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

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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 allyltriphenylstannanes has been widely studied.1 From the view point of asymmetric reactions, there have been a number of reports which include the use of allylmetal compounds bearing chiral ligands,2 chiral aldehydes3 and chiral Lewis acid mediators.4 In the course of our studies on the asymmetric cycloaddition employing chiral sulfoxides,5 we were intrigued by the use of a chiral sulfinyl furfural for the reaction mediated by a Lewis acid. Despite of numerous efforts6 for asymmetric condensations using α-sulfinyl carbonyl compounds, little work has been done on the asymmetric addition to β-sulfinyl carbonyl compounds. This is presumably because of its low performance in chelation control.3a Our interest in Lewis acid-mediated reactions prompted us to investigate the possibility of asymmetric condensation of β-sulfinyl carbonyl compounds. Reported herein is a highly diastereoselective condensation of β-sulfinyl carbonyl compounds (i.e. 3-sulfinyl furfural) with allyltriphenylstannane in the presence of a Lewis acid.
To evaluate the diastereoselectivity for the addition, three types of sulfinyl-substituted furylaldehydes (±)-1–3 were selected and the results are summarized in Table 1. Aldehydes used were easily prepared by the modified methods previously described. For aldehydes ((+)-1 and (+)-2), upon treatment with allyltriphenylstannane or allyltrimethylsilane in the presence of a Lewis acid, the two homoallylic alcohols ((±)-4 and (±)-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 ((+)-3) with allyltriphenylstannane in the presence of TiCl₄ afforded the alcohol (±)-6 with a high degree of diastereoselectivity (Entry 5). 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 TiCl₄ 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 (±)-3 with TiCl₄ followed by addition of the allylstannane to afford (±)-6 predominantly. On the other hand, when the Lewis acid was added to the allylstannane prior to pre-complexation of the aldehyde, the reaction proceeded with lower diastereoselectivity (Entry 7), accompanied by a substantial amount of the diastereoisomer (±)-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 allylmetal competes with that of the formation of chelation from TiCl₄ and aldehyde.
Table 1 Reaction of sulfinyl furfurals (1)–(3) with allylmetal compounds

<table>
<thead>
<tr>
<th>Entry</th>
<th>Aldehyde</th>
<th>Allylmetal compound (equiv.)</th>
<th>Lewis acid (equiv.)</th>
<th>Reaction conditions</th>
<th>Proportions% of diastereoisomers</th>
<th>Isolated yield / %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>allyltriphenylstannane (2.0)</td>
<td>TiCl₄ (2.0)</td>
<td>2</td>
<td>-84</td>
<td>4a:4b (1:1)</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>allyltrimethylsilane (1.0)</td>
<td>SnCl₄ (2.0)</td>
<td>2</td>
<td>-78</td>
<td>5a:5b (1.8:1)</td>
</tr>
<tr>
<td>3</td>
<td>2</td>
<td>allyltriphenylstannane (2.0)</td>
<td>TiCl₄ (2.0)</td>
<td>2</td>
<td>-84</td>
<td>5a:5b (1:1)</td>
</tr>
<tr>
<td>4</td>
<td>3</td>
<td>allyltrimethylsilane (1.2)</td>
<td>TiCl₄ (2.0)</td>
<td>1</td>
<td>-78</td>
<td>6:7 (5.8:1)</td>
</tr>
<tr>
<td>5</td>
<td>3</td>
<td>allyltriphenylstannane (2.0)</td>
<td>TiCl₄ (2.0)</td>
<td>1.5</td>
<td>-84</td>
<td>6:7 (19.4:1)</td>
</tr>
<tr>
<td>6</td>
<td>3</td>
<td>allyltriphenylstannane (2.0)</td>
<td>TiCl₄ (2.0)</td>
<td>1</td>
<td>-20</td>
<td>6:7 (1.5:1)</td>
</tr>
<tr>
<td>7</td>
<td>3</td>
<td>allyltriphenylstannane (2.0)</td>
<td>TiCl₄ (2.0)</td>
<td>1</td>
<td>-84</td>
<td>6:7 (2.1:1)</td>
</tr>
<tr>
<td>8</td>
<td>3</td>
<td>allyltriphenylstannane (1.5)</td>
<td>SnCl₄ (2.0)</td>
<td>1</td>
<td>-84</td>
<td>6:7 (1.9)</td>
</tr>
<tr>
<td>9</td>
<td>3</td>
<td>allyltriphenylstannane (2.0)</td>
<td>SnCl₄ (2.0)</td>
<td>1</td>
<td>-84</td>
<td>6:7 (1:6.4)</td>
</tr>
</tbody>
</table>

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

Next, we examined the reaction of (±)-3 with another Lewis acid, SnCl₄ (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 SnCl₄, it is no importance of the order of the addition of the reagents (Entry 8 vs. 9). The use of BF₃-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 (S₅)-3 and the transformation of an optically active alcohol (6)¹⁰ into the compound (8) with known absolute configuration.¹¹ Optically pure
sulfoxide (S)-3 can be easily obtained from (+)-(S)-p-tolyl 3-furyl sulfoxide, as described in the preparation of a racemic series. The homoallylic furyl alcohol ((S)-6), obtained from the reaction of (S)-3, was transformed into (S)-2-hydroxypentanoic acid (8) by a 4-step reaction sequence: i) acetylation of the hydroxy group, ii) hydrogenation, iii) oxidative degradation of the furan ring with RuO₄, and iv) mild saponification of the acetyl group. The absolute configuration and the enantiomeric excess (e.e. ≥94%) of synthetic 8 ([α]D²¹ -6.8° (c 0.2, H₂O) as Ba salt) was confirmed by the comparison with the reported value (lit., [α]D²⁵ -6.0° (c 1, H₂O) as Ba salt) and by high-performance chiral ligand exchange chromatography.

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. Since the reaction of 2-sulfinyl-3-furylaldehyde (I) gave no satisfactory stereocontrol, coordination of the Sn atom of the allylstannane with the oxygen atom of the furan ring may also be of importance for performance of the diastereoselectivity. The detailed mechanistic study is in progress.

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REFERENCES AND NOTES


7. Sulfoxide ((±)-1) was prepared by the following sequence: i) treatment of 3-furyl alcohol with BuLi and di-p-tolyl disulfide,8a 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.8b 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.8c


10. Typical Procedures.—To a solution of (S3)-sulfoxide (3) ([α]D20 289.7° (c 2, CHCl3), 500 mg, 2.13 mmol) in dry CH2Cl2 (50 ml) at −84 °C was added a solution of TiCl4 (4.27 ml, 4.27 mmol, 1 mol dm−3 in CH2Cl2) via a syringe. After being stirred at that temperature for 20 min, allyltribphenylstannane (1.669 g, 4.27 mmol) in dry CH2Cl2 (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 CH2Cl2 (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, CHCl$_3$); $\nu_{\text{max}}$ (CHCl$_3$) / cm$^{-1}$ 3320, 1490, 1120, 1080, 1030; $\delta$ (270 MHz; CDCl$_3$) 2.68 (2 H, t, J 7, 2-H), 4.1 (1 H, d, J 7, OH), 5.01 (1 H, q, J 7, 1-H), 5.13 (1 H, dm, J 10, 4-H$^a$), 5.15 (1 H, dm, J 17, 4-H$^b$), 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 (M$^+\cdot$OH), 235, 217, 143, 127, 123, 91. X-Ray analysis details of 7 will be published elsewhere.


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