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Synthesis and Reactivity of Enantiomerically Pure *N*-Acyl *N*-Alkyl *p*-Toluenesulfinamides†

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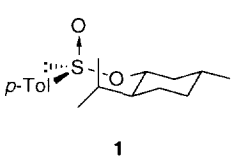
Abstract: The syntheses of different enantiomerically *N*-acyl *N*-alkyl *p*-toluenesulfinamides **5**, by *N*-sulfinylation of primary amines with (*S*)-menthyl-*p*-tolylsulfinate followed by *N*-acylation of the resulting sulfinamides are reported. Their reactions with some C-nucleophiles take place at the sulfur atom exclusively with complete retention of the enantiomeric purity, revealing their ability as sulfinylating agents. In this sense, their comparison with other reagents popularly used, revealed that **5** have some important advantages.

The commercially available enantiomerically pure (+) and (-)-menthyl sulfinates (**1**) are the most popular and used sources of the homochiral *p*-tolylsulfinyl groups.[2] Recently, two seminal contributions to the chemistry of sulfinylamides have evidenced their relevance in the preparation of enantiomerically pure sulfoxides. Evans et al.[3] have established that diastereo- and enantiomerically pure *N*-sulfinyloxazolidinones **2** and **3** are valuable reagents to transfer homochiral sulfinyl moieties to a variety of nucleophiles. In this sense, these compounds are probably the most powerful reagents so far described. On the other hand, Wills et al.[4] have reported several papers which demonstrate that cyclic sulfinamide **4** can also be used as a recoverable source of chiral sulfoxides and it has been used to achieve sulfinylations not possible by using the menthyl sulfinate. In addition to the sulfur atom, compounds **2-4** exhibit at least one more stereogenic centre apparently without any relevant role in their main application, the R-SO group transference. It suggests that the more simple *N*-sulfinylamides, **5**, could act as efficient sulfinylating agents. In this sense, the scope of compounds **5** would be limited to the synthesis of *p*-tolyl sulfinyl derivatives. Nevertheless, this would not be a serious inconvenient because they are the usual sulfoxides involved in asymmetric transformations. As additional interest, these compounds could be used to get asymmetric transformations at their acyl moiety, taking advantage of the ability of the sulfinyl oxygen to form chelates,[5] whose structures would be similar to those of **6** and **7**, respectively derived from *N*-acyl oxazolidinones[6] and *N*-acryloyl oxazolidinones,[7] which have been extensively used in asymmetric synthesis.

As a part of a general programme concerning the asymmetric synthesis based on the use of the sulfinyl group as chiral inductor, [8] we were interested in the search for new sulfinylating reagents. Thus, taking into account the above considerations, *N*-acylsulfinamides **5** were interesting candidates for study.



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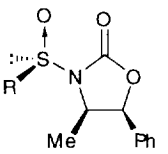
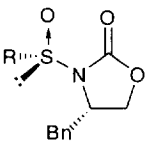
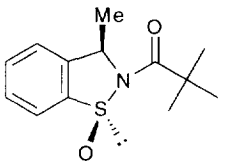


2a, R=Ph
2b, R=*p*-Tol



3a, R=Me
3b, R=*t*-Bu
3c, R=Ph
3d, R=*p*-Tol



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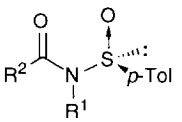

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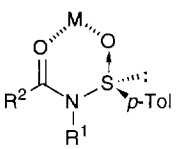

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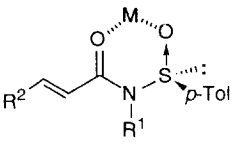

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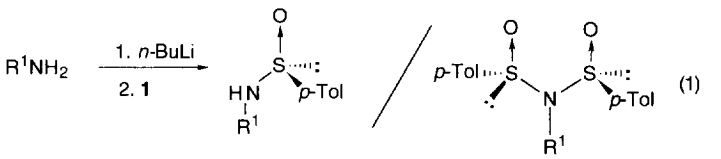
In this paper we report a general method that allows an easy access to enantiomerically pure *N*-acyl *N*-alkyl sulfinamides (**5**) as well as the preliminary results on their reactivity with C-nucleophiles which illustrate their ability as chiral sulfinyl transfer reagents.

Results and Discussion

Compounds **5** were prepared by a two steps sequence involving the sulfinylation of the amines **9** (Eq. 1) followed by acylation of the resulting sulfinamides **8** (Eq. 2).[9]

Enantiomerically pure sulfinamides **8** (>98% ee) have been prepared in yield higher than 80% (after flash chromatography) by reaction of the colored solution of the lithium amide, obtained by addition of two equivalents of *n*-BuLi to the corresponding amines **9**, to (*S*)-menthyl *p*-toluenesulfinate (**1**) (Eq 1). The reaction mode is critical in order to get high enantiomeric purity. Thus, the very quick addition of the amide anion resulting from **9a** on the sulfinate **1** is completely necessary to achieve **8a** in ee higher than 97%. Otherwise, samples with lower enantiomeric excess (even almost racemic) were obtained. The influence of the addition mode seems to be less important in the synthesis of **8b**. As sulfinamides **8** are configurationally stable under basic conditions, [10] the partial racemization observed by slow addition of the amide anion derived from **9** to the sulfinate **1** could be a consequence of the formation of the bis-sulfinylamines **10** (by reaction of the sulfinylamide **8** anions with **1**) which would also act as sulfinylating agent (much better than **1**) of the anion of the amide **9** later added. As the sulfur configuration is the opposite in **1** and **10**, one can expect the formation of both enantiomers of the sulfinamides **8**. The lower reactivity of the anion derived from **8b** due to steric factors, could be responsible of the lower incidence of the addition mode on its enantiomeric purity.

We have assigned the *S* configuration to the scalemic sulfinamides **8** by assuming the total inversion of configuration at the sulfur centre of sulfinate **1**.[11] To the best of our knowledge this is the first time that scalemic *N*-monoalkyl sulfinamides (>98% ee) have been obtained by means of a sulfinate as chiral sulfinyl transfer reagent,[12] probably due to the very critical experimental conditions required.

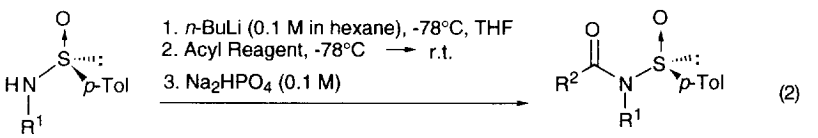


9a R^1= Bn **8a** R^1= Bn (>98% ee) [a]
9b R^1= *t*-Bu **8b** R^1= *t*-Bu (>98% ee)[b] **10**

[a] It could not be directly measured with chiral shift reagent tris[3-(trifluoromethylhydroxymethylene) camphorato] $Eu(tfc)_3$ (signals of the racemic **8a** were not separated by addition of the chiral shift reagent) either with (*R*)-(-)-*N*-(3,5-dinitrobenzoyl)-α-phenylethylamine (Deshmukh, M., Dunach, E., Juge, S.S., Kagan, H.B., *Tetrahedron Lett.*, **1984**, *25*, 3467), in this case it was not possible to accurately measure high enantiomeric excesses). Therefore it was deduced from the ee measured for its acyl derivative. [b] Determined by chiral shift reagent $Eu(tfc)_3$

N-acyl sulfinamides **5** were prepared by acylation of sulfinamides **8** in basic medium[13] (Eq. 2). We tried several acylating agents in order to obtain **5a** (Table I). The reactions of propionyl chloride with the lithium anion obtained from **8a** and *n*-BuLi,[14] (Entry 2) or its trimethylsilyl derivative[15] (Entry 3), afforded **5a** in very poor chemical yield, however propionic anhydride (Entry 1) was much more efficient. The remaining of *N*-acyl sulfinamides **5b-e** (Entries 4-7) were therefore prepared by using *n*-BuLi as base followed by treatment with the neat appropiate anhydride being obtained in a range from 72 to 86% chemical yield in high enantiomeric purity. Except the trifluoroacetyl derivative **5f**, which undergoes extensive decomposition during the purification process, all the *N*-acyl sulfinamides prepared are stable for months under refrigerator (T<5°C). In this sense, the thermal stability of sulfinamides **5**[16] seems to be slightly higher than that of compounds **2** and **3** reported by Evans, which need to be maintained below -20°C.

Table I. Preparation of *N*-Acyl *N*-Alkyl *p*-Toluenesulfinamides 5. (Eq 2)

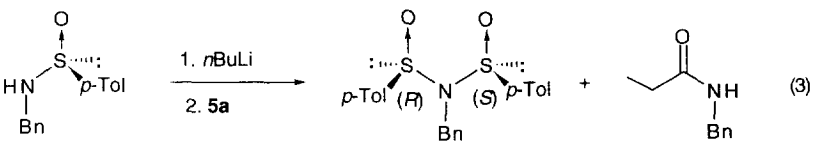


8 **5**

Entry	*Starting Material*	R^1	Acyl Reagent	Product	R^2	Yield (%)[a]	$[\alpha]_D$[b]	ee(%)
1	**8a**	Bn	$(EtCO)_2O$	**5a**	Et	86	+66.2	>98[c]
2	**8a**	Bn	ClCOEt	**5a**	Et	2	0	0
3	**8a**	Bn	ClTMS, ClCOEt	**5a**	Et	25	+66.2	>98[c]
4	**8b**	*t*-Bu	$(EtCO)_2O$	**5b**	Et	83	-29.5	*d*
5	**8a**	Bn	$(MeCO)_2O$	**5c**	Me	80	+84.5	*d*
6	**8a**	Bn	(*E*)-$(CH_3CH{=}CHCO)_2O$	**5d**	(*E*)-$CH_3CH{=}CH$	72	-33.2	>98[c]
7	**8b**	*t*-Bu	(*E*)-$(CH_3CH{=}CHCO)_2O$	**5e**	(*E*)-$CH_3CH{=}CH$	86	-51.1	*d*
8	**8b**	*t*-Bu	$(CF_3CO)_2O$	**5f**	CF_3	35	—	—

[a] After flash chromatography. [b] c=2, acetone. [c] Determined by using the chiral shift reagent $Eu(tfc)_3$. [d] It could not be determined because the addition of $Eu(tfc)_3$ does not separate the signals of the racemic compounds.

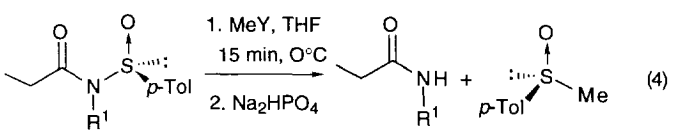
Concerning the enantiomeric purity of the obtained *N*-acylsulfinamides, the enantiomeric excess strongly dependent on the addition mode of the reagents. Enantiomerically pure **5a** (>98% ee) could be prepared by fast addition of the neat propionic anhydride (excess) to a solution containing the lithium anion from **8a** (obtained with *n*-BuLi at -78°C). Samples with lower enantiomeric purity (even racemic) are obtained with a slow addition, or by inverting the reagent addition order. This behaviour may be explained by assuming that the anion of **8a** reacts with the acetyl derivative **5a** yielding the bis-sulfinylamines **10** and the anion of **11**.[17] As **10** is a *meso*-form (it exhibits the opposite configuration at both sulfur atoms), the attack of **11** generates both enantiomers **5a** and **5a**. On the other hand, the attack of **11** on **5a** also generates the enantiomer **5a** (See Eq. 3). The fast addition of excess of anhydride to **8a** determines the inmediate and complete disapearance of the sulfinamide, precluding its later evolution and thus preserving the optical integrity of the acyl derivative **5a**.



8 **10a** **11a** (3)

Table II shows our preliminary results on the reactivity of *N*-acyl sulfinamides **5a** and **5b** with C-nucleophiles.

Table II. Reactivity of *N*-alkylsulfinamides 5a-b with MeY (Y=Li,MgI) (Eq 4)



R^1=Bn, **5a**
R^1=*t*-Bu, **5b**

11 (-)-(*S*)-**12** (4)

Entry	Starting material	R^1	Y	$[\alpha]_D$ acetone, c=2	ee, (%)[a]	T (°C)	Config. at sulfur
1	**5a**	Bn	Li	-10.5	7	0	S
2	**5b**	*t*-Bu	Li	-81	56	0	S
3	**5a**	Bn	MgI	-142	97	0	S
4	**5b**	*t*-Bu	MgI	-142	97	0	S
5	**5b**	*t*-Bu	MgI	-139	95	reflux	S

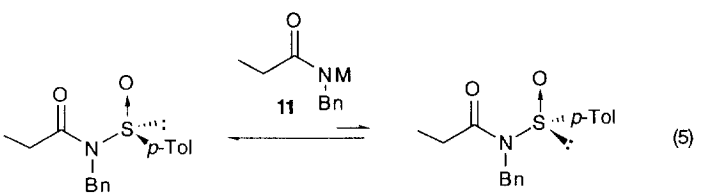
[a] Determined by comparison of the optical rotation to the maximun rotation ($[\alpha]_D$=+146°, (c=2, acetone)) reported in the literature (Mislow, K.; Axelrod, M.; Rayner, D.R.; Gotthardt, H.; Coyne, L.M.; Hammond, G.S. *J. Am. Chem. Soc.* **1965**, *87*, 4958) for (+)-(*R*)-**12** or directly measured with (*R*)-(-)-*N*-(3,5-dinitrobenzoyl)-α-phenylethylamine.

The addition of 1 equivalent of MeY (Y=Li or MgI) to a THF solution of these sulfinamides at 0°C gives, quantitatively, methyl *p*-tolylsulfoxide **12** and the corresponding amides **11**. As expected, the sign of the specific rotation measured for compound **12** evidences, in all cases, a *S* configuration at the sulfur centre.

However, a strong influence to both the nature of the metal used and the *N*-alkyl group, on the enantiomeric purity of **12** is observed. Thus, higher enantiomeric excesses of **12** are observed starting from **5b,** regardless of the reagent used. It is remarkable that the high enantiomeric purity of **12** is obtained in conditions of entry 5 (reflux in THF), despite the temperature used in the trial. On the other hand, the partial racemization observed for compound **12** obtained by using MeLi (entries 1 and 2) contrasts with the fact that almost enantiomerically pure **12** is obtained in reactions with MeMgI (entries 3 and 4).

The easier epimerization observed with MeLi could be explained as a consequence of the ability of the reagent to racemise methyl phenyl sulfoxide,**11a** or as a consequence of the reaction of the organometallic with **5** (enantiomers of **5**) resulting in the attack of the *N*-alkyl amide anion **11** (generated from **5** and MeY) on the *N*-sulfinyl amide **5**. The latter explained the behaviour observed for *N*-sulfinyloxazolidinone (*S*)-**3d**, which was equilibrated faster by its lithiated oxazolidinone (1 min at -78°C) than by the magnesium one (3h at 0°C).[3] To clarify this point, we evaluated the configurational stability of the sulfinamides **5** in the presence of the amide anion **11** (Table III). As we could see, lithium amides effect the complete racemization of **5a** in very few minutes, even at -78° (Entries 1-3), whereas magnesium amides require much longer reaction times (Entries 3 and 4) to effect only partial racemization (after 1 day, *ee* of **5a** is 62%). This demonstrates that the presence of the anion amide **11** only has significant consequences for the epimerization of **5a** in the case of the lithium derivatives.

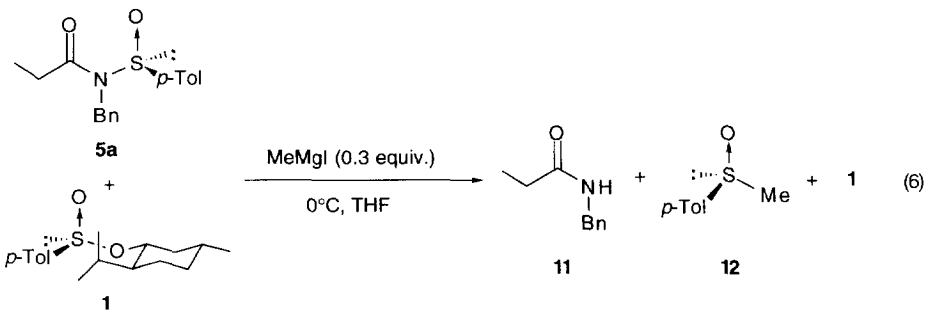
Table III. Reactivity of *N*-alkylsulfinamide 5a with the *N*-alkyl amide anion 11 (Eq 5).



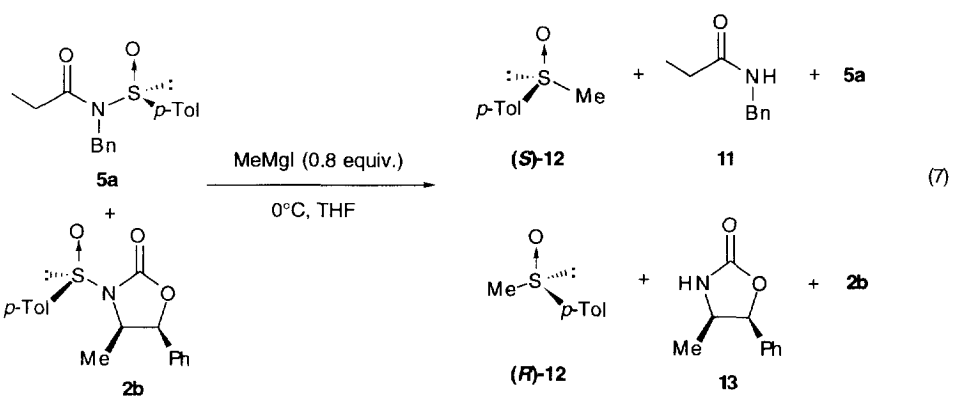
Entry	M	t(°C)	t(min)	$[\alpha]_D^a$	ee, (%)	Config. at sulfur
1	Li	0	1	+2	3	*S*
2	Li	0	10	0	0	——
3	Li	-78	1	+4	6	*S*
4	MgBr	0	180	+64	97	*S*
5	MgBr	0	1440	+41	62	*S*

[a] Optical rotation recorded in (c=2, acetone).

In order to check the ability of the *N*-acyl sulfinamides **5** as sulfinylating agent, we have carried out several competition experiments. First of all, we studied the reaction of a 1:1 mixture of **5a** and menthyl sulfinate **1** with 0.3 equivalents of MeMgI at 0°C (Eq 5). The reaction mixture was analyzed by 1H-NMR spectroscopy. Within the detection limits of the experiment (1%), the signals corresponding to menthol were not observed, which indicates that none of the menthyl sulfinate **1** had been transformed. It demonstrates that *N*-acyl sulfinamide **5a** is at least two orders of magnitude more reactive than the corresponding menthyl sulfinate **1** (eq 6).



In a second experiment, we studied the reaction of a 1:1 mixture of **5a** and **2b** with 0.8 eq. of MeMgI at 0°C (Eq. 7). After protonation, the ^{1}H-NMR spectrum of the reaction crude reveals the presence of the signals corresponding to **5a**, **11** (resulting from **5a**), **2b** and **13** (resulting from **2b**). The integration of the signals of the methylene group α to the carbonyl groups in **5a** and **11** and those of the methyl groups in **2b** and **13**, which appear perfectly separated in the mixture, reveals that their relative proportions are 1.13 (**5a**):1(**11**);1(**2b**):1.13(**13**). This indicates a similar ability to transfer the sulfinyl group for **5a** and **2b** (the second seems to be 1.1 times more reactive). On the other hand, as the nucleophilic attack of MeMgI on **5a** and **2b** yields respectively (*S*)- and (*R*)- methyl-*p*-tolylsulfoxide, the *ee* of this compound can be used as a measure of the relative reactivity of both sulfinyl amides. The specific rotation of **12** ($[\alpha]_D$ = +21 (c=1, acetone)) reveals an *ee*= 14% (being *R* the major enantiomer), which suggests that the relative reactivity of **5a** and **2b** is very similar to that established from the ^{1}H-NMR data.



In conclusion, we have reported the precise conditions to synthesize enantiomerically pure *N*-sulfinylamides by direct sulfinylation of primary amines, their acylation and the use of the obtained *N*-acyl *N*-alkyl *p*-toluenesulfinamides as a new kind of sulfinylating agents which exhibit a much more simple structure and a similar reactivity than those of the best sulfinylating agents so far reported.

Experimental Section

General procedure for the preparation of *N*-alkyl-*p*-toluenesulfinamides (8). To a solution of the corresponding amine (1.07 eq.) in THF (0.98 M) under argon at -78°C, *n*-BuLi (in hexane, 2 eq.) was added. The solution was stirred at -78°C for 15 min. and then it was added very quickly on a solution of (*S*)-menthyl-*p*-toluenesulfinate (1 eq.) in THF (0.44 M) at room temperature (the very quick addition is neccessary in order to get high enantiomeric excess, see Results and Discussion part). The temperature was allowed to reach room temperature and the mixture was stirred for 1.3 h. for **8a** and 2.5 h. for **8b**. Then it was quenched with Na_2HPO_4 (0.1 M) and extracted with CH_2Cl_2. The organic layer was dried over $MgSO_4$ and the solvent was evaporated. The residue was purified by flash chromatography (Et_2O/Hexane 1:2, silica gel had to be treated previously with a solution of the eluent and Et_3N, 5% v/v).

(+)-(*S*)-*N*-benzyl-*p*-toluenesulfinamide (8a). Yield. 80%. ^{1}H-NMR (200 MHz, $CDCl_3$) δ 7.66, 7.32 (AA'BB' system, 4H), 7.29 (m, 5H), 4.30-3.85 (m, 3H), 2.42 (s, 3H); ^{13}C-NMR (50.3 MHz, $CDCl_3$) δ 141.3, 140.8, 137.7, 129.6, 128.6, 128.3, 127.6, 125.9, 44.5, 21.3; IR ($CHCl_3$) 3330, 2980, 2920, 2860, 1595, 1485, 1450, 1390, 1075, 1055, 1020, 810 cm^{-1}; m.p.: 77-79°C; [α]= +40 (c= 2, acetone); Anal. Calcd. for $C_{14}H_{15}NSO$: C, 68.55, H, 6.17; N, 5.71. Found: C, 68.99; H, 6.26; N, 5.36; E.M. 245 (M^+, 10.1), 227 (12.4), 197 (52.4), 181 (2.1), 167 (4.0), 154 (3.5), 139 (76.5), 123 (14.7), 111 (11.7), 106 (99.4), 91 (100.0), 77 (53.7), 65 (43.5).

(+)-(*S*)-*N*-*tert*-butyl-*p*-toluenesulfinamide (8b). Yield. 80%. ^{1}H-NMR (200 MHz, $CDCl_3$) δ 7.57, 7.28 (AA'BB' system, 4H), 3.81 (broad s, 1H), 2.41 (s, 3H), 1.40 (s, 9H); ^{13}C-NMR (50.3 MHz, $CDCl_3$) δ 143.1, 140.4, 129.0, 125.3, 53.7, 30.7, 20.9; IR ($CHCl_3$) 2980, 1600, 1370, 1200, 1090, 1060, 955, 930, 850 cm^{-1}; m.p.: 50-52 °C; [α]= +135 (c= 2, acetone); HRMS Calcd. for $C_{11}H_{17}NSO$, 211.1030. Found, 211.1002; E.M. 211 (M^+, 6.5), 195 (17.0), 163 (10.7), 139 (100.0), 123 (14.6), 107 (15.8), 91 (33.9), 77 (8.6), 65 (8.9), 58 (33.0).

General procedure for the preparation of *N*-alkyl-*N*-acyl-*p*-toluenesulfinamides (5). To a solution of *N*-alkyl-*p*-toluenesulfinamides (**8**) in THF under argon at -78°C, *n*-BuLi (in hexane, 1.1 eq.) was added. After 10 minutes at this temperature, neat propionic anhydride (3 eq.) was quickly added (the very quick addition is neccesary in order to get high enantiomeric excess, see Results and Discussion part). The mixture was allowed to reach room temperature and quenched, with Na_2HPO_4 (0.1 M). It was extracted with CH_2Cl_2. The organic layer was dried over $MgSO_4$ and the solvent was evaporated. The residue was purified by flash chromatography (silica gel had to be previously treated with a solution of the eluent and Et_3N, 5%v/v).

(+)-(*S*)-*N*-Propanoyl-*N*-benzyl-*p*-toluenesulfinamide (5a). Reaction time: 10 min. Eluent: Et_2O/Hexane 1:3. Yield 86%. ^{1}H-NMR (200 MHz, $CDCl_3$) d 7.47, 7.35 (AABB system, 4H), 7.21-6.99 (m, 5H), 4.46, 4.33 (AB system, 2H, J= 15.4 Hz), 2.82 (q, 2H, J= 7.3 Hz), 2.39 (s, 3H), 1.26 (t, 3H); ^{13}C-NMR (50.3 MHz, $CDCl_3$) d 174.6, 142.3, 138.2, 136.8, 129.6, 128.3, 127.6, 126.4, 125.0, 43.2, 28.15, 21.0, 9.0; IR ($CHCl_3$) 3140, 3100, 1770, 1580, 1540, 1520, 1460, 1440, 1280, 1190, 1160, 1100, 1140, 940, 780 cm^{-1}; m.p.: 57-58°C; [a]= +66 (c= 2, acetone); HRMS Calcd for $C_{17}H_{19}NSO_2$, 301.1136.

Found, 301.1135; E.M. 301 (M^+, 24.8), 229 (2.14), 210 (22.1), 197 (2.3), 163 (16.3), 139 (51.3), 123 (9.8), 106 (55.6), 91 (100.0), 77 (15.6), 65 (13.3), 57 (35.4).

***N*-Benzyl-bis-*p*-toluenesulfinamide (10)** (as a mixture of diastereoisomers). ^{1}H-NMR (200 MHz, $CDCl_3$) δ 7.00 (m, 10H), 7.6, 7.32 (AABB system, 4H), 7.51, 7.19 (AABB system, 4H), 4.22 (s, 2H), 4.20, 3.99 (AB system, 2H, J= 15.8 Hz), 2.41 (s, 3H), 2,36 (s, 3H).

(-)-(*S*)-*N*-Propanoyl-*N*-*tert*-butyl-*p*-toluenesulfinamide (5b). Reaction time: 30 min. Eluent:Et_2O/hexane 1:10. Yield. 83%. ^{1}H-NMR (200 MHz, $CDCl_3$) δ 7.47, 7.33 (AABB system, 4H), 2.42 (q, 2H, J= 7.3 Hz), 2.42 (s, 3H), 1.61 (s, 9H), 0.75 (t, 3H, J= 7.3 Hz); ^{13}C-NMR (50.3 MHz, $CDCl_3$) δ 178.5, 141,9, 141.2, 130.0, 125.3, 62.2, 32.6, 30.0, 21.1, 8.8. IR ($CHCl_3$) 2980, 2440, 1690, 1610, 1490, 1430, 1400, 1230, 1090, 1060, 930, 800 cm^{-1}; [α]= -29 (c= 2, acetone); E.M. 267 (M^+, 4.3), 211 (80.7), 194 (17.0), 182 (1.5), 163 (10.8), 139 (100.0), 123 (11.4), 108 (48.8), 91 (38.1), 77 (10.5).

(+)-(*S*)-*N*-Acetyl-*N*-benzyl-*p*-toluenesulfinamide (5c). Reaction time: 30 min. Eluent: Et_2O/hexane 1:3.Yield: 80% ^{1}H-NMR (200 MHz, $CDCl_3$) δ 7.47, 7.26 (AABB system, 4H), 7.12 (m, 5H), 4.46, 4.34 (AB system, 2H, J= 25.4 Hz), 2.49 (s, 3H), 2.39 (s, 3H); ^{13}C-NMR (50.3 MHz, $CDCl_3$) δ 171.3, 142.7, 138.4, 136.8, 129.8, 128.0, 127.9, 126.8, 125.2, 43.5, 23.0, 21.3; IR ($CHCl_3$) 3000, 2400, 1675, 1595, 1490, 1430, 1370, 1300, 1280, 1250, 1100, 1070, 1030, 1020, 960, 915, 855, 700 cm^{-1}; m.p. 49-51°C; [α]= +84 (c= 2, acetone); HRMS Calcd for $C_{16}H_{17}NSO_2$, 287.0980. Found, 287.0980; E.M. 287 (M^+, 47.2), 196 (33.9), 155 (7.3), 139 (67.7), 123 (9.5), 106 (75.3), 91 (100.0), 65 (31.3).

(-)-(*S*)-*N*-(*E*)-2-Butenoyl-*N*-benzyl-*p*-toluenesulfinamide (5d). Reaction time: 40 min. Eluent: Et_2O/hexane 1:3. Yield: 72%. ^{1}H-NMR (200 MHz, $CDCl_3$) δ 7.47, 7.23 (AABBsystem, 4H), 7.14 (m, 5H), 7.15 (dq, 1H, J= 15.0, 6.8 Hz), 6.76 (dq, 1H, J= 15.0, 1.6 Hz), 4.47 and 4.36 (AB system, 2H, J= 22.4 Hz), 2.39 (s, 3H), 1.95 (dd, 3H, J= 6.8, 1.6 Hz); ^{13}C-NMR (50.3 MHz, $CDCl_3$) δ 166.3, 145.1, 142.1, 138.4, 136.7, 129.4, 127.6, 127.4, 126.3, 124.8, 120.9, 42.7, 20.9, 17.9; IR ($CHCl_3$) 3000, 2380, 1665, 1630, 1490, 1440, 1430, 1365, 1325, 1290, 1190, 1100, 1070, 1010, 960, 925, 880; m.p. 75-77°C; [α]= -33 (c= 2, acetone); HRMS Calcd for $C_{18}H_{19}NSO_2$, 313.1136. Found, 313.1125. E.M. 313 (M^+, 21.1), 222 (20.2), 174 (6.7), 139 (41.5), 123 (8.1), 106 (34.2), 91 (87.7), 77 (21.9), 69 (100.0).

(-)-(*S*)-*N*-(*E*)-2-Butenoyl-*N*-*tert*-butyl-*p*-toluenesulfinamide (5e). Reaction time: 5 min. Eluent: Et_2O/hexane 1:8. Yield: 86%. ^{1}H-NMR (200 MHz, $CDCl_3$) δ 7.42, 7.27 (AABB system, 4H), 6.48 (dq, 1H, J= 16.5, 6.6 Hz), 6.25 (dq, 1H, J= 16.5, 1.5 Hz), 2.39 (s, 3H), 1.65 (s, 9H), 1.65 (dd, 3H, J= 6.6, 1.5 Hz); ^{13}C-NMR (50.3 MHz, $CDCl_3$) δ 169.9, 142.3, 141.5, 141.1, 129.5, 127.4, 126.2, 125.2, 61.4, 30.0, 28.7, 21.2, 17.6; IR ($CHCl_3$) 2926, 1660, 1625, 1435, 1390, 1360, 1320, 1280, 1170, 1080, 1060, 970, 940, 890, 800 cm^{-1}; [α]= -51 (c= 2, acetone); E.M. 279 (M^+, 9.1), 223 (88.6), 194 (31.4), 175 (27.2), 154 (10.7), 139 (100.0), 126 (27.9).

(*S*)-*N*-Trifluoroacetyl-*N*-*tert*-butyl-*p*-toluenesulfinamide (5f). Reaction time: 15 min. Eluent: Et_2O/hexane 1:1. Yield: 35%. ^{1}H-NMR (200 MHz, $CDCl_3$) δ 7.89, 7.39 (AABB system, 4H), 2.47 (s, 3H),

1.31 (s, 9H); ^{13}C-NMR (50.3 MHz, $CDCl_3$) δ 163.8, 145.9, 137.6, 130.3, 128.0, 115.7, 58.6, 30.3, 29.7, 21.7; IR ($CHCl_3$) 2960, 2400, 2300, 1721, 1360, 1270, 1190, 1130, 970, 700 cm^{-1}; m.p. 154-156°C; E.M. 267.1 (62.0), 211.0 (57.9), 171.0 (4.6), 154.0 (51.2), 140.0 (2.7), 139.0 (27.0), 106.0 (21.0), 91.0 (6.7), 69 (13.9), 58.0 (100), 57.1 (39.7).

General procedure for the reaction with nucleophiles. To a solution of the *N*-alkyl-*N*-acyl-*p*-toluenesulfinamide in THF under argon at 0°C, the organometallic (1.1 eq.) was added dropwise. The solution was stirred at 0°C for 15 min. and then quenched with Na_2HPO_4 (0.1M), extracted with CH_2Cl_2 and dried over $MgSO_4$. After the solvent was evaporated, the (*S*)-methyl-*p*-tolylsulfoxide was purified by flash chromatography (AcOEt/ hexane 1:3).

Configurational stability of (+)-(*S*)-*N*-propanoyl-*N*-benzyl-*p*-toluenesulfinamide (5a) in presence of the amide anion (11). To a solution of *i*-Pr_2NM (M= Li, MgBr, 1.2 eq) in THF (M= Li) or in benzene (M= MgBr), amide anion (**11**, 54 mg, 0.33 mmol, 1 eq) was added. After 30 min. at 0°C, (+)-(*S*)-*N*-propanoyl-*N*-benzyl-*p*-toluenesulfinamide (**5a**, 0.1 g, 0.33 mmol, 1 eq) was added (see temperature and reaction time in table III of Results and Discussion part). The mixture was quenched with Na_2HPO_4 (0.1 M) and extracted with CH_2Cl_2. Compound **5a** was purified by flash chromatography Et_2O/hexane 1:4.

Competition experiment between (*S*)-(-)-menthyl-*p*-toluenesulfinate (1) and (+)-(*S*)-N-propanoyl-N-benzyl-*p*-toluenesulfinamide (5a). A solution of methyl magnesium iodide (3M in ether, 66 µl, 0.2 mmol, 0.3 eq.) was added slowly to a solution of (*S*)-(-)-menthyl-*p*-toluenesulfinate (**1**) (0.19 g, 0.66 mmol) and (+)-(*S*)-*N*-propanoyl-*N*-benzyl-*p*-toluenesulfinamide (**5a**) (0.2 g, 0.66 mmol) in THF (7 ml) at 0°C under argon atmosphere. The solution was stirred at 0°C for 1h. and then quenched with saturated aqueous ammonium chloride and diluted with diethyl ether. The mixture was extracted with Et_2O, dried over $MgSO_4$ and the solvent evaporated. The crude of reaction shows that **5a** is at least two orders of magnitude more reactive than **1**, because the signals of (-)-menthol did not appear in the ^{1}H-NMR spectrum.

Competition experiment between (+)-(*S*)-*N*-propanoyl-*N*-benzyl-*p*-toluenesulfinamide (5a) and (4*R*,5*S*)-4-methyl-5-phenyl-3-[(*R*)-*p*-tolylsulfinyl]-2-isoxazolidinone (2b). A solution of methyl magnesium iodide (3M in ether, 87 µl, 0.26 mmol, 0.8 eq.) was added slowly to a solution of (+)-(*S*)-*N*-propanoyl-*N*-benzyl-*p*-toluenesulfinamide (**5a**, 0.1 g, 0.33 mmol) and (4*R*,5*S*)-4-methyl-5-phenyl-3-[(*R*)-*p*-tolylsulfinyl]-2-isoxazolidinone (**2b**, 0.1 g, 0.33 mmol) in THF (6 ml) at 0°C under argon atmosphere. The solution was stirred at 0°C for 10 min. and then quenched with saturated aqueous ammonium chloride, extracted with CH_2Cl_2, dried over $MgSO_4$ and the solvent evaporated. Analysis of the crude of reaction by ^{1}H-NMR and measure of the optical rotation of (*S*)-methyl-*p*-tolylsulfoxide isolated (by flash chromatography, AcOEt/hexane, 1:2) showed a similar reactivity in the two compounds (see Results and Discussion part).

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References and Notes

† Dedicated to the late Professor Francisco Fariña.

1 Present address: Instituto de Química Orgánica. CSIC. Juan de la Cierva 3, 28006-Madrid, Spain

2 Walker, A.J. *Tetrahedron Asymmetry*, **1992**, *3*, 961.

3 Evans, D.A.; Faul, M.M.; Colombo, L.; Bisaha, J.J.; Clardy, J.; Cherry, D. *J. Am. Chem. Soc.*, **1992**, *114*, 5977 (For a previous work about *N*-sulfinylcarbamates see: Whitesell, J.R.; Carpenter, J.F.; Yaser, H.K.; Machajewski, T. *J. Am. Chem. Soc.*, **1990**, *112*, 7653).

4 a) Oppolzer, W.; Wills, M.; Starkemann, C.; Bernardinelli, G. *Tetrahedron Lett.* **1990**, *31*, 4117. b) Wills, M.; Butlin, R.J.; Linney, I.D.; Gibson, R.W. *J. Chem. Soc. Perkin Trans. 1*, **1991**, 3383. c) Wills, M.; Butlin, R.J.; Linney, I.D. *Tetrahedron Lett.* **1992**, *33*, 5427. d) Butlin, R.J.; Linney, I.D.; Critcher, D.J.; Mahon, M.F.; Molloy, K.C.; Wills, M. *J. Chem. Soc. Perkin Trans. 1*, **1993**, 1581. e) Linney, I.D.; Tye, H.; Wills, M.; Butlin, R.J. *Tetrahedron Lett.* **1994**, *35*, 1785.

5 The concrete and fixed substitution at nitrogen exhibited by compounds **2-4** make them unsuitable for this application, which restricts their usefulness, so far limited to be used as sulfinylating agents.

6 (a) Evans, D.A.; Bartroli, J.; Shih, T.L. *J. Am. Chem. Soc.*, **1981**, *103*, 2127. (b) Evans, D.A.; Ennis, M.D.;Mathre, D.J. *J. Am. Chem. Soc.*, **1982**, *104*, 1737. (c) Boger, D.L.; Honda, T. *Tetrahedron Lett.* **1993**, *34*, 1567. d) Hashimoto,N.; Ishizuka, T:; Kunieda, T. *Tetrahedron Lett.* **1994**, *35*, 721. e) Iseki,K.; Asada, D.; Takahashi, M.; Nagai, T.; Kobayashi, Y. *Tetrahedron Lett.* **1994**, *35*, 7399.

7 Evans, D.A.; Chapman, K.T.; Bisaha, J. *J. Am. Chem. Soc.*, **1988**, *110*, 1238.

8 For nucleophilic additions to β-ketosulfoxides, see García Ruano, J.L.; Martín, A.M.; Rodríguez, J.H. *J. Org. Chem.* **1994**, *59*, 533.Escribano, A.; García Ruano, J.L.; Martín, A.M.; Rodríguez, J.H. *Tetrahedron*, **1994**, *50*, 7567. Solladié, G.; Huser, N.; García Ruano, J.L.; Adrio, J.; Carreño, M.C.; Tito, A. *Tetrahedron Lett.* **1994**, *29*, 5296 and references cited therein. For the use of sulfinyl dienophiles and dienes in asymmetric Diels-Alder reactions see: Alonso, I.; Carretero, J.C.; García Ruano, J.L. *J. Org. Chem.* **1994**, *59*, 1499. Arce, E.; Carreño, M.C.; Cid, M.B.; García Ruano, J.L. *J. Org. Chem.* **1994**, *59*, 3421 and references cited therein.

9 The sulfinylation of the N-alkylamides with (*S*)-menthyl sulfinate (**1**) was unsuccesful.

10 It was inferred from the fact that when a THF solution of scalemic sulfinamides **8** (ee>98%) was treated with *n*-BuLi (0.6M in hexane) ad aliquots parts, collected at different times, were then protonated with Na_2HPO_4 (0.1M), unaltered enantiomerically pure sulfinamides **8** were isolated in all cases.

11 a) Jacobus, J.; Mislow, K. *J. Am. Chem. Soc.*, **1967**, *89*, 5228. b) Montanari, F.; Colonna, S.; Giovini, R. *J. Chem. Soc. Chem Commun.*, **1968**, 253. c) References 3 and 4.

12 Scalemic *N*-phenyl sulfinamide has been reported (Nudelman, A.; Cram, D.J. *J. Am. Chem. Soc.*, **1968**, *90*, 3869). On the other hand, optically pure monoalkylsulfinamides have been recently reported by DIBAL reduction of the corresponding sulfimides (Hose, D.R.J.; Wills, M.; Raynham, T. *Tetrahedron Lett.* **1994**, *35*, 5303).

13 In general sulfinamides are sensitive to acids. For example: racemic sulfinamides **5** are obtained by stirring at room temperature of scalemic sulfinamides **5** (>98%) solution with silica gel (60 Merck 230-400.mesh). See for example Mikolajcyk, M.; Drabowicz, J.; Bujnicki, B. *J. Chem. Soc. Chem. Commun.*, **1976**, 568. b) Hua, D.H.; Miao, S.W.; Chen, J.S.; Iguchi, S. *J. Org. Chem.* **1991**, *56*, 4.

14 The use of NaH or LDA as bases gives poor chemical and optical yields in **8a** when ClCOEt was used as acylating reagent.

15 a) Thom, C.; Kocienski, P. *Synthesis*, **1992**, 582. b) Curran, D.P.; Rebek, J.Jr; Stack, J.G.; Geib, S.V.; Ballester, P. *J. Am. Chem. Soc.*, **1992**, *114*, 7007.

16 Thermal stability of **5b** is slighty lower than that of **5a**. Taking into account the similar reactivity of both compounds (deduced from a competition experiment), the studies concerning the reactivity of these sulfinamides was made on **5a**.

17 When the reaction of **8a** and propionic anhydride is made by slow addition, compounds **10** (two diastereoisomers) and **11** (M=H) have been isolated and characterized.

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