# (S,S)-bis-p-Tolylsulfinylmethane and Carbonyl Compounds : Reactivity and Asymmetric Induction

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Abstract : (S,S)-bis p-Tolylsulfinylmethane was shown to react with aromatic aldehydes with a high diastereoselectivity. In contrast,  $\beta$ -unsaturated aldehydes, giving only the elimination products, are in one step transformed into 4-substituted (E, E)-(S,S)-1, 1-bis (p-tolylsulfinyl)-1, 3-butadiene.

In spite of many efforts, the condensation of the (+)-(R)-methyl p-tolylsulfoxide anion to various carbonyl compounds shows always a poor diastereoselectivity<sup>1-3</sup>. An improvement in the diastereoselectivity was however observed in the case of benzaldehyde, only after transmetallation of the lithiated sulfinyl anion with zinc chloride, leading to a 80% d.e. but only a 28% chemical yield<sup>4</sup>. In sharp contrast, optically active  $\alpha$ -sulfinyl esters<sup>5</sup> (or amides<sup>6</sup>) give a high diastereoselectivity in aldol-type condensations due to the chelation effect of the ester (or amide) function.  $\alpha$ -Sulfinylsulfides<sup>7</sup> show also a moderate to good asymmetric induction in their condensation with aldehydes.



In this context, we became interested by B-disulfoxides with a  $C_2$  axis of symmetry such as (S,S)-bis-p-tolylsulfinylmethane 1, prepared many years ago by Kunieda<sup>8</sup> from optically pure menthyl sulfinate and (+)-(R)-methyl-p-tolylsulfoxide.

The best experimental conditions (base, temperature, reaction time) for the condensation of the anion of the disulfoxide 1 were determined in the case of benzaldehyde (Table I).

#### Table I : Condensation of 1 to benzaldehyde

Base	Reaction time (t°C)	2a (Yield %)	d.r. (SSS/RSS)
(i-Pr) <sub>2</sub> NMgBr	30 min. (-78)	26	> 98/2
	3.30 h (-40)		
n-BuLi	30 min. (-78)	75	90/10
t-BuMgBr	2 h (-78)	22	> 98/2

The diastereomeric ratio (d.r.) was determined by the NMR of the signals of  $H^1$  in compound **2a** (3.56 ppm,  $J_{1-2}=1.2Hz$  in the SSS configuration and 3.92 ppm,  $J_{1-2}=9Hz$ , in the RSS configuration). The absolute configuration of the main diastereomer was established by chemical correlation : mono-desulfurization with aluminium amalgam to the known<sup>1</sup>  $\beta$ -hydroxysulfoxide 3.

The results of table I show that the best diastereoselection was obtained using a magnesium containing base. Unfortunately we have been unable to improve the chemical yield and therefore we used only n-BuLi as a base for all the experiments reported in table II.



The results from table II show that the disulfoxide 1 gives a high diastereoselectivity only with aromatic aldehydes, in contrast with (+)-(R)-methyl p-tolylsulfoxide which gives poor d.e. The presence of one electron-donating group such as a methoxy group on the aromatic ring decreases the chemical yield, while two electron-donating groups inhibited the reaction.

The absolute configuration of the main diastereomer was deduced from its NMR characteristics by comparison with the known benzaldehyde adduct 2a (smaller chemical shift and  $H_1$ - $H_2$  coupling constant around 2 Hz in the (SSS) diastereomer).

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R	R'	Yield %	d.r.	δ Η <sub>1</sub> (SSS)- <b>2<sup>b</sup></b>	6 H <sub>1</sub> (RSS)-2 <sup>с</sup>
С <sub>б</sub> Н5	н	70	90/10	3.56	3.92
p-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	Н	93	85/15	3.56	3.83
p-MeOC <sub>6</sub> H <sub>4</sub>	н	37	84/16	3.51	4.12
3,4-Cl2C6H3	Н	85	74/26	3.59	3.80
p-MeO <sub>2</sub> C-C <sub>6</sub> H <sub>4</sub>	Н	75	85/15	3.55	3.86
C5H11	Н	60	60/40	3.33	3.63
i-C <sub>3</sub> H <sub>7</sub>	Н	56	55/45	3.49	3.75
EtO <sub>2</sub> C	CH3	60	73/25	4.18	4.30

## Table II : Condensation of 1 to carbonyl compounds R-CO-R'a

<sup>a</sup> No reaction with 3,4-dimethoxybenzaldehyde, p-benzyloxybenzaldehyde, phenylethylketone and p-nitroacetophenone. <sup>b</sup> main isomer :  $J \approx 2$  Hz between H<sub>1</sub> and H<sub>2</sub> = R. <sup>c</sup> minor isomer :  $J \approx 9$  Hz.<sup>d</sup> All the adducts from the above aldehydes are solid, the diastereomers can be separated by flash chromatography (EtOAc/Hexane/CH<sub>2</sub>Cl<sub>2</sub>:5/4/1).



A chelated model very similar to the one we have proposed<sup>5</sup> for the aldol condensation of  $\alpha$ -sulfinyl esters appears to allow a predic-tion of the absolute configuration of the main diastereomer. In this model, the electronic interaction between the axial lone pair of sulfur and the aromatic ring on the prochiral center (equatorial) is minimized.

When we attempted to apply this reaction to  $\alpha$ ,  $\beta$ -unsaturated aldehydes, we observed a completely different pathway, giving in one step the elimination product, the corresponding 4-substituted (3E)-(S,S)-1,1-bis-(p-tolylsulfinyl)-1,3 butadiene 4 (Table III).



### Table III : Formation of dienes 4 by condensation of 1 with $\alpha$ , $\beta$ -unsaturated aldehydes

R	Yield %	[a]D	m.p.°C
СН <sub>3</sub>	64 <sup>a</sup>	-22° (c 1.9, acetone)	121-3
$C_2H_5$	81b	-24° (c 0.7, acetone)	112-4
C <sub>6</sub> H <sub>5</sub>	80 <sup>c</sup>	-94° (c 0.9, CHCl <sub>3</sub> )	182-3
$2 - MeOC_6H_4$	81 <sup>c</sup>	-109° (c 2.1, CHCl <sub>3</sub> )	155-7

<sup>a</sup> Trans isomer,  $J_{3.4} = 14.5$  Hz; <sup>b</sup> trans isomer,  $J_{3.4} = 14.9$  Hz; <sup>c</sup> the coupling constant  $J_{3.4}$  could not be determined, the aromatic protons shielding the H<sub>3</sub> and H<sub>4</sub> signals.

It has been shown by  $Evans^9$  that racemic phenylsulfinyl butadiene is an effective diene in Diels-Alder reaction with electron-rich and electron-deficient dienophiles. Our results describe the first very short synthesis of optically pure substituted bis (p-tolylsulfinyl) butadienes with a  $C_2$  axis of symmetry which could be useful in asymmetric cycloadditions.

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