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

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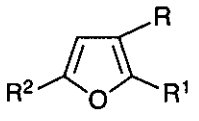
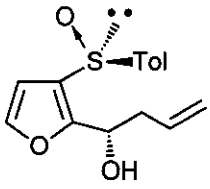
Abstract —The addition of allyltriphenylstannane to 3-sulfinylfurfural (**3**) in the presence of titanium(IV) tetrachloride proceeded with high diastereoselectivity to give the furyl alcohol (**6**), whereas the similar treatment with tin(IV) tetrachloride afforded the other diastereoisomeric alcohol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

Lewis acid-promoted allylation of aldehydes using allylmetal compounds such as allyltrialkylsilanes and allyltriarylstannanes 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 aldehydes[3] 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 efforts[6] 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.



1 R = CHO, R^1 = S(O)Tol-*p*, R^2 = H
2 R = H, R^1 = S(O)Tol-*p*, R^2 = CHO
3 R = S(O)Tol-*p*, R^1 = CHO, R^2 = H
4 R = $CH(OH)C_3H_5$, R^1 = S(O)Tol-*p*, R^2 = H
5 R = H, R^1 = S(O)Tol-*p*, R^2 = $CH(OH)C_3H_5$



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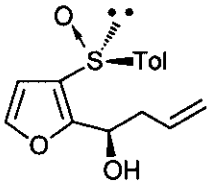

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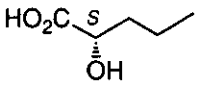

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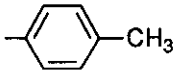
p-Tol = 

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.[7] 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 $TiCl_4$ afforded the alcohol ((±)-**6**) with a high degree of diastereoselectivity (Entry 5).[9] 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 $TiCl_4$ 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 $TiCl_4$ followed by addition of the allylstannane to afford (±)-**6** predominantly. On the other hand, when the Lewis acid was added to the allylstannnane prior to pre-complexation[9] 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 $TiCl_4$ and aldehyde.[9]

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

Entry	Aldehyde	Allylmetal compound (equiv.)	Lewis acid (equiv.)	Reaction conditions: Time (t / h)	Reaction conditions: Temp. (T /°C)	Proportions[a] of diastereoisomers	Isolated yield / %
1	**1**	allyltriphenylstannane (2.0)	$TiCl_4$ (2.0)	2	−84	**4a**:**4b** (1:1)	94
2	**2**	allyltrimethylsilane (1.0)	$SnCl_4$ (2.0)	2	−78	**5a**:**5b** (1.8:1)	63
3	**2**	allyltriphenylstannane (2.0)	$TiCl_4$ (2.0)	2	−84	**5a**:**5b** (1:1)	77
4	**3**	allyltrimethylsilane (1.2)	$TiCl_4$ (2.0)	1	−78	**6**:**7** (5.8:1)	80
5	**3**	allyltriphenylstannane (2.0)	$TiCl_4$ (2.0)	1.5	−84	**6**:**7** (19.4:1)	94
6	**3**	allyltriphenylstannane (2.0)	$TiCl_4$ (2.0)	1	−20	**6**:**7** (1.5:1)	8[b]
7	**3**	allyltriphenylstannane (2.0)	$TiCl_4$[c] (2.0)	1	−84	**6**:**7** (2.1:1)	94
8	**3**	allyltriphenylstannane (1.5)	$SnCl_4$ (2.0)	1	−84	**6**:**7** (1:9)	87
9	**3**	allyltriphenylstannane (2.0)	$SnCl_4$[c] (2.0)	1	−84	**6**:**7** (1:6.4)	89

[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, $SnCl_4$ (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 $SnCl_4$, it is no importance of the order of the addition of the reagents (Entry 8 *vs.* 9). The use of BF_3-ether complex as a Lewis acis 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_S)-**3** and the transformation of an optically active alcohol (**6**)[10] into the compound (**8**) with known absolute configuration.[11] Optically pure

sulfoxide (S_S)-**3** can be easily obtained from (+)-(S_S)-*p*-tolyl 3-furyl sulfoxide,[12] as described in the preparation of a racemic series. The homoallylic furyl alcohol[13] ((S_S)-**6**), obtained from the reaction of (S_S)-**3**, was transformed into (*S*)-2-hydroxypentanoic acid (**8**)[11] by a 4-step reaction sequence: i) acetylation of the hydroxy group, ii) hydrogenation, iii) oxidative degradation of the furan ring with RuO_4, and iv) mild saponification of the acetyl group. The absolute configuration and the enantiomeric excess (e.e. ≥94%) of synthetic **8** {$[\alpha]_D^{21}$ −6.8° (*c* 0.2, H_2O) as Ba salt} was confirmed by the comparison with the reported value {lit., [11] $[\alpha]_D^{25\text{-}27}$ −6.0° (*c* 1, H_2O) as Ba salt} and by high-performance chiral ligand exchange chromatography.[14]

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.[15] 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[16] may also be of importance for performance of the diastereoselectivity. The detailed mechanistic study is in progress.

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10. Typical Procedures.– To a solution of (S_S)-sulfoxide (**3**) ($[\alpha]_D^{20}$ −289.7° (*c* 2, $CHCl_3$), 500 mg, 2.13 mmol) in dry CH_2Cl_2 (50 ml) at −84 °C was added a solution of $TiCl_4$ (4.27 ml, 4.27 mmol, 1 mol dm^{-3} in CH_2Cl_2) *via* a syringe. After being stirred at that temperature for 20 min, allyltriphenylstannane (1.669 g, 4.27 mmol) in dry CH_2Cl_2 (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_2Cl_2 (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° (*c* 1.8, $CHCl_3$); ν_{max} ($CHCl_3$) /cm^{-1} 3320, 1490, 1120, 1080, 1030; δ_H (270 MHz; $CDCl_3$) 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^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^+-OH), 235, 217, 143, 127, 123, 91. X-Ray analysis details of **7** will be published elsewhere.

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