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Enantioselective Conjugate Addition of Diethylzinc to Chalcone Catalyzed by Chiral Tricarbonyl(arene)chromium/Nickel (II)

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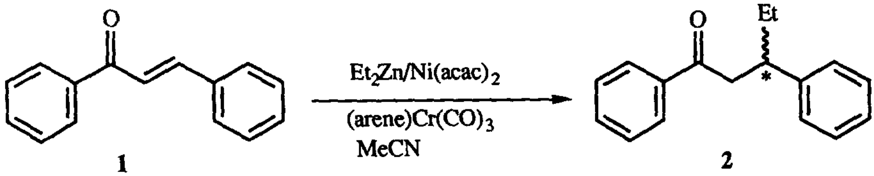
Abstract: Enantioselective conjugate addition of diethylzinc to chalcone in the presence of $Ni(acac)_2$ complexed with chiral tricarbonyl(1,2-disubstituted arene)chromium gave addition products with up to 78 % ee depending upon the amounts of Ni(II) and chiral arene chromium complexes.

There has been great interest in catalytic enantioselective conjugate addition of organometallic reagents to prochiral enones. Chiral β-amino alcohols and the related compounds have been recently proven to be effective ligands for asymmetric synthesis of optically active β-substituted ketones catalyzed by the presence of transition metals.[1,2] In a continuation of our studies into the asymmetric reactions[3] of chiral (1,2-disubstituted arene)chromium complexes possessing both benzylic amino and hydroxy groups (δ-amino alcohols), we wish to describe herein the enantioselective conjugate addition of diethylzinc to chalcone.

The chiral (1,2-disubstituted arene)chromium complexes **3**-**5** as the ligands were prepared stereoselectively from tricarbonyl(*N,N*-dimethyl α(*R*)-phenylethylamine)chromium according to the reported procedure.[4] The reaction conditions and results for the Ni(II)-catalyzed enantioselective conjugate addition reactions are summarized in Table 1. Reaction of chalcone with 2 eq of diethylzinc in the presence of nickel catalyst, generated in situ by mixing 1 mol % of $Ni(acac)_2$ and 10 mol % of the ligand **3** (R = Ph) with phenyl substituted (*S*)-configuration at the α'-position possessing benzylic hydroxy group, gave (*R*)-1,3-diphenylpentan-1-one (**2**) with 36 % ee (entry 1). The asymmetric induction is highly dependant on the amount of chiral catalyst. The



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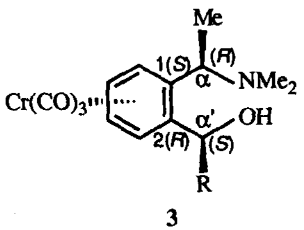

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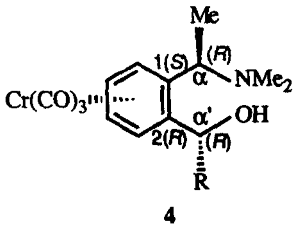

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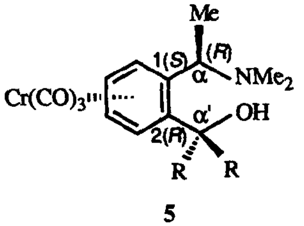

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enantioselectivity increased to 62 % ee when 5 mol % of the catalyst was used. Stoichiometric conditions gave 78 % ee of the conjugate addition product (entry 3). From the results, the phenyl substituted chiral ligand **3** (R = Ph) was found to be effective for high enantioselective conjugate addition, regardless of the chiral δ-amino alcohol. α'(*S*)-Ethyl substituted chromium complex **3** (R = Et), an efficient ligand for the enantioselective addition of diethylzinc to benzaldehyde,[3] resulted in lower selectivity. With a stereoisomeric α'-(*R*)-ethyl substituted complex **4** (R = Et) gave low enantioselectivity of the same (*R*)-product (entry 7). Disubstituted complex **5** with phenyl substituent resulted in 62 % ee of the addition product under stoichiometric conditions (entry 8). Diethyl substituted complex **5** (R = Et) produced racemic product under catalytic conditions, but a use of stoichiometric amount of the ligand and Ni(II) increased to up 37 % ee.

Since it is easily possible to modify the chiral ligands (e.g.; conversion of one of tricarbonyl to other group or modification of the phenyl ring at the α'-position), it seems that there is plenty of room for further improvement in this class of the chiral (arene)chromium complexes.

Table 1 Asymmetric Conjugate Addition of Diethylzinc to Chalcone[a]

entry	(η^6-arene)Cr(CO)$_3$	mol % Ni(acac)$_2$	ratio of Ni(II) : chiral ligand	yield (%)[b]	% ee[c] (config)
1	**3** (R = Ph)	1	1 : 10	66	36 (*R*)
2	**3** (R = Ph)	5	1 : 10	90	62 (*R*)
3	**3** (R = Ph)	100	1 : 1	70	78 (*R*)
4[d]	**3** (R = Et)	7	1 : 2.5	78	26 (*R*)
5	**3** (R = Et)	5	1 : 10	91	43 (*R*)
6	**3** (R = Et)	100	1 : 1	73	53 (*R*)
7	**4** (R = Et)	100	1 : 1	78	50 (*R*)
8	**5** (R = Ph)	100	1 : 1	71	62 (*R*)
9	**5** (R = Et)	5	1 : 10	92	1 (*R*)
10	**5** (R = Et)	100	1 : 1	70	37 (*R*)

[a] All conjugate addition reactions were carried out with 2 eq of diethylzinc at -30 °C for 18 h in acetonitrile in the presence of the chiral catalyst which was prepared in situ by mixing Ni(acac)$_2$ with the chiral (arene)chromium complex in acetonitrile at room temperature for 1 h. [b] Isolated yield after column chromatography. [c] Determined by HPLC (Daicel Chiralcel OD, Eluent 0.2 % 2-propanol in hexane). [d] Presence of 7 mol % of 2,2'-dipryridyl.

References and Notes

1 (a) Soai, K.; Hayasaka, T.; Ugajin, S. *J. Chem. Soc., Chem. Commun.* **1989**, 516; Soai, K.; Yokoyama, S.; Hayasaka, T.; Ebihara, K. *J. Org. Chem.* **1988**, *53*, 4149; Soai, K.; Hayasaka, T.; Ugajin, S.; Yokoyama, S. *Chem. Lett.* **1988**, 1571. (b) Bolm, C.; Ewald, M. *Tetrahedron Lett.* **1990**, *31*, 5011.

2 (a) Villacorta, G. M.; Rao, C. P.; Lippard, S. J. *J. Am. Chem. Soc.* **1988**, *110*, 3175. (b) Jansen, J. F. G. A.; Feringa, B. L. *J. Org. Chem.* **1990**, *55*, 4168. (c) Ahn, K-H.; Klassen, R. B.; Lippard S. J. *Organometallics*, **1990**, *9*, 3178.

3 Enantioselective addition of diethylzinc to benzaldehyde; Uemura, M.; Miyake, R.; Hayashi, Y. *J. Chem. Soc., Chem. Commun.* **1991**, 1696.

4 (a) Blagg, J.; Davies, S. G.; Goodfellow, C. L.; Sutton, K. H. *J. Chem. Soc., Perkin Trans I*, **1987**, 1805; (b) Heppert, J. A.; Aubé, J.; Thomas-Miller, M. E.; Milligan, M. L.; Takusagawa, F. *Organometallics*, **1990**, *9*, 727; (c) Uemura, M. Miyake, R.; Shiro, M.; Hayashi, Y. *Tetrahedron Lett.* **1991**, 4569.