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Preliminary communication

Optically active phenanthrolines in asymmetric catalysis. Rhodium-catalyzed asymmetric transfer hydrogenation of acetophenone

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Abstract

The catalyst formed in situ from [Rh(1,5-cyclooctadiene)Cl]$_2$ and (+)-(*S*)-3-s-butyl-1,10-phenanthroline promotes the asymmetric transfer hydrogenation of acetophenone in isopropanol solution; optical yields of up to 31% are obtained.

We previously reported that the asymmetric transfer hydrogenation of acetophenone can be accomplished, albeit with moderate stereoselectivity, by use of rhodium(I) catalysts containing optically active alkyl 2,2′-bipyridines [1]. In continuation of our studies in the field of the synthesis of optically active nitrogen heterocycles, we recently prepared some optically active alkyl 1,10-phenanthrolines, the first representatives of a new class of chiral chelating nitrogen ligands [2].

As an initial example of the application of these compounds in the field of asymmetric catalysis, we describe here preliminary results obtained in the asymmetric hydrogen transfer from propan-2-ol to acetophenone promoted by the catalytic system rhodium(I)/(+)-(*S*)-3-s-butyl-1,10-phenantroline (**1**).

$$C_6H_5(CH_3)C{=}O + (CH_3)_2CHOH \rightleftharpoons C_6H_5(CH_3)CHOH + (CH_3)C{=}O$$

The chiral auxiliary has been synthesized from 8-aminoquinoline (**2**) and (+)-2-s-butylacrolein (**3**) by a modified Doebner–Miller reaction, as outlined in Scheme 1. Compound **1** was isolated in 30% yield as light yellow crystals (m.p. 92–93°C; $[\alpha]_D^{25}$ +22.4 (c = 1.04; EtOH 95%) after column chromatography and several crystallizations. Its identity was confirmed spectroscopically.

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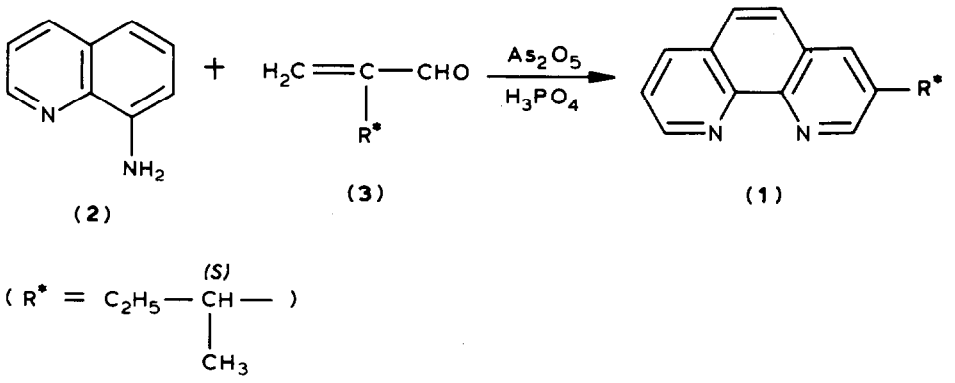

Scheme 1.

The enantiomeric purity of **1** has not yet been directly determined, but it reasonably can be assumed to be the same as that of the parent chiron **3** (91%) by analogy with the results observed in the case of the synthesis of chiral 3-alkylpyridines [3].

The catalytic experiments were carried out under nitrogen in isopropanol solution (45 ml) containing potassium hydroxide (5×10^{-4} mol). The pro-catalyst was prepared in situ by addition of suitable amount of the chiral ligand to $[Rh(COD)Cl]_2$ (2.5×10^{-5} mol). The solution was then refluxed for 1 h in order to activate the catalytic system, and then acetophenone (0.01 mol) was added and the reduction was carried out at reflux temperature. Table 1 summarizes the experimental conditions and the results obtained in a set of catalytic runs. In keeping with previous observations [4,5], the catalytic system appears quite sensitive to the experimental conditions and to the preactivation procedure, so that even slight modifications give rise to marked differences in the reaction rates and stereoselectivities.

These discrepancies may sometimes be related to a reduced homogeneity of the catalytic system, which became evident in a few runs by separation of a black

Table 1

Reduction of acetophenone by hydrogen transfer from isopropanol catalyzed by $[Rh(COD)Cl]_2$ and (+)-(*S*)-3-s-butyl-1,10-phenanthroline (Reaction conditions: 2.5×10^{-5} mol of $[Rh(COD)Cl]_2$ in 45 ml of isopropanol; KOH/Rh = 10; *T* 83° C)

Run	[S]/[Rh]	[Rh]/[Ligand]	TN [a]	Optical yield [b] (%)
1	200	2	360	25.5
2	200	4	144	20.5
3	200	10	88	17.2
4	200	25	45	10.0
5	100	2	368	5.0
6	100	4	372	31.1
7	1000	2	45	13.2
8	1000	4	22	15.4

[a] TN = turnover number = mols of substrate converted per hour and g-atom of rhodium. [b] Extrapolated to 100% optical purity of the ligand. In all the experiments the predominant enantiomer had the (*S*) configuration.

precipitate during the reaction. We emphasize, however, that this behaviour is unusual, and almost all the experiments proceeded under strictly homogeneous conditions even at the lowest ligand-to-metal ratios.

In general the best stereoselectivities are associated with the highest reaction rates and with the lowest substrate-to-metal ratios. This is probably a consequence of the short contact times required in these runs, which limit the racemization of the reaction product which is rather labile under the conditions. The same feature may account at least in part, for the decrease in the stereoselectivity associated with increase in the ligand-to-metal ratio. In this case, however, other factors seem also to be involved, and further investigation is required.

Comparison of these results with those obtained in the same process with the structurally related (+)-(*S*)-5-s-butyl-2,2′-bipyridine shows that, while the general features are similar, with the new catalyst the sign of the asymmetric induction is always opposite to those obtained with the latter catalyst and the optical yields are usually more than one order of magnitude higher. These substantial differences are impressive in that they result from a structural change in the ligand that does not directly involve either the asymmetric unit responsible for the chiral information (a s-butyl substituent in both cases) or its disposition with respect to the putative reactive site of the catalyst, or the size of the chelate ring in the metal complex.

The inversion of the topicity of the asymmetric induction and the remarkable enhancement of the stereoselectivity of the process must be associated with the greater rigidity of the phenanthroline than of the bipyridine ligand. The restriction of the conformational possibilities for the Rh/phenantroline catalyst allows an efficient transfer of the chiral information through four bonds to a metal center rather remote from the asymmetric carbon. We expect that this effect can be increased by reducing the distance between the catalytic and the asymmetric centres, and work along this line is in progress.

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References

1 C. Botteghi, G. Chelucci, G. Chessa, G. Delogu, S. Gladiali and F. Soccolini, J. Organomet. Chem., 304 (1986) 217.
2 S. Gladiali, G. Chelucci, G. Chessa, G. Delogu, F. Soccolini and C. Botteghi, Ital. Patent Application A/86,21517 (1986).
3 U. Azzena, G. Chelucci, G. Delogu, S. Gladiali, M. Marchetti, F. Soccolini and C. Botteghi, Gazz. Chim. Ital., 116 (1986) 307.
4 G. Zassinovich and F. Grisoni, J. Organomet. Chem., 247 (1983) C24.
5 R. Spogliarich, J. Kaspar, M. Graziani and F. Morandini, J. Organomet. Chem., 306 (1986) 407.