Chiral (η^6-Arene)chromium Complexes as Catalysts for the Enantioselective Addition of Diethylzinc to Benzaldehyde

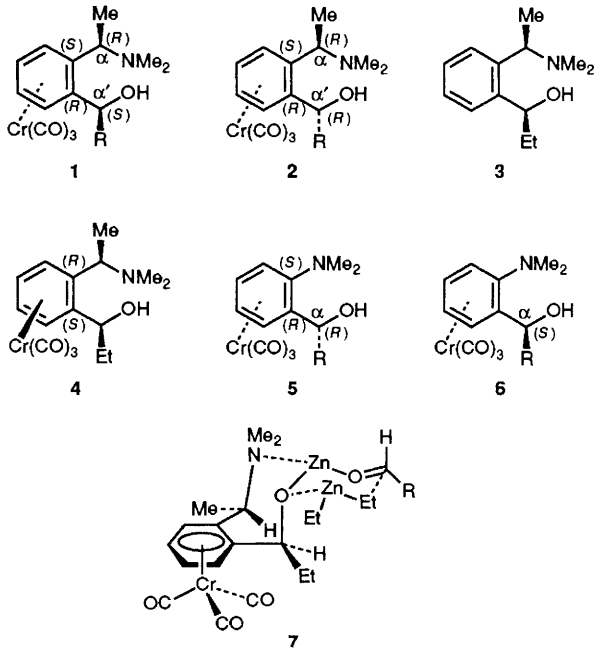
Motokazu Uemura,* Ryuta Miyake and Yuji Hayashi

Faculty of Science, Osaka City University, Sugimoto 3-3-138, Sumiyoshi-ku, Osaka 558, Japan

Chiral (η^6-1,2-disubstituted arene)chromium complexes possessing amino and hydroxy groups catalyse the addition of diethylzinc to benzaldehyde with highly enantioselective induction.

An enantioselective reaction through a catalytic process is now recognized as one of the most important and challenging problems in organic synthesis. It has been reported[1] by several groups that chiral amino alcohols not only accelerate but also direct the stereochemical outcome in the absolute sense. Among these alcohols, chiral β-amino alcohols as ligands have been mostly used to achieve high enantioselectivity in the asymmetric alkylation of aldehydes. Tricarbonyl(η^6-arene)-chromium complexes can exist in two enantiomeric forms when the phenyl ring has two different substituents at the *ortho*- or *meta*-positions. Therefore, these types of chromium complexes possessing chiral centres in the side chains are attractive compounds as asymmetric ligands, because they have both chiral centre and facial chirality. We report here the asymmetric ethylation of benzaldehyde with diethylzinc catalysed by chiral (1,2-disubstituted arene)chromium complexes possessing amino and hydroxy groups in the side chain.

The requisite chiral δ-amino alcohol 1,2-disubstituted arene chromium complexes are prepared stereoselectively as follows. Diastereoselective *ortho* lithiation[2] of (*R*)-tricarbonyl(*N*,*N*-dimethyl-α-phenylethylamine)chromium followed by reaction with aldehydes produces predominantly Ar(*S*,*R*,α*R*,α′*S*) chromium complexes **1**† in a ratio of 92–94 : 8–6. The newly created stereogenic centre at the C-α′ position was found to have the (*S*)-configuration by X-ray crystallography. The corresponding stereoisomeric chromium complexes **2** with the (*R*) configuration at C-α′ were easily synthesized as major products† in a ratio of 66–99 : 34–1 by the reaction of Ar(*S*,*R*,α*R*)tricarbonyl(2-formyl-*N*,*N*-dimethyl-α-phenethylamine)chromium‡ with aryl- or alkyl-lithiums. The corresponding chromium complex **4** with opposite aromatic face chirality was prepared *via* the chromium-free compound **3** from **1** (R = Et) by oxidative (air) decomplexation and re-complexation with (naphthalene)chromium.[3] The homologous chiral γ-amino alcohol chromium complex **5**† with α(*R*)-configuration was obtained by the reaction of organolithiums with (−)-tricarbonyl(2-formyldimethylaniline)chromium.[4] The corresponding stereoisomeric complex **6**† with α(*S*)-configuration was synthesized from **5** by oxidation with active manganese dioxide and subsequent reduction with $LiAlH_4$.



Since the chiral (1,2-disubstituted arene)chromium complexes with amino and hydroxy groups at the side chain can be easily prepared stereoselectively, we next examined the catalytic asymmetric ethylation of benzaldehyde utilizing the chiral (arene)chromium complexes. Reaction results are summarized in Table 1. Among these chiral chromium complexes, complex **1** with the Ar(*S*,*R*,α*R*,α′*S*)-configuration gave a high degree of enantioselectivity in the catalytic ethylation of benzaldehyde despite the fact that the chromium complex **1** are δ-amino alcohols (resulting in a seven-membered ring *via* coordination of the zinc with two heteroatoms in the transition states). The complex with α′(*S*)-ethyl group gave the highest enantioselectivity (entry 3). The stereoisomeric complex **2** with the (*R*)-configuration at the α′-position and unsubstituted complex **1** (R = H) without chirality of the hydroxy group gave lower enantioselectivity (entries 7 and 1). Therefore, the asymmetric carbon bearing the hydroxy group is required to be in the (*S*)-configuration for the achievement of high enantioselectivity. The corresponding $Cr(CO)_3$-free chiral δ-amino alcohol **3** resulted in only 24% e.e. to give the (*S*)-alcohol under the same conditions (entry 8). Thus, $Cr(CO)_3$ complexation of the

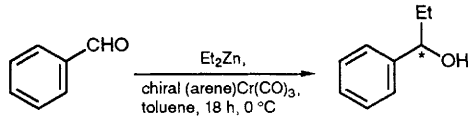


Table 1 Asymmetric ethylation of benzaldehyde catalysed by chiral (arene)$Cr(CO)_3$[a]

Entry	Complex	Yield (%)[b]	Optical yield (% e.e.)[c]	Absolute configuration[d]
1	**1** (R = H)	70	15	*S*
2	**1** (R = Me)	83	63	*S*
3	**1** (R = Et)	87	93	*S*
4	**1** (R = *o*-$CF_3C_6H_4$)	97	89	*S*
5	**1** (R = *m*-$CF_3C_6H_4$)	96	88	*S*
6	**1** (R = C_6F_5)	98	87	*S*
7	**2** (R = Et)	87	50	*S*
8	**3**	71	24	*S*
9	**4**	79	30	*R*
10	**5** (R = Me)	49	6	*S*
11	**6** (R = Me)	56	12	*S*

[a] Reaction was carried out in toluene at 0 °C for 18 h in the presence of 5 mol% of catalyst. [b] Isolated yield. [c] The enantiomeric excess (e.e.) was measured by HPLC using DAICEL CHIRALPAK OB (eluent: 10% propan-2-ol in hexane). [d] The absolute configuration of 1-phenyl-propyl alcohol was determined by optical rotation.

† All new compounds gave satisfactory analyses and spectral data.

‡ The complex was stereoselectively synthesized by *ortho* lithiation and subsequent trapping with dimethylformamide according to the literature method; see ref. 2.

ligands has a large effect on the enantioselectivity in the asymmetric ethylation. The face-inverted complex **4** gave the (*R*)-alcohol in 30% e.e. (entry 9). From these results, direction of $Cr(CO)_3$ complexation to the arene ring is also a significant factor for high enantioselectivity. The homologous γ-amino alcohol chromium complexes **5** and **6** gave poor enantioselectivity, although the transition states formed were six-membered cyclic intermediates by the coordination of the zinc and two heteroatoms.

In conclusion, the direction of $Cr(CO)_3$ complexation and the chirality of the benzylic alcohol are important factors. The molecular model of catalyst **1** suggests that the zinc alkoxide formed a seven-membered ring with a chair conformation[7] in an *exo*-configuration to the $Cr(CO)_3$ group, and the ethylation can be interpreted in terms of a six-membered cyclic transition state **7**. Nucleophilic attack of the ethyl group from the *Si*-face of the aldehyde in the transition state leads to the *S*-isomer. Similarly, the chiral ferrocenyl complexes with δ-amino alcohols catalysed ethylation of aldehydes in high enantioselectivity.[5]

Received, 1st August 1991; Com. 1/04007C

References

1 A review: R. Noyori and M. Kitamura, *Angew. Chem., Int. Ed. Engl.*, 1991, **30**, 49. Some representative examples; N. Oguni, Y. Matsuda and T. Kaneko, *J. Am. Chem. Soc.*, 1988, **110**, 7877; M. Kitamura, S. Okada, S. Suga and R. Noyori, *J. Am. Chem. Soc.*, 1989, **111**, 4028; K. Soai, A. Ookawa, K. Ogawa and T. Kaba, *J. Am. Chem. Soc.*, 1987, **109**, 7111; E J. Corey, P. W. Yuen, F. J. Hannon and D. A. Wierda, *J. Org. Chem.*, 1990, **55**, 784; W. Oppolzer and R. N. Radinov, *Tetrahedron Lett.*, 1988, **29**, 5645; N. N. Joshi, M. Srebnik and H. C. Brown, *Tetrahedron Lett.*, 1989, **30**, 5551; K. Takano, H. Ushio and H. Suzuki, *J. Chem. Soc., Chem. Commun.*, 1989, 1700.

2 J. Blagg, S. G. Davies, C. L. Goodfellow and K. H. Sutton, *J. Chem. Soc., Perkin Trans. 1*, 1987, 1805; J. A. Heppert, J. Aube, M. E. Thomas-Miller, M. L. Milligan and F. Takusagawa, *Organometallics*, 1990, **9**, 727.

3 M. Uemura, T. Kobayashi, K. Isobe, T. Minami and Y. Hayashi, *J. Org. Chem.*, 1986, **51**, 2859.

4 The optically active complex was obtained by kinetic resolution; L. A. Bromley, S. G. Davies and C. L. Goodfellow, *Tetrahedron Asymm.*, 1991, **2**, 139.

5 M. Watanabe, S. Araki, Y. Butsugan and M. Uemura, *J. Org. Chem.*, 1991, **56**, 2218.