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OPTICALLY ACTIVE BIPYRIDINES IN NICKEL CATALYZED ENANTIOSELECTIVE CONJUGATE ADDITION TO ENONES

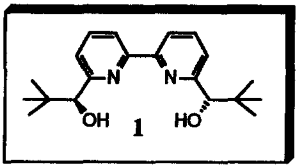
Carsten Bolm* and Martina Ewald

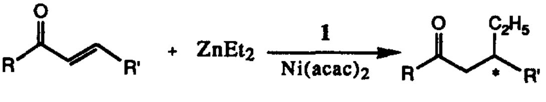
*Institut für Organische Chemie der Universität, St. Johanns-Ring 19,
CH-4056 Basel (Switzerland)*

Abstract: In the presence of catalytic amounts of $Ni(acac)_2$ and a chiral bipyridine, diethyl zinc adds enantioselectively to enones to give optically active β-substituted ketones in good yields.

Optically active bipyridine **1** has proved to be an efficient catalyst for the enantioselective addition of diethyl zinc to aldehydes.[1] The resulting alcohols were obtained in good yields and with high enantiomeric excess. **1** is readily available in both enantiomeric forms by asymmetric synthesis.[1] Many methods have been reported for the asymmetric conjugate addition of chirally modified organometallic reagents to enones.[2] In general, they require stoichiometric or even excess amounts of chiral reagent. Only a few reports have focused on catalytic enantioselective addition to enones.[3]

In our studies, we were interested in the catalytic use of nickel complexes of bipyridine **1** for the enantioselective addition of organozinc reagents to α,β-unsaturated ketones.[4] We now report that ethyl transfer from diethyl zinc to chalcone (**2a**) and other aryl substituted enones can be catalyzed by the combination of nickel acetylacetonate [$Ni(acac)_2$] and bipyridine **1**. Optically active β-substituted ketones are obtained in high yields and with good asymmetric induction.[5] The optically active ligand **1** can be separated by column chromatography and recycled without loss of optical purity.





2a/3a $R = C_6H_5$, $R' = C_6H_5$
2b/3b $R = p\text{-}CH_3OC_6H_4$, $R' = C_6H_5$
2c/3c $R = CH_3$, $R' = C_6H_5$

The asymmetric induction is highly dependant on the Ni : ligand ratio (see table), the solvent and temperature. When 20 mol% of **1** was used, as little as 1 mol% of $Ni(acac)_2$ was required for effective catalysis (yield for **3a**: 75%, ee = 72%). The selectivity decreased to 54% ee when the Ni : ligand ratio was reduced to 1 : 10 (1 mol% of $Ni(acac)_2$, 10 mol% of **1**). Increasing the amount of **1** to 30 mol% did not raise the enantiomeric excess. Comparison between entries 4 / 5 and 6 / 7 demonstrates the dependance of the optical purity on the catalyst concentration. The reactions were carried out in acetonitrile under heterogeneous conditions at -30°C. In toluene, THF, or DMF, products with lower enantiomeric excess were obtained. Conjugate addition to 4'-methoxy-

Table. Enantioselective conjugate addition to enones catalyzed by $Ni(acac)_2$/(*S,S*)-**1**.

Entry	Substrate	mol% $Ni(acac)_2$	Ratio Ni : **1**	Yield[b] [%]	ee[c] [%]
1	**2a**	1	1 : 30	55	72
2	**2a**	1	1 : 20	75	72
3	**2a**	1	1 : 10	82	54
4	**2a**	1	1 : 5	74	20
5	**2a**	2	1 : 5	66	48
6	**2a**	2	1 : 3	73	18
7	**2a**	5	1 : 3	58	58
8	**2a**	5	1 : 1	69	18
9	**2b**	5	1 : 10	68	74
10	**2c**	5	1 : 5	76	2[d]

[a] The diethyl zinc was added as a 1 M solution in hexane. [b] After column chromatography. [c] Determined by HPLC analysis using a chiral column (see experimental); major for **3a** and **3c**: (*R*)-configuration; for **3b**: undetermined. [d] According to rotation value.[6]

chalcone (**2b**) afforded **3b** with an enantiomeric excess of 74%. In the case of the methyl-substituted derivative **2c**, the product was obtained in good yields but was essentially racemic.

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(5) Experimental: In a flame-dried flask 3 mg (0.01 mmol) of $Ni(acac)_2$ (acac = acetylacetonate) and 66 mg (0.20 mmol) of (*S,S*)-**1** in 2 ml of dry acetonitrile were stirred at 73°C under argon for 1 h. The suspension was cooled to room temperature and a solution of 208 mg (1.00 mmol) 1,3-diphenylpropenone in 2 ml of dry acetonitrile was added. The mixture was cooled to -30°C and 1.5 ml of a 1 M solution of diethyl zinc in hexane (1.50 mmol) were added dropwise. After 18 h at -30°C, the reaction was quenched with 10 ml of 1 M hydrochloric acid. The mixture was extracted three times with 20 ml of dichloromethane. The combined organic layers were washed with brine and dried over sodium sulfate. Evaporation under reduced pressure gave a crude product that was purified by column chromatography (silica gel, eluent: petrolether : ethyl acetate 100 : 1). 176 mg (76%) of 1,3-diphenylpentan-1-one (**3a**) was obtained (72% ee; determined by HPLC analysis using a chiral column: CHIRACEL OD, 0.25% 2-propanol in hexane; flow rate: 1.0 ml/min, UV detector (254 nm); retention time for **3a**: (*S*)-enantiomer 15.8 min. (minor), (*R*)-enantiomer 18.0 min. (major); optical rotation: $[a]_D$ -8.2° (c 2.62, EtOH) [78% ee, based on reported value[6]].
1 was recovered by eluting the column with ethyl acetate and recrystallization of the crude crystals from hexane.

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