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Enantioselective conjugate addition of diethylzinc to chalcone catalyzed by $\text{Co}(\text{acac})_2$ and chiral amino alcohols

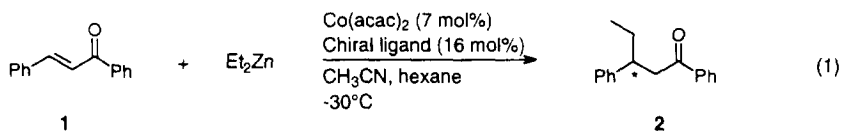
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Abstract: $\text{Co}(\text{acac})_2$ in the presence of chiral ligands has been employed as catalyst for the enantioselective conjugate addition of diethylzinc to chalcone. With chiral amino alcohols derived from (+)-camphor, enantioselectivities up to 83% were achieved. © 1997 Elsevier Science Ltd

Conjugate addition reactions of carbon nucleophiles to α,β -unsaturated compounds are among the most widely used methods for carbon–carbon bond formation in organic synthesis.¹ Asymmetric conjugate addition reactions, however, still lack the ‘ideal chiral catalyst’ which promotes enantioselective conjugate addition of readily available organometallic reagents to a wide variety of substrates.² Considerable progress has been made with the copper catalyzed conjugate addition of Grignard reagents³ and the nickel catalyzed conjugate addition of diethylzinc.⁴ Also a copper catalyzed 1,4-addition of diethylzinc to cyclohexenone has been reported.⁵ Recently, we and others have found the first catalytic system capable of the enantioselective conjugate addition of dialkylzinc reagents to *both* cyclic and acyclic substrates.⁵

Although transmetallation reactions of organozinc reagents to several metal salts have been proposed,⁶ Knochel and co-workers recently reported the first synthetically useful transmetallations of organozinc reagents to *cobalt* in acylation and allylation reactions.⁷ The use of organocobalt reagents in conjugate addition reactions has been limited.⁸ Herein we describe catalytic enantioselective conjugate addition reactions of diethylzinc to chalcone using $\text{Co}(\text{acac})_2$ and chiral amino alcohols (Equation 1).



When $\text{Co}(\text{acac})_2$ (7 mol%) and chiral amino alcohol **3** (16 mol%) were employed in the model reaction the 1,4-product **2** was isolated in 61% yield (70% conversion according to GC analysis, after 16 h at -30°C).⁹ No 1,2-addition was observed and chiral HPLC analysis⁹ revealed an enantioselectivity of 67%.

Three other chiral amino alcohol ligands **4–6** were also examined in the model reaction. With ligand **4** product **2** was isolated in 73% yield with an e.e. of 83%. Ligands **5**¹⁰ and **6** gave substantial lower conversions to the 1,4-product (~50%) and moderate e.e.'s (see Figure 1).

Using chiral amino alcohols the cobalt catalyzed conjugate addition is relatively slow compared to the nickel catalyzed reaction (>95% conversion to the 1,4-product **2** after 2 h at -30°C)^{4c} and a considerable amount (5% with ligands **3** and **4**, 20% with ligands **5** and **6**) of the reduced by-product 1,3-diphenylpropan-1-one has been detected.¹¹ However, relatively high enantioselectivities were found in this reaction and moreover transmetallation processes of organozinc reagents to cobalt seem to have a greater applicability in (enantioselective) organic reactions⁷ than transmetallation to

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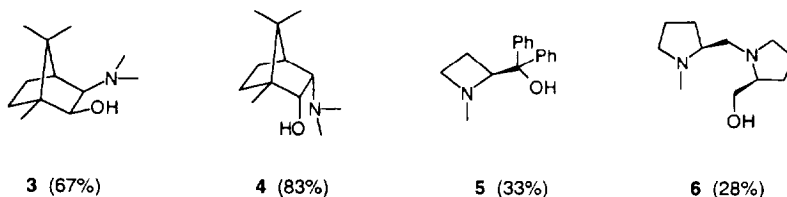


Figure 1. Chiral amino alcohols used in the $\text{Co}(\text{acac})_2$ catalyzed addition of Et_2Zn to **1**. In brackets the e.e. of product **2** achieved with the given ligand.

other metal salts.¹² Therefore, further studies involving enantioselective cobalt mediated reactions of organozinc reagents are in progress in our laboratories.

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