehyde **34**, resulting in a normal Pummerer reaction. As the acidity of the NH group at **32** is higher than that of any carbamate, the fact that this substrate does not undergo the non-oxidative Pummerer reaction suggests that these reactions evolve through a six membered σ-sulfuranes as intermediates (instead of a four membered σ-sulfuranes), only possible for carbamates. However, the observed evolution for **31** could be due to the lower reactivity of the *N*-sulfonylamides.



Experimental Section

Addition of Enantiopure Alkyl *p*-Tolyl Sulfoxide Anions to *N*-Sulfinylketimines. General Procedure (Tables 1 and 2). To a solution of $^{i}Pr_2NH$ (24.0 mmol) in THF (30 mL) at 0 °C was added a 2.5 M solution of *n*-BuLi in hexane (24.0 mmol). After 30 min of stirring, the mixture was cooled at −78 °C and a solution of the alkyl sulfoxide (**1** or **2**, 24.0 mmol) in THF (20 mL) was then added. After the mixture was stirred for 30 min at −78 °C, a solution of the *N*-sulfinylketimine (**3** or **4**, 12.0 mmol) in THF (10 mL) was added at the temperature indicated in Tables 1 and 2. After the reaction finished (24 h), a saturated NH_4Cl aqueous solution (10 mL) was added. The organic phase was extracted with ethyl acetate (3 × 10 mL) and dried with anhydrous Na_2SO_4 and the solvent evaporated under vacuum. The crude product was purified by flash column chromatography with the solvent indicated in each case.

(*S*)-*N*-[(1*S*,*S*$_S$)-1-Methyl-1-phenyl-2-(*p*-tolylsulfinyl)ethyl]-*p*-toluenesulfinamide (5A). The product was prepared from (*S*)-**1** and (*S*)-**3** at 0 °C. It was obtained, after column chromatography (AcOEt/hexane, 1:1), as a white crystalline solid: yield 67%; mp 66−67 °C; $[\alpha]^{20}_D = -58.0$ (*c* 0.5, $CHCl_3$); ^{1}H NMR (200 MHz) δ 7.72 (m, 2H), 7.58 (m, 2H), 7.42−7.25 (m, 9H), 5.94 (bs, 1H), 3.49 (d, *J* = 13.4 Hz, 1H), 3.41 (d, *J* = 13.4 Hz, 1H), 2.41 (s, 3H), 2.39 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (50 MHz) δ 143.9, 143.0, 141.3, 141.1, 129.9, 129.6, 128.6, 127.8, 126.0, 125.5, 124.0, 71.2, 61.1, 43.8, 27.2, 21.2; MS (electrospray) *m*/*z* 412 (M + 1). Anal. Calcd for $C_{23}H_{25}NO_2S_2$: C, 67.12; H, 6.12; N, 3.40; S, 15.58. Found: C, 67.25; H, 6.28; N, 3.37; S, 15.60.

(*S*)-*N*-[(1*R*,*S*$_S$)-1-Methyl-1-phenyl-2-(*p*-tolylsulfinyl)ethyl]-*p*-toluenesulfinamide (5B). The product was obtained from (*S*)-**1** and (*S*)-**3** at −78 °C as the minor isomer of a 80:20 mixture of diastereomers **5A**/**5B**. Both diastereomers were separated by flash chromatography (AcOEt/hexane, 1:1), and the spectroscopic data were taken from a mixture of **5B** uncontaminated with the starting sulfoxide (*S*)-**1**: ^{1}H NMR (200 MHz) δ 7.58−7.25 (m, 13H), 5.97 (s, 1H), 3.05 (AB-system, Δν = 102.0 Hz, *J* = 13.2 Hz, 2H), 2.64 (s, 3H), 2.37 (s, 3H),

2.33 (s, 3H); ^{13}C NMR (50 MHz) δ 143.9, 143.0, 131.3, 141.1, 129.9, 129.6, 128.6, 128.4, 127.7, 126.0, 125.5, 125.2, 124.9, 124.0, 123.8, 71.7, 65.7, 61.8, 29.8, 21.3.

(*S*)-*N*-[(1*S*,R_S)-1-Methyl-1-phenyl-2-(*p*-tolylsulfinyl)ethyl]-*p*-toluenesulfinamide (6A). The product was prepared from (*R*)-**1** and (*S*)-**3** at 0 °C. It was obtained, after column chromatography (ether), as a white crystalline solid: yield 65%; mp 64−65 °C; $[\alpha]^{20}_D = +290.0$ (*c* 0.5, $CHCl_3$); ^{1}H NMR (200 MHz) δ 7.77 (m, 2H), 7.57 (m, 2H), 7.53−7.25 (m, 9H), 6.35 (s, 1H), 3.48 (AB system, $\Delta\nu$= 138.0 Hz, J = 13.4 Hz, 2H), 2.42 (s, 3H), 2.39 (s, 3H), 2.01 (s, 3H); ^{13}C NMR (50 MHz) δ 141.1, 143.1, 142.0, 141.3, 140.8, 130.1, 129.8, 128.7, 125.8, 125.2, 124.6, 68.7, 62.0, 29.7, 29.2, 21.4. Anal. Calcd for $C_{23}H_{25}NO_2S_2$: C, 67.12; H, 6.12; N, 3.40; S, 15.58. Found: C, 66.94; H, 6.32; N, 3.55; S, 15.47.

(*S*)-*N*-[(1*R*,R_S)-1-Methyl-1-phenyl-2-(*p*-tolylsulfinyl)ethyl]-*p*-toluenesulfinamide (6B). The product was obtained from (*R*)-**1** and (*S*)-**3** at −78 °C as the minor isomer of a mixture of diastereomers **6A**/**6B**. Both diastereomers were separated, and the spectroscopic data were taken from a mixture of **6B** uncontaminated with the starting sulfoxide (*R*)-**1**: ^{1}H NMR (200 MHz) δ 7.70−7.25 (m, 13H), 6.95 (s, 1H) 3.52 (AB system, $\Delta\nu$ = 14.0 Hz, J = 13.4 Hz, 2H), 2.42 (s, 3H), 2.39 (s, 3H), 2.21 (s, 3H).

(*S*)-*N*-[(1*S*,R_S)-1-Methyl-1-phenyl-2-(*p*-tolylsulfinyl)ethyl]-2-methoxy-1-naphthalenesulfinamide (8A). The product was obtained as a unique diasteromer from (*R*)-**1** and (*S*)-**4** at −78 °C. After column chromatography (ether), it was obtained as a white crystalline solid: yield 83%; mp 145−146 °C; $[\alpha]^{20}_D = +210.0$ (*c* 0.5, $CHCl_3$); ^{1}H NMR (200 MHz) δ 8.52 (d, J = 8.6 Hz, 1H), 7.96 (m, 2H), 7.85 (d, J = 8.1 Hz, 1H), 7.55−7.27 (m, 12H), 4.20 (s, 3H), 3.48 (AB system, $\Delta\nu$= 94.0 Hz, J = 13.5 Hz, 2H), 2.40 (s, 3H), 2.12 (s, 3H); ^{13}C NMR (50 MHz) δ 155.3, 144.3, 141.7, 141.0, 133.1, 130.2, 130.0, 128.8, 128.6, 128.4, 127.8, 127.4, 126.3, 125.9, 124.3, 124.2, 122.4, 113.6, 70.5, 61.9, 56.8, 29.4, 21.4; MS (electrospray) *m*/*z* 478 (M + 1).

(*S*)-*N*-[(1*S*,2*S*,S_S)-1-Methyl-1-phenyl-2-(*p*-tolylsulfinyl)propyl]-*p*-toluenesulfinamide (12A). It is obtained from (*S*)-**3** and (*S*)-**2** as the minor isomer of a mixture of diastereomers, **12A**/**12B**. After column chromatography (hexane/AcOEt, 2:1), the product was obtained as a white solid: yield 12%; mp 78 °C; $[\alpha]^{20}_D = -98.0$ (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz) δ 7.60 (m, 4H), 7.47−7.22 (m, 9H), 5.11 (s, 1H), 2.85 (q, J = 7.0 Hz, 1H), 2.38 (s, 3H), 2.34 (s, 3H), 2.27 (s, 3H), 0.98 (d, J = 7.0 Hz, 3H); ^{13}C NMR (75 MHz) δ 143.3, 142.5, 141.2, 140.8, 139.0, 129.6, 128.5, 127.9, 127.4, 125.0, 123.8, 71.1, 64.0, 27.0, 21.2, 4.3; MS (electrospray) *m*/*z* 426 (M + 1).

(*S*)-*N*-[(1*S*,2*R*,S_S)-1-Methyl-1-phenyl-2-(*p*-tolylsulfinyl)propyl]-*p*-toluenesulfinamide (12B). The product was obtained as a unique diastereomer from (*S*)-**3** and (*S*)-**2** at room temperature. After column chromatography (hexane/AcOEt, 2:1), it was obtained as a yellow solid: mp 81−83 °C; yield 80%; mp 62 °C; $[\alpha]^{20}_D = -82.0$ (*c* 0.3, $CHCl_3$); IR (film) 3348, 1597, 1493, 1445 cm^{-1}; ^{1}H NMR (300 MHz) δ 7.78 (m, 4H), 7.47 −7.22 (m, 13H), 2.82 (q, J = 7.0 Hz, 1H), 2.39 (s, 3H), 2.17 (s, 3H), 1.88 (s, 3H), 0.81 (d, J = 7.0 Hz, 3H); ^{13}C NMR (75 MHz) δ 146.9, 140.6, 140.0, 129.7, 128.4, 126.8, 125.2, 123.9, 70.5, 63.9, 29.6, 21.3, 4.2; MS (electrospray) *m*/*z* 426 (M + 1).

(*S*)-*N*-[(1*S*,2*R*,R_S)-1-Methyl-1-phenyl-2-(*p*-tolylsulfinyl)propyl]-*p*-toluensulfinamide (13A). The product was obtained from (*S*)-**3** and (*R*)-**2** as the minor isomer of a mixture of diastereomers **13A**/**13B**. After column chromatography (hexane/AcOEt, 2:1) the product was obtained as a yellow solid: mp 73−76 °C; solid; $[\alpha]^{20}_D = +134.0$ (*c* 0.5, $CHCl_3$); IR (film) 3436, 3203, 1596, 1492, 1446, 1086, 1048 cm^{-1}; ^{1}H NMR (300 MHz) δ 7.78 (m, 4H), 7.52−7.22 (m, 9H), 4.78 (s, 1H), 3.05 (q, J = 7.0 Hz, 1H), 2.38 (s, 3H), 2.38 (s, 3H), 2.22 (s, 3H), 0.85 (d, J = 7.0 Hz, 3H); ^{13}C NMR (75 MHz) δ 143.9, 142.7, 141.4, 140.9, 140.4, 129.8, 129.7, 128.6, 127.6, 126.2, 126.0, 123.8, 71.1, 64.2, 26.9, 21.3, 4.4; MS (FAB) *m*/*z* 426 (M + 1). Anal. Calcd for $C_{24}H_{27}NO_2S_2$: C, 67.73; H, 6.39; N, 3.29; S, 15.07. Found: C, 67.56; H, 6.66; N, 3.24; S, 14.91.

(*S*)-*N*-[(1*S*,2*S*,R_S)-1-Methyl-1-phenyl-2-(*p*-tolylsulfinyl)propyl]-*p*-toluenesulfinamide (13B). The product was obtained from (*S*)-**3** and (*R*)-**2** as the major isomer of a mixture of both diastereomers **13A** and **13B**. After column chromatography (hexane/AcOEt, 2:1), the product was obtained as a white solid: yield 54%; mp 79 °C; $[\alpha]^{20}_D = +128.0$ (*c* 1.0, $CHCl_3$); IR (film) 3454, 2978, 1636, 1493, 1448, 1213, 1189 cm^{-1}; ^{1}H NMR (300 MHz) δ 7.71 (m, 4H), 7.57 (m, 4H), 7.48−7.31 (m, 5H), 5.49 (s, 1H), 2.92 (q, J = 7.0 Hz, 1H), 2.38 (s, 3H), 2,38 (s, 3H), 2.01 (s, 3H), 1.05 (d, J = 7.0 Hz, 3H);^{13}C NMR (75 MHz) δ 143.3, 141.3, 141.0, 138.9, 129.8, 128.7, 127.9, 126.6, 125.2, 124.0, 70.4, 65.0, 25.5, 21.3, 4.9; MS (electrospray) *m*/*z* 426 (M + 1). Anal. Calcd for $C_{24}H_{27}NO_2S_2$: C, 67.73; H, 6.39; N, 3.29; S, 15.07. Found: C, 67.83; H, 6.28; N, 3.13; S, 14.90.

(*S*)-*N*-[(1*S*,2*R*,R_S)-1-Methyl-1-phenyl-2-(*p*-tolylsulfinyl)propyl]-2-methoxy-1-naphthalenesulfinamide (15A). The product was obtained from (*S*)-**4** and (*R*)-**2** as the minor isomer of a mixture of both diastereomers **15A** and **15B**. After column chromatography (hexane/AcOEt, 2:1) the product was obtained as a white solid: yield 22%; $[\alpha]^{20}_D = +51.0$ (*c* 0.4, $CHCl_3$); ^{1}H NMR (200 MHz) δ 8.50 (d, J = 8.6 Hz, 1H), 7.96 (m, 2H), 7.82 (d, J = 8.1 Hz, 1H), 7.55−7.20 (m, 11H), 7.02 (s, 1H), 4.17 (s, 3H), 2.89 (q, J = 7.0 Hz, 1H), 2.36 (s, 3H), 2.03 (s, 3H), 0.95 (d, J = 7.0 Hz, 3H); ^{13}C NMR (50 MHz) δ 155.1, 144.7, 140.8, 140.0, 133.2, 130.2, 129.7, 129.0, 128.7, 128.0, 127.7, 127.4, 126.7, 124.4, 123.8, 122.1, 113.7, 71.1, 63.8, 57.0, 26.8, 21.3, 4.4; MS (electrospray) *m*/*z* 492 (M + 1).

(*S*)-*N*-[(1*S*,2*S*,R_S)-1-Methyl-1-phenyl-2-(*p*-tolylsulfinyl)propyl]-2-methoxy-1-naphthalenelsulfinamide (15B). The product was obtained at 0 °C from (*S*)-**4** and (*R*)-**2** as the major isomer of a 30:70 mixture of both diastereomers **15A** and **15B**. After column chromatography (hexane/AcOEt, 2:1), the product was obtained as a white solid: yield 50%; mp 133 °C; $[\alpha]^{20}_D = -11.6$ (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz) δ 8.33 (d, J = 8.2 Hz), 7.96 (m, 2H), 7.82 (d, J = 8.0 Hz, 1H), 7.55−7.20 (m, 12H), 4.21 (s, 3H), 2.89 (q, J = 7.0 Hz, 1H), 2.34 (s, 3H), 2.15 (s, 3H), 1.10 (d, J = 7.0 Hz, 3H); ^{13}C NMR (75 MHz) δ 155.1, 144.3, 140.7, 139.2, 132.8, 130.2, 129.6, 128.7, 128.4, 128.3, 127.7, 127.5, 127.0, 126.5, 124.3, 123.8, 123.7, 122.2, 113.7, 71.2, 64.8, 56.9, 25.6, 21.2; MS (electrospray) *m*/*z* 492 (M + 1). Anal. Calcd for $C_{28}H_{29}NO_3S_2$: C, 68.40; H, 5.95; N, 2.85; S, 13.04. Found: C, 68.44; H, 6.18; N, 2.70; S, 12.59.

Desulfinylation of *N*-(*β*-Sulfinylalkyl)sulfinamides. General Procedure. To a stirred solution of the corresponding *N*-(*β*-sulfinylalkyl)sulfinamide (12.4 mmol) in methanol (120 mL) was added TFA (61.8 mmol, 4.7 mL). After the mixture was stirred for 3 h at 0 °C, the solvent was evaporated under vacuum and the residue obtained was chromatographed on a SCX column, affording the corresponding *β*-aminosulfoxide.

(1*S*,R_S)-1-Methyl-1-phenyl-2-(*p*-tolylsulfinyl)ethylamine (9). The product was obtained as a colorless oil from **5A**: yield 90%; $[\alpha]^{20}_D = +114.0$ (*c* 0.6, $CHCl_3$); ^{1}H NMR (300 MHz) δ 7.55 (m, 2H), 7.41−7.22 (m, 7H), 3.48 (AB system, $\Delta\nu$ = 24.0 Hz, J = 13.4 Hz, 2H), 2.34 (s, 3H), 2.19 (bs, 2H), 1.61 (s, 3H); ^{13}C NMR (75 MHz) δ 146.6, 141.6, 141.2, 129.8, 128.5, 127.0, 125.1, 123.7, 73.3, 55.6, 32.1, 21.3.

(1*S*,S_S)-1-Methyl-1-phenyl-2-(*p*-tolylsulfinyl)ethylamine (10). The product was obtained as a colorless oil from **6A**: yield 90%; $[\alpha]^{20}_D = -99.0$ (*c* 0.5, $CHCl_3$); ^{1}H NMR (300 MHz) δ 7.49−7.43 (m, 4H), 7.32−7.22 (m, 5H), 3.01 (AB system, $\Delta\nu$ = 61 Hz, J = 13.5 Hz, 2H), 2.34 (s, 3H), 2.09 (bs, 2H), 1.84 (s, 3H); ^{13}C NMR (75 MHz): δ 147.3, 141.4, 141.2, 129.8, 128.3, 126.9, 124.8, 123.7, 72.9, 55.1, 29.7, 21.2.

(1*S*,2*R*,R_S)-1-Methyl-1-phenyl-2-(*p*-tolylsulfinyl)propylamine (16A). The product was obtained as a white solid from **15A**: yield 90%; mp 33 °C; $[\alpha]^{20}_D = +137.0$ (*c* 0.5, $CHCl_3$); IR (film) 3369 (bs), 1598, 1493, 1445, 1084 cm^{-1}; ^{1}H NMR (300 MHz) δ 7.47 (m, 2H), 7.36−7.25 (m, 7H) 3.45 (bs, 2H), 2.85 (q, J = 6.95 Hz, 1H), 2.37 (s, 3H), 1,88 (s, 3H), 0.85 (d, J = 6.95

Hz, 3H); ^{13}C NMR (75 MHz) δ 145.9, 140.7, 139.5, 129.7, 128.5, 127.1, 125.1, 123.8, 70.2, 58.4, 29.0, 21.2, 4.2; HRMS calcd for $C_{17}H_{21}NOS$ [M^+] 287.13438, found 287.13460. Anal. Calcd for $C_{17}H_{21}NOS$: C, 71.04; H, 7.36. Found: C, 70.96; H, 7.49.

(1*S*,2*S*,*R*$_S$)-1-Methyl-1-phenyl-2-(*p*-tolylsulfinyl)propylamine (16B). The product was obtained as a white solid from **15B**: yield 90%; mp 123 °C; $[\alpha]^{20}_D = +110.0$ (*c* 0.6, $CHCl_3$); ^{1}H NMR (200 MHz) δ 7.56 (m, 2H), 7.42−7.23 (m, 7H), 2.83 (q, J = 6.95 Hz, 2H), 2.35 (s, 3H), 2.06 (s, 2H), 1.62 (s, 3H), 0.97 (d, J = 6.95 Hz, 3H); ^{13}C NMR (50 MHz) δ 147.1, 140.4, 140.3, 129.5, 128.4, 127.0, 125.6, 123.8, 71.7, 57.9, 28.1, 21.2, 4.5; HRMS calcd for $C_{17}H_{21}NOS$ [M^+] 287.13438, found 287.13495. Anal. Calcd for $C_{17}H_{21}NOS$: C, 71.04; H, 7.36. Found: C, 69.91; H, 7.58.

(1*S*,2*R*,*S*$_S$)-1-Methyl-1-phenyl-2-*p*-tolylsulfinylpropylamine (17B). The product was obtained as a colorless oil from **12B**: yield 93%; $[\alpha]^{20}_D = +15.6$ (*c* 1.7 $CHCl_3$); ^{1}H NMR (300 MHz) δ 7.54 (d, J = 8.2 Hz, 2H), 7.26 (t, J = 7.3 Hz, 2H), 7.35−7.20 (m, 5H), 2.83 (q, J = 6.9 Hz, 1H), 2.41 (bs, 2H), 2.35 (s, 3H),0.97 (d, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz): δ 146.9, 140.4, 140.1, 129.5, 129.5, 127.1, 125.6, 123.8, 71.6, 58.0, 28.0, 21.2, 4.5. Anal. Calcd for $C_{17}H_{21}NOS$: C, 71.04; H, 7.36. Found: C, 71.11; H, 7.65.

(*R*)-2-Phenyl-2-butylamine (18).[18] To a stirred solution of the corresponding β-amino sulfoxide **17B** or **16A/16B** (0.2 mmol) in THF (2 mL) was added a suspension of activated Raney-nickel (1.2 g) in THF. The reaction was stirred for 2 h, and then the crude was purified by SCX column to afford the amine: yield 69% from **17B** and 58% from **16A**/**16B**; $[\alpha]^{20}_D$ = +15.6 (*c* 0.5,EtOH) [lit.[18] $[\alpha]^{20}_D = +16.0$ (*c* 0.6, EtOH)]; ^{1}H NMR (300 MHz) δ 7.49 (d, J = 7.1 Hz, 2H), 7.40−7.24 (m, 3H), 2.05 (m, 2H), 1.72 (s, 3H), 0.80 (t, J = 7.5, 3H).

Boc-Protection of β-Sulfinylamines. General Procedure. To a solution of the corresponding β-aminosulfoxide (0.5 mmol) in CH_3CN (2 mL) and triethylamine (180 μL, 1.25 mmol) was added (*t*-BuOCO)$_2$O (0.65 mmol). After the mixture was stirred for 15 h at room temperature, 10% HCl aqueous solution was added and the mixture extracted with AcOEt (4 × 25 mL). The organic phase was dried over Na_2SO_4, evaporated under vacuum, and purified by column chromatography on silica gel (AcOEt/hexane, 1:1) to give the corresponding carbamate.

***tert*-Butyl *N*-[(1*S*,*R*$_S$)-1-Methyl-1-phenyl-2-*p*-tolylsulfinylethyl]carbamate (19).** The product was obtained as a white solid from **9**: yield 45%; mp 70 °C; $[\alpha]^{20}_D = +82.0$ (*c* 0.5, $CHCl_3$); ^{1}H NMR (300 MHz) δ 7.52 (m, 2H), 7.32−7.21 (m, 7H), 5.99 (s, 1H), 3.51(AB system, $\Delta\nu$ = 114.0 Hz, J = 13.3 Hz, 2H), 2.39 (s, 3H), 1.81 (s, 3H), 1.45 (s, 9H); ^{13}C NMR (75 MHz) δ 154.5, 141.2, 129.9, 128.6, 127.0, 123.7, 68.7, 57.7, 30.3, 28.3, 27.3, 21.3.

***tert*-Butyl *N*-[(1*S*,2*S*,*R*$_S$)-1-Methyl-1-phenyl-2-(*p*-tolylsulfinyl)propyl]carbamate (20).** The product was obtained as a colorless oil from **16B**: yield 42%; $[\alpha]^{20}_D = +54.0$ (*c* 0.5, $CHCl_3$); ^{1}H NMR (300 MHz) δ 7.49 (m, 2H), 7.46−7.24 (m, 7H), 6.00 (bs, 1H), 3.19 (m, 1H), 2.37 (s, 3H), 1.89 (s, 3H), 1.43 (s, 9H), 1.05 (d, J = 6.96 Hz, 3H).^{13}C NMR (75 MHz) δ 154.9, 144.7, 140.7, 139.0, 129.6, 128.4, 127.2, 125.7, 123.9, 79.4, 68.0, 61.2, 28.3, 25.3, 21.3, 4,6.

1,3-Bis[(1*S*,*S*$_S$)-1-methyl-1-phenyl-2-(*p*-tolylsufinyl)ethyl]-urea (21). The product was obtained as a byproduct from **9**, together with the corresponding Boc-amine **19**: white solid; mp 148−150 °C; yield 40%; $[\alpha]^{20}_D = +41.1$ (*c* 1.3, $CHCl_3$); IR (film) 3353, 1682, 1547, 1493, 1445 cm^{-1}; ^{1}H NMR (300 MHz) δ 7.41−7.05 (m, 18H), 3.75 (AB system, $\Delta\nu$ = 30.0 Hz, J = 13.5 Hz, 4H), 2.34 (s, 3H), 1.64 (s, 3H); ^{13}C NMR (75 MHz) δ 155.9, 147.7, 141.0, 140.1, 129.7, 128.3, 126.2, 124.1, 123.9, 67.7, 56.7, 32.0, 21.2.

***N*,*N*-Diethyl-*N*′-[(1*S*,2*S*,*R*$_S$)-1-Methyl-1-phenyl-2-(*p*-tolylsulfinyl)propyl]urea (22).** The product was obtained as a byproduct from **16B**, together with the corresponding Boc-amine **20**: white solid;, mp 147−149 °C; yield 41%; $[\alpha]^{20}_D$ = +43.1 (*c* 1.5, $CHCl_3$); IR (film) 3371, 1681, 1547, 1493, 1446 cm^{-1}; ^{1}H NMR (300 MHz) δ 7.42 (m, 2H), 7.29 (m, 7H), 6.28 (s, 1H), 3.42 (q, 2H, J = 6.9 Hz), 3.29 (q, 2H, J = 6.9 Hz), 2.92 (m, 1H), 2.37 (s, 3H), 2.09 (s, 3H), 1.20 (m, 9H); ^{13}C NMR (75 MHz) 156.6, 145.6, 140.8, 138.5, 129.7, 129.6, 128.4, 127.0, 125.7, 123.9, 70.0, 62.1, 41.2, 27.0, 21.3, 13.9.

Cbz-Protection of β-Sulfinylamines. General Procedure. To a solution of the corresponding β-amino sulfoxide (1.0 mmol) in THF (4 mL) at rt was added NaH (2 mmol). After the solution was stirred for 2 min, benzyl chloroformate (1.05 mmol) was added. After an additional 5 h of stirring, a solution of saturated NH_4Cl aqueous solution was added slowly. The mixture was extracted with diethyl ether (2 × 10 mL), washed with brine, and dried over $MgSO_4$ and the solvent evaporated under vacuum. The desired protected amine was isolated in pure form by column chromatography (hexane−AcOEt, 3:1).

Benzyl *N*-[(1*S*,2*S*,*R*$_S$)-1-Methyl-1-phenyl-2-(*p*-tolylsulfinyl)propyl]carbamate (26). The product was obtained as a colorless oil from **16B**: yield 86%; $[\alpha]^{20}_D = -172.2$ (*c* 0.4, $CHCl_3$); IR (film) 3314, 2983, 1712, 1599, 1522, 1336, 1253 cm^{-1}; ^{1}H NMR. (300 MHz) δ 7.42−7.23 (m, 14H), 6.25 (bs, 1H), 5.09 (AB system, $\Delta\nu$ = 30.0 Hz, J = 132.3 Hz, 2H), 2.81 (m, 1H), 2.38 (s,3H), 2.24 (s, 3H), 0.76 (d, J = 7.0 Hz, 3H); ^{13}C NMR (75 MHz) δ 155.1, 142.5, 141.0, 138.7, 136.6, 129.7, 128.4, 128.3, 128.0, 127.9, 127.2, 125.8, 124.0, 69.0, 66.4, 61.3, 25.7, 21.3, 4.2. Anal. Calcd for $C_{25}H_{27}NO_3S$: C, 71.23; H, 6.46. Found: C, 71.31; H, 6.62.

Benzyl *N*-[(1*S*,2*R*,*R*$_S$)-1-Methyl-1-phenyl-2-(*p*-tolylsulfinyl)propyl]carbamate (27). The product was obtained as a colorless oil from **16A**: yield 84%; $[\alpha]^{20}_D = -92.4$ (*c* 0.7, $CHCl_3$); ^{1}H NMR (300 MHz) δ 7.42−7.23 (m, 14H), 6.24 (bs, 1H), 5.09 (AB system, $\Delta\nu$= 30.0 Hz, J = 12.3 Hz, 4H), 2.82 (m, 1H), 2.39 (s, 3H), 2.24 (s, 3H), 0.76 (d, J = 7.0 Hz, 3H); ^{13}C NMR (75 MHz) δ 155.1, 142.6, 141.0, 138.8, 136.5, 129.8, 128.4, 128.3, 128.0, 127.9, 127.3, 125.8, 124.0, 69.0, 66.4, 61.3, 25.7, 21.3, 4.2. Anal. Calcd for $C_{25}H_{27}NO_3S$: C, 71.23; H, 6.46. Found: C, 71.01; H, 6.72.

Benzyl *N*-[(1*S*,2*R*,*S*$_S$)-1-Methyl-1-phenyl-2-(*p*-tolylsulfinyl)propyl]carbamate (28). The product was obtained as a colorless oil from **17B**: yield 77%; IR (film) 3301, 1729, 1521, 1448 cm^{-1}; $[\alpha]^{20}_D = -68.2$ (*c* 0.4, $CHCl_3$); ^{1}H NMR (300 MHz) δ 7.42−7.23 (m, 14H), 6.24 (bs, 1H), 5.08 (m, 2H), 2.82 (m, 1H), 2.39 (s,3H), 2.24 (s, 3H), 0.76 (d, J = 7.0 Hz, 3H); ^{13}C NMR (75 MHz) δ 155.1, 142.7, 141.0, 138.8, 136.6, 129.8, 128.4, 128.3, 128.0, 127.9, 127.3, 125.8, 124.0, 69.0, 66.5, 61.3, 25.8, 21.3, 4.3; Anal. Calcd for $C_{25}H_{27}NO_3S$: C, 71.23; H, 6.46. Found: C, 71.21; H, 6.52.

Pummerer Reaction and Deprotection of Boc-Protected β-Amino Sulfoxides. To a stirred solution of the β-(*N*-Boc-amino)sulfoxide **19** or **20** (1.0 mmol) and *sym*-collidine (0.42 mL, 3.0 mmol) in acetonitrile (10 mL) at 0 °C was added trifluoroacetic anhydride (0.8 mL, 5.0 mmol) dropwise. After the solution was stirred for 5 min, a 20% K_2CO_3 aqueous solution was added until basic pH was reached. The mixture was warmed to room temperature and, after 5 min, quenched with saturated NH_4Cl aqueous solution (5 mL), and the organic phase was extracted with ethyl acetate (5 × 10 mL). The organic layers were treated with 10% HCl aqueous solution (5 mL) to remove the excess *sym*-collidine, dried over Na_2SO_4, and evaporated under vacuum. The crude mixture was treated with a mixture of 1 N HCl aqueous solution (3 mL) and THF (2 mL). After 48 h of vigorous stirring, the crude product was extracted with CH_2Cl_2 (10 mL), and the aqueous layer was evaporated under vacuum, affording the corresponding β-amino alcohol hydrochloride.

(2*S*)-2-Amino-2-phenylpropan-1-ol Hydrochloride (11). This compound was obtained from **19** as a colorless oil: yield 80%; $[\alpha]^{20}_D = +17.0$ (*c* 0.5, H_2O); IR (film): 3286, 1601, 1485, 1027 cm^{-1}; ^{1}H NMR (200 MHz) δ 7.26 (m, 5H), 3.65 (AB system, $\Delta\nu$ = 17.0 Hz, J = 12.3 Hz, 2H),1.98 (s, 3H, CH_3); ^{13}C NMR (50 MHz) δ 145.4, 127.4, 125.8, 124.2, 70.7, 55.3, 26.1;

(2*R*,3*S*)-3-Amino-3-phenylbutan-2-ol Hydrochloride (25). This compound was obtained from **20** as a colorless oil: yield

70%; $[\alpha]^{20}_D = -4.0$ (*c* 0.5, H_2O); ^1H NMR δ 7.45−7.22 (m, 5H), 4.12 (q, $J = 6.5$ Hz, 1H), 1.6 (s, 3H), 0.94 (d, $J = 6.5$ Hz, 3H).

Pummerer Reaction of Cbz-Protected β-Aminosulfoxides. General Procedure. To a stirred solution of the corresponding β-(*N*-Cbz-amino)sulfoxide (1.0 mmol) **26**−**28** and *sym*-collidine (0.42 mL, 3.0 mmol) in acetonitrile (10 mL), under a nitrogen atmosphere at 0 °C, was added trifluoroacetic anhydride (0.8 mL, 5.0 mmol) dropwise. After the solution was stirred for 5 min, a 20% K_2CO_3 aqueous solution was added until basic pH was reached. $NaBH_4$ (excess) was then added portionwise at 0 °C, and the mixture was warmed to room temperature. When the reaction was completed as evidenced by TLC, it was quenched with a saturated NH_4Cl aqueous solution and extracted with AcOEt. The organic layer was dried over $MgSO_4$, evaporated under vacuum, and purified by column chromatography on silica gel (hexane/AcOEt, 2:1) to give the corresponding Cbz-protected amino alcohol.

Benzyl *N*-[(1*S*,2*R*)-1-Methyl-1-phenyl-2-hydroxypropyl]-carbamate (29). This compound was obtained from **26** as a colorless oil: yield 64%; $[\alpha]^{20}_D = +5.2$ (*c* 0.3, $CHCl_3$); ^1H NMR (300 MHz) δ 7.40−7.23 (m, 10H), 5.6 (bs, 1H), 5.06 (s, 2H), 3.99 (m, 1H), 1.75 (s, 3H), 1.11 (d, $J = 6.4$ Hz, 3H); ^{13}C NMR (75 MHz) δ 156.0, 143.8, 136.5, 128.6, 128.5, 128.3, 128.1, 127.2, 125.7, 74.7, 66.6, 62.3, 21.6, 17.3.

Benzyl*N*-[(1*S*,2*S*)-1-Methyl-1-phenyl-2-hydroxypropyl]-carbamate (30). This compound was obtained as a white solid from **27** (68% yield) or **28** (75% yield): $[\alpha]^{20}_D = +10.8$ (*c* 1.4, MeOH); IR (film) 3403, 2984, 1705, 1497, 1454 cm^{-1}; ^1H NMR (400 MHz) δ 7.40−7.20 (m, 10H), 5.50 (m, 1H), 5.13 (m, 1H), 5.00 (m, 2H), 3.85 (q, $J = 6.4$ Hz, 1H), 1.75 (s, 3H), 0.95 (t, $J = 6.4$ Hz, 3H); ^{13}C NMR (100 MHz) δ 156.0, 141.7, 136.5, 135.3, 128.6, 128.5, 128.3, 128.2, 128.1, 127.2, 126.3, 74.1, 67.8, 66.6, 22.4, 17.8; MS (FAB) *m*/*z* 300 (M + 1, 85), 254 (70), 238 (54), 210 (100); HRMS calcd for $C_{18}H_{21}NO_3$ [M + 1] 300.1600, found 300.1606.

***N*-[1,1-Diphenyl-2-*p*-tolylsulfinylethyl]-*p*-toluenesulfonamide (31).** To a solution of $^iPr_2NH$ (1.20 mmol) in THF (5 mL) at 0 °C was added a 2.5 M solution of *n*-BuLi in hexane (1.20 mmol). After 20 min of stirring, the mixture was cooled at −78 °C and a solution of racemic methyl *p*-tolyl sulfoxide (1.20 mmol) in THF (2 mL) was then added. After the mixture was stirred for 30 min at −78 °C, a solution of the *N*-sulfonylketimine **35**[25] (1.20 mmol) in THF (4 mL) was added at −78 °C. After the reaction finished (2 h), a saturated NH_4Cl aqueous solution (10 mL) was added. The organic phase was extracted with ethyl acetate (3 × 10 mL) and dried with anhydrous Na_2SO_4 and the solvent evaporated under vacuum. The crude product was purified by flash column chromatography with 3/1 hexane−AcOEt. It was obtained as a white solid: yield 68%; IR (film) 3165 (bs), 1595, 1493, 1446, 1326 cm^{-1}; ^1H NMR (300 MHz) δ 7.55−7.29 (m, 12H), 7.11 (d, $J = 8.4$ Hz, 2H), 7.00−6.91 (m, 4H), 3.70 (AB-system, $\Delta\upsilon = 222.0$ Hz, $J = 12.9$ Hz, 1H), 3.33 (d, $J = 12.9$ Hz, 1H), 2.42 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (75 MHz) δ 142.0, 141.9, 141.8, 140.2, 139.4, 139.0, 129.9, 129.2, 128.6, 128.3, 127.7 (2C), 127.6, 127.2, 126.7, 124.0, 68.2, 66.6, 21.3, 21.2. Anal. Calcd for $C_{28}H_{27}NO_3S_2$: C, 68.68; H, 5.56. Found: C, 68.75; H, 5.52.

***N*-(1,1-Diphenyl-1-formylethyl)-*p*-toluenesulfonamide (34).** To a stirred solution of **31** (0.02 mmol) and *sym*-collidine (0.1 mL, 0.07 mmol) in dry acetonitrile (5 mL), under a nitrogen atmosphere at 0 °C, was added trifluoroacetic anhydride (0.2 mL, 0.10 mmol) dropwise. After the solution was stirred for 5 min, a 20% K_2CO_3 aqueous solution was added until basic pH was reached. $NaBH_4$ (excess) was then added portionwise at 0 °C, and the mixture was warmed to room temperature. When the reaction was completed as evidenced by TLC, it was quenched with a saturated NH_4Cl aqueous solution and extracted with AcOEt. The organic layer was dried over $MgSO_4$, evaporated under vacuum, and purified by column chromatography on silica gel (hexane/AcOEt, 6:1) to give the corresponding aldehyde. It was obtained as a colorless oil: yield 55%; IR (film) 1715, 1659, 1597, 1591, 1556, 1277 cm^{-1}; ^1H NMR (400 MHz) 9.63 (s, 1H), 7.80 (d, $J = 8.0$ Hz, 2H), 7.58 (t, $J = 7.2$ Hz, 2H), 7.47 (t, $J = 7.6$ Hz, 2H), 7.35−7.24 (m, 5H), 7.00 (d, $J = 8.0$ Hz, 2H), 6.95 (d, $J = 8.0$ Hz, 2H), 2.26 (s, 3H); ^{13}C NMR (100 MHz) 190.6, 139.8, 137.7, 137.6, 136.7, 132.4, 130.0, 129.6, 129.5, 128.3, 128.2, 127.9, 126.1, 70.8, 21.2. Anal. Calcd for $C_{21}H_{19}NO_3S$: C, 69.02; H, 5.24. Found: C, 69.29; H, 5.66.

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Supporting Information Available: NMR study of nonoxidative Pummerer reaction. Synthesis and ^1H NMR spectra of Mosher esters of Cbz-protected amino alcohols **29a**,**b** and **30a**,**b**.Copies of ^1H and the ^{13}C NMR spectra of compounds **5B**, **8A**, **12A**,**B**, **15A**, **9**, **10**, **18**−**20**, **22**, **11**, **29**, and **21**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(25) *N*-Sulfonylimine was prepared following the procedure described in the following reference: Ram, R. N.; Khan, A. A. *Synth. Commun.* **2001**, *31*, 841.