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속 보

키랄 Thiazolidine 촉매에 의한 알데히드에 Dialkylzinc의 거울상선택적 부가반응

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Enantioselective Addition of Dialkylzinc to Aldehydes Catalyzed by Chiral Thiazolidine

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Catalytic enantioselective addition of dialkylzinc reagent to aldehydes has proved to be a convenient and powerful methodology for the synthesis of optically active *sec*-alcohols.[1] Successful results have been obtained by using mainly chiral aminoalcohols, chiral diamines, and their derivatives, which not only accelerate the reaction but also cause asymmertic induction in the formation of the corresponding alcohols.[2,3] In the course of our studies on the development and applicability of new catalysts, we found that chiral thiazolidine **1** can behave as an effective asymmetric catalyst for enantioselective dialkylzinc-aldehyde addition. Pyridinylthiazolidines have been proved to be effective ligands for asymmetric hydrosilylation.[4] However, to the best of our knowledge, thiazolidines of cyclic amino sulfide type have not been used before as catalysts for the dialkylzinc-aldehyde addition. It is interesting to note that the thiazolidine **1** can give high yields as well as high enantioselectivities in the reactions. Homochiral (*R*)-2,2-dimethyl-4-carboethoxy-1,3-thiazolidine **1**[5] was easily synthesized by condensation of acetone with readily accessible L-cysteine ethyl ester hydrochloride in 95% yield. Reactions of diethylzinc to aldehydes were carried out in the presence of a catalytic amount of the thiazolidines **1**. Typical experimental procedure is illustrated as follows: To a stirred solution of catalyst (0.05~0.1 mmol) in toluene (3 mL) was added diethylzinc (2 mL, 1.0 M in Hexane) at 0 ℃ under nitrogen atmosphere and the mixture was stirred at RT for 20 min. Aldehyde (1.0 mmol) was slowly added at 0 ℃. The mixture was allowed to warm to RT and react for 10 h, observing the progress of the reaction by TLC. The reaction was quenched at 0 ℃ by addition of 10% HCl and extracted with CH_2Cl_2. The yield was calculated by GLC at this stage. The residue was purified by flash chromatography on silical gel (hexane/AcOEt=9/1). The enantiomeric excess was determined by HPLC analysis using chiral column.[6] Absolute configuration was assigned from the elution order or optical rotation.[6,7] As shown in *Table* 1, different aromatic aldehydes were alkylated enantioselectively with relatively high reactivity. 1-Arylpropanols with (*S*)-

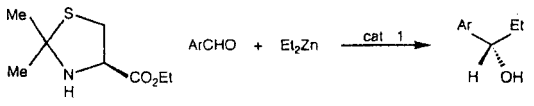

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Table 1. Enantioselective addition of diethylzinc to aldehydes

Ar	mol% of cat	time h	Optically active carbinol	
			conversion[a] %	ee[b] %
C_6H_5	6	15	88	90
C_6H_5	8	14	95	90
C_6H_5	10	14	99	89
p-ClC_6H_5	4	14	82	83
p-ClC_6H_5	6	14	95	85
p-ClC_6H_5	8	12	99	90
p-ClC_6H_5	10	12	93	88
p-$MeOC_6H_5$	8	16	80	81
o-$MeOC_6H_5$	8	15	100	83

[a]Calculated by GLC. [b]Determined by HPLC analysis using chiralcel OD column (eluent: 2.5% isopropanol in hexane).

absolute configuration were preferentially formed in all the examined cases. The data of the *Table* 1 indicate that asymmetric induction is somewhat dependent on the amount of the chiral catalyst, in which the highest enantioselectivities are achieved with 8 mol% of catalyst. In the cases of benzaldehyde and p-chlorobenzaldehyde, optically active alcohols of up to 90% ee were obtained with high chemical yield. The ee's of the addition to p- and o-methoxybenzaldehyde with this catalyst were relatively satisfactory levels.

We believe that this results may open the way to the use of chiral thiazolidines of aminosulfide type in the design of new stereoselective ligands. Efforts for the synthesis of further chiral thiazolidine ligands to improve the enantioselectivity are currently under way in this laboratory.

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5. colorless liquid, $[\alpha]=-178.6$ (c=1.4, $CHCl_3$), ^1H NMR ($CDCl_3$, 250 MHz) δ 4.18 (q, J=7.2 Hz, 2H, CH_2CH_3), 4.02(dd, J=9.1, 7.0 Hz, 1H, SCH_2CH), 3.38(dd, J=10.5, 7.0 Hz, 1H, SCH_2CH), 3.1~2.9(br s, 1H, NH), 2.96(dd, J=10.3, 9.2 Hz, 1H, SCH_2CH), 1.65(s, 3H, CCH_3), 1.47(s, 3H, CCH_3), 1.24(t, J=7.1 Hz, 3H, CH_2CH_3).
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