

**DIASTEREOSELECTIVE ADDITION OF ALLYLTRIPHENYLSTANNANE TO 3-SULFINYLFURFURAL MEDIATED BY TITANIUM(IV) TETRACHLORIDE AND TIN(IV) TETRACHLORIDE**

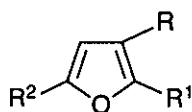
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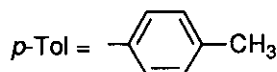
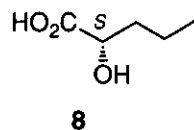
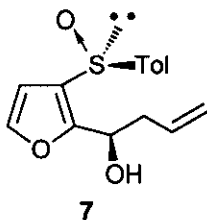
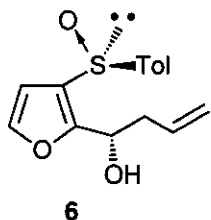
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**Abstract** —The addition of allyltriphenylstannane to 3-sulfinylfurfural (**3**) in the presence of titanium(IV) tetrachloride proceeded with high diastereoselectivity to give the furyl alcohol (**6**), whereas the similar treatment with tin(IV) tetrachloride afforded the other diastereoisomeric alcohol (**7**), exclusively.

Lewis acid-promoted allylation of aldehydes using allylmetal compounds such as allyltrialkylsilanes and allyltriarylstannanes has been widely studied.<sup>1</sup> From the view point of asymmetric reactions, there have been a number of reports which include the use of allylmetal compounds bearing chiral ligands,<sup>2</sup> chiral aldehydes<sup>3</sup> and chiral Lewis acid mediators.<sup>4</sup> In the course of our studies on the asymmetric cycloaddition employing chiral sulfoxides,<sup>5</sup> we were intrigued by the use of a chiral sulfinyl furfural for the reaction mediated by a Lewis acid. Despite of numerous efforts<sup>6</sup> for asymmetric condensations using  $\alpha$ -sulfinyl carbonyl compounds, little work has been done on the asymmetric addition to  $\beta$ -sulfinyl carbonyl compounds. This is presumably because of its low performance in chelation control.<sup>3a</sup> Our interest in Lewis acid-mediated reactions prompted us to investigate the possibility of asymmetric condensation of  $\beta$ -sulfinyl carbonyl compounds. Reported herein is a highly diastereoselective condensation of  $\beta$ -sulfinyl carbonyl compounds (*i.e.* 3-sulfinyl furfural) with allyltriphenylstannane in the presence of a Lewis acid.



- 1 R = CHO, R<sup>1</sup> = S(O)Tol-*p*, R<sup>2</sup> = H  
 2 R = H, R<sup>1</sup> = S(O)Tol-*p*, R<sup>2</sup> = CHO  
 3 R = S(O)Tol-*p*, R<sup>1</sup> = CHO, R<sup>2</sup> = H  
 4 R = CH(OH)C<sub>3</sub>H<sub>5</sub>, R<sup>1</sup> = S(O)Tol-*p*, R<sup>2</sup> = H  
 5 R = H, R<sup>1</sup> = S(O)Tol-*p*, R<sup>2</sup> = CH(OH)C<sub>3</sub>H<sub>5</sub>



To evaluate the diastereoselectivity for the addition, three types of sulfanyl-substituted furfuraldehydes ( $\pm$ )-1-3 were selected and the results are summarized in Table 1. Aldehydes used were easily prepared by the modified methods previously described.<sup>7</sup> For aldehydes ( $\pm$ )-1 and ( $\pm$ )-2, upon treatment with allyltriphenylstannane or allyltrimethylsilane in the presence of a Lewis acid, the two homoallylic alcohols ( $\pm$ )-4 and ( $\pm$ )-5 were produced as nearly an equal amount of two diastereoisomers, respectively, indicating the low diastereoselectivities of the reaction (Entries 1-3).

In sharp contrast, the reaction of the aldehyde ( $\pm$ )-3 with allyltriphenylstannane in the presence of TiCl<sub>4</sub> afforded the alcohol ( $\pm$ )-6 with a high degree of diastereoselectivity (Entry 5).<sup>9</sup> The use of a smaller amount (*e.g.* 1 equiv.) of allyltriphenylstannane, however, resulted in low yields of the product under the same conditions. Moreover, when the reaction was carried out at an elevated temperature (-20 °C), neither the diastereoselectivity nor the yield was improved (Entry 6). Instead, the corresponding furyl chloride was produced in 60% yield as the major product in a ratio of *ca.* 2:1. In the reactions with TiCl<sub>4</sub> the order of the addition of reagents have a great influence on the selectivity. In a standard way the reaction was conducted by treatment of a solution of ( $\pm$ )-3 with TiCl<sub>4</sub> followed by addition of the allylstannane to afford ( $\pm$ )-6 predominantly. On the other hand, when the Lewis acid was added to the allylstannane prior to pre-complexation<sup>9</sup> of the aldehyde, the reaction proceeded with lower diastereoselectivity (Entry 7), accompanied by a substantial amount of the diastereoisomer ( $\pm$ )-7 whose relative stereochemistry was established by X-ray analysis. It seems likely that in the inverse addition, the rate of nucleophilic addition of the allylmethyl competes with that of the formation of chelation from TiCl<sub>4</sub> and aldehyde.<sup>9</sup>

**Table 1** Reaction of sulfinyl furfurals (1)–(3) with allylmetal compounds

Entry	Aldehyde	Allylmetal compound (equiv.)	Lewis acid  (equiv.)	Reaction conditions		Proportions <sup>a</sup> of diastereoisomers	Isolated yield  / %
				Time ( <i>t</i> / h)	Temp. ( <i>T</i> / °C)		
1	1	allyltriphenylstannane (2.0)	TiCl <sub>4</sub> (2.0)	2	–84	4a:4b (1:1)	94
2	2	allyltrimethylsilane (1.0)	SnCl <sub>4</sub> (2.0)	2	–78	5a:5b (1.8:1)	63
3	2	allyltriphenylstannane (2.0)	TiCl <sub>4</sub> (2.0)	2	–84	5a:5b (1:1)	77
4	3	allyltrimethylsilane (1.2)	TiCl <sub>4</sub> (2.0)	1	–78	6:7 (5.8:1)	80
5	3	allyltriphenylstannane (2.0)	TiCl <sub>4</sub> (2.0)	1.5	–84	6:7 (19.4:1)	94
6	3	allyltriphenylstannane (2.0)	TiCl <sub>4</sub> (2.0)	1	–20	6:7 (1.5:1)	8 <sup>b</sup>
7	3	allyltriphenylstannane (2.0)	TiCl <sub>4</sub> <sup>c</sup> (2.0)	1	–84	6:7 (2.1:1)	94
8	3	allyltriphenylstannane (1.5)	SnCl <sub>4</sub> (2.0)	1	–84	6:7 (1:9)	87
9	3	allyltriphenylstannane (2.0)	SnCl <sub>4</sub> <sup>c</sup> (2.0)	1	–84	6:7 (1:6.4)	89

<sup>a</sup> Proportions were determined by integration of the olefinic signals of the crude product in the <sup>1</sup>H nmr spectra. <sup>b</sup> The major product, the corresponding furyl chloride, was produced in 60% yield as roughly a 2:1 mixture of diastereoisomers. <sup>c</sup> Inverse addition (see text).

Next, we examined the reaction of (±)-3 with another Lewis acid, SnCl<sub>4</sub> (Entries 8 and 9). Interestingly, in each case the diastereoisomer (±)-7 was produced as the major product in a diastereoselective manner (up to 80% d.e.). With SnCl<sub>4</sub>, it is no importance of the order of the addition of the reagents (Entry 8 vs. 9). The use of BF<sub>3</sub>-ether complex as a Lewis acid did not improve the diastereoselectivity. The other Lewis acid such as magnesium bromide did not effect the reaction, resulting in a recovery of starting material even at an elevated temperature (25 °C) and for a prolonged reaction period (20 h).

Based upon these results in a racemic series of 3, we undertook the synthesis of (*S*)-3 and the transformation of an optically active alcohol (6)<sup>10</sup> into the compound (8) with known absolute configuration.<sup>11</sup> Optically pure

sulfoxide ( $S_S$ )-**3** can be easily obtained from (+)-( $S_S$ )-*p*-tolyl 3-furyl sulfoxide,<sup>12</sup> as described in the preparation of a racemic series. The homoallylic furyl alcohol<sup>13</sup> (( $S_S$ )-**6**), obtained from the reaction of ( $S_S$ )-**3**, was transformed into ( $S$ )-2-hydroxypentanoic acid (**8**)<sup>11</sup> by a 4-step reaction sequence: i) acetylation of the hydroxy group, ii) hydrogenation, iii) oxidative degradation of the furan ring with  $\text{RuO}_4$ , and iv) mild saponification of the acetyl group. The absolute configuration and the enantiomeric excess (e.e.  $\geq 94\%$ ) of synthetic **8**  $\{[\alpha]_D^{21} -6.8^\circ$  ( $c$  0.2,  $\text{H}_2\text{O}$ ) as Ba salt} was confirmed by the comparison with the reported value {lit., <sup>11</sup>  $[\alpha]_D^{25-27} -6.0^\circ$  ( $c$  1,  $\text{H}_2\text{O}$ ) as Ba salt} and by high-performance chiral ligand exchange chromatography.<sup>14</sup>

As regards the reaction mechanism of this reaction induced by a Lewis acid, we believe that different reaction mechanisms are involved in these two Lewis acids. Although it is unclear at present, the Lewis acid should coordinate to the carbonyl and/or the sulfinyl oxygen.<sup>15</sup> Since the reaction of 2-sulfinyl-3-furylaldehyde (**1**) gave no satisfactory stereocontrol, coordination of the Sn atom of the allylstannane with the oxygen atom of the furan ring<sup>16</sup> may also be of importance for performance of the diastereoselectivity. The detailed mechanistic study is in progress.

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  - Sulfoxide ((±)-1) was prepared by the following sequence: i) treatment of 3-furyl alcohol with BuLi and di-*p*-tolyl disulfide,<sup>8a</sup> ii) pyridinium dichromate oxidation of the resultant alcohol, and iii) 3-chloroperoxybenzoic acid (*m*-CPBA) oxidation. Sulfoxide ((±)-2) was obtained by treatment of 2-(*p*-tolylsulfinyl)furan with *N,N*-dimethylformamide and lithium diisopropylamide.<sup>8b</sup> Sulfoxide ((±)-3) was prepared from 3-bromofuran by a 3-step sequence: i) treatment with BuLi and di-*p*-tolyl disulfide, ii) *m*-CPBA oxidation, and iii) formylation.<sup>8c</sup>
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  - Typical Procedures.— To a solution of (*S*<sub>s</sub>)-sulfoxide (**3**) ( $[\alpha]_{\text{D}}^{20} -289.7^\circ$  (*c* 2, CHCl<sub>3</sub>), 500 mg, 2.13 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (50 ml) at -84 °C was added a solution of TiCl<sub>4</sub> (4.27 ml, 4.27 mmol, 1 mol dm<sup>-3</sup> in CH<sub>2</sub>Cl<sub>2</sub>) *via* a syringe. After being stirred at that temperature for 20 min, allyltriphenylstannane (1.669 g, 4.27 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (15 ml) was added to the mixture *via* a syringe. The mixture was stirred for 1 h, then was quenched with saturated sodium hydrogen carbonate (30 ml), and the mixture was stirred for 2 h. The organic phase was separated and the aqueous layer was extracted with CH<sub>2</sub>Cl<sub>2</sub> (60 ml). The combined organic phase was washed with saturated sodium hydrogen carbonate (50 ml x 2), saturated brine (50 ml),

dried and concentrated. The residue (2.35 g) was purified by column chromatography on silica with hexane-ethyl acetate (3:1→3:2) as eluent to give **6** (526 mg, 89%) from early fractions, and a mixture (30 mg, 5%) of **6** and **7** from later fractions. Compound (**6**): a colorless liquid;  $[\alpha]_D^{21} -2.3^\circ$  ( $c$  1.8,  $\text{CHCl}_3$ );  $\nu_{\text{max}}$  ( $\text{CHCl}_3$ )/ $\text{cm}^{-1}$  3320, 1490, 1120, 1080, 1030;  $\delta_{\text{H}}$  (270 MHz;  $\text{CDCl}_3$ ) 2.68 (2 H, t,  $J$  7, 2-H), 4.11 (1 H, d,  $J$  7, OH), 5.01 (1 H, q,  $J$  7, 1-H), 5.13 (1 H, dm,  $J$  10, 4-H<sup>a</sup>), 5.15 (1 H, dm,  $J$  17, 4-H<sup>b</sup>), 5.82 (1 H, ddt,  $J$  17, 10, 7, 3-H), 6.24 (1 H, d,  $J$  2, 4'-H), 7.29 (2 H, d,  $J$  8, ArH), 7.30 (1 H, d,  $J$  2, 5'-H), 7.58 (2 H, d,  $J$  8, ArH);  $m/z$  259 ( $\text{M}^+ - \text{OH}$ ), 235, 217, 143, 127, 123, 91. X-Ray analysis details of **7** will be published elsewhere.

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