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# CHIRAL AMINO AND DIAMINO PHOSPHINES AS LIGANDS FOR ASYMMETRIC HYDROGENATION CATALYSTS

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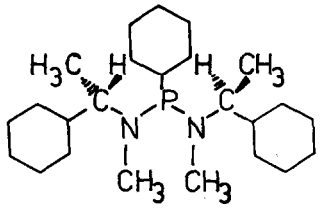
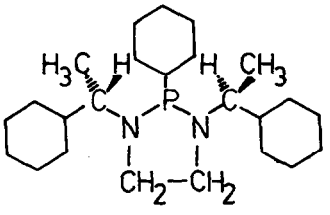
A recent communication by Fiorini et al. [1] on asymmetric hydrogenations by means of a chiral bis(aminophosphine) chlororhodium complex induces us to publish some own results on a very similar topic, obtained by us parallel to the work cited above. Starting investigations on the ability of optically active amides of phosphinous and phosphonous acids to act as asymmetry inducing ligands (notice also l.c. [2] ), we compared the stereoselective effects of Rh(I) complexes with the ligands I - III in asymmetric hydrogenation of aminoacid precursors IVa and IVb. Each of these ligands contains 2 chiral $\alpha$-phenylethyl groups combined in a different manner and with different degrees of conformational flexibility.



I



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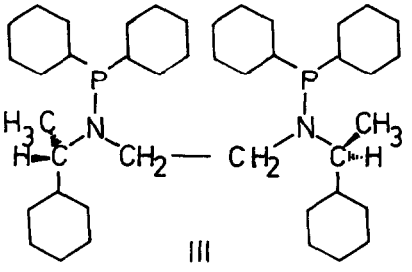

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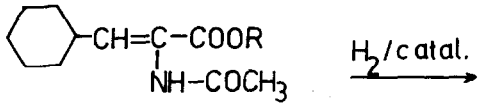
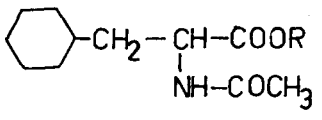


IV



V

IVa: R = H
IVb: R = $CH_3$

Va: R = H
Vb: R = $CH_3$

Phenylphosphonous acid bis[N-methyl-(S)-$\alpha$-phenylethylamide] I was prepared by reacting 4 moles of (S)(-)-N-methyl $\alpha$-phenylethylamine with $PhPCl_2$ in

$Et_2O$; yield 76 %; m.p. 79 - 81 °C, from acetone; $[\alpha]_D^{24}$+80.5° (c 0.79; $C_6H_6$). N.N'-Bis[(S)-α-phenylethyl] ethylenediamine VI, the common precursor of II and III, was obtained from oxalic acid bis[N-(S)-α-phenylethylamide] and $LiAlH_4$ in boiling tetrahydrofurane; yield 80 - 88 %; $[\alpha]_D^{20}$-72.9° (c 9.7; EtOH).

Cyclocondensation of VI and $PhPCl_2$ with $Et_3N$ in $Et_2O$ gave 1.3-bis [(S)-α-phenylethyl]-2-phenyl-2-phosphaimidazolidine II; yield 69 %, colourless viscous liquid, polymerizing partially on distillation at 120 - 130 °C (bath)/ $10^{-4}$ Torr; $[\alpha]_D^{19}$-19.9° (c 2.7; benzene).

The amide III, described already in l.c. [1], was synthesized in an analogous manner from VI and 2 moles of $Ph_2PCl$; m.p. 135 - 136.5 °C, from $Et_2O$; $[\alpha]_D^{25}$-102.7° (c 1.6; $C_6H_6$); $[\alpha]_D^{25}$-103.7° (c 1.3; $CHCl_3$).

Compounds I, II, III and VI analyzed correctly for C, H, N, and P and gave reasonable i.r. and mass spectra.

The catalysts were prepared in situ from the ligands I - III and $[Rh(C_2H_4)_2Cl]_2$ (Rh:P = 1:2) in benzene, and injected under anaerob conditions into the thermostated normal pressure hydrogenation apparatus. The results of the hydrogenation experiments are summarized in table 1.

Asymmetric hydrogenation of methyl α-acetamidocinnamate (IVb) in benzene solution led in all three cases to relatively small optical yields ($p \leqslant 20$ % ee), the catalyst derived from I being the most stereoselective one.

Surprisingly, substitution of I for II lowers the activity of the Rh-complexes seriously, in spite of the close structural relationship between both compounds. This might be caused by the rigid conformation of II, leading to extremely strong shielding of the coordination centre by 4 bulky α-phenylethyl groups. In these experiments with II-Rh-complexes we obtained usually low chemical yields and no unequivocally reproducible stereoselectivity.

Using methanol instead of benzene as the solvent changes the picture drastically. In this solvent, the chlororhodium complex of I was less active and stereoselective than in benzene, the hydrogen uptake usually ceasing before reaching the calculated amount. This might be due - at least in part - to rapid methanolysis of P-N-bonds during the catalytic process, as indicated by an alcaline reaction of the solution after hydrogenation.

On the other hand, in the case of III•RhCl MeOH strongly enhanced rate and stereospecificity of the catalysis. When hydrogenating the free acid IVa in MeOH, we observed p = 80 % ee (lit. [1] : p = 84 %), and for the corresponding ester IVb p = 66 % ee (lit. [1] : p = 49 %). Looking for an explanation of this surprising solvent effect, three possibilities seemed worthwhile discussion:

(1.) Direct participation of the methanol OH-bond in one step of the catalytic cycle by protolysis of the intermediate alkyl rhodium complex.
(2.) Ionization of the chloro complex in the more polar solvent, yielding a catalytically more active and stereoselective cationic rhodium species.

Table 1: Asymmetric hydrogenations of α-acetamido cinnamic acid (IVa) and its ester (IVb) using Rh(I)-complexes of ligands I, II, and III at normal pressure of $H_2$

| Catalyst [a] (c [mM]) | | Substrate (c [mM]) | | Solvent | Temp. | half life [h] [b] | chem. yield [c] | optical yield [% ee] (configuration) |
|---|---|---|---|---|---|---|---|---|
| $RhClL_2$ | , L = I (4.53) | IVb | (45.6) | $C_6H_6$ | 31 °C | 6 | 87 % | 19.7 % (R) |
| " | , L = II (4.57) | IVb | (45.6) | " | 31 °C | ≫25 | 35 % | d) |
| " | , $L_2$ = III (4.93) | IVb | (45.6) | " | 31 °C | 0.58 | 87 % | 9.0 % (R) |
| " | , L = I (4.55) | IVb | (45.6) | MeOH | 31 °C | >40 | 61 % | 4.2 % (R) |
| " | , L = II (4.66) | IVb | (45.6) | " | 31 °C | 24 | 75 % | d) |
| " | , $L_2$ = III (0.18) | IVb | (91.7) | " | 25 °C | 0.30 | 89 % | 66.2 % (R) |
| " | , $L_2$ = III (0.60) | IVa | (195) | " | 25 °C | 0.63 | 99 % | 79.8 % (R) |
| $[RhL_2]^+BF_4^-$ | , L = I (3.67) | IVb | (45.6) | $C_6H_6$ | 31 °C | 5.5 | 87 % | 17.2 % (R) |
| " | , L = II (4.58) | IVb | (45.6) | " | 31 °C | 4.8 | 76 % | d) |
| " | , $L_2$ = III (0.39) | IVb | (43.2) | " | 25 °C | 0.16 | 90 % | 82.5 % (R) |
| " | , $L_2$ = III (0.39) | IVb | (45.6) | MeOH | 25 °C | 0.08 | 91 % | 66.8 % (R) |
| " | , $L_2$ = III (0.42) | IVa | (44.7) | " | 25 °C | 0.03 | 90 % | 81.7 % (R) |

a) The formula does'nt take into account solvatation or dimerization.

b) in rapid reactions possibly influenced by diffusion.

c) The chemical yield of the reactions IVb ⟶ Vb was determined by hydrolysis of the evaporated reaction mixture with 5 N HCl (15 h, 20 °C) and extraction of the free acid Va. The optical purity was not changed by this process. Because of slight hydrolysis of the N-acetyl group, the given chemical yields may be a little lower than the true ones of the hydrogenation.

d) low and difficult to be reproduced.

(3.) General solvent effects, e.g. by H-bonding between solvent and substrate or by donor-acceptor interaction between solvent and catalyt.

Alternative (1) could be excluded by means of tracer experiments. The use of $CH_3OD$ instead if $CH_3OH$ caused neither changes in rate or p nor incorporation of D into the product (D-content of Vb neglegible; HD-content of the excess $H_2$ after hydrogenation $\leq 3.7$ %).

On the other hand, (2) could be clearly shown to explain the experimental data. The cationic complex $[L_2Rh(Solv.)_x]^+BF_4^-$ ($L_2$ = III), prepared in situ from $L_2RhCl(Solv.)_y$ and $AgBF_4$, proved in benzene solution to be even more active and stereoselective than the chloro complex in methanol, the optical yields of Vb from IVb reaching up to 82 % ee.

In striking contrast to benzene as solvent, we found for MeOH solutions no significant differences between the catalytic behaviour of the neutral chloro and the cationic complexes in hydrogenations of IVa to Va and IVb to Vb. This points to a high degree of dissociation of the chloro complex. Glaser et al. [3] reported the corresponding cationic Rh(I)-DIOP complex in EtOH, compared with the RhCl-DIOP complex in EtOH, to be slightly more active, but equally stereoselective. It might be concluded that in this case also the steric course of the hydrogenation is determined nearly totally by the cationic species. The slightly lower p obtained with the cationic complex of III in MeOH vs. benzene should be due to some additional solvent effect.

The hitherto unknown drastic unfluence of catalyst dissociation upon stereoselectivity might be understood in several ways, based on considerations of Gelbard, Kagan, and Stern [4] about the mechanism of asymmetric catalysis by DIOP complexes. However, more detailed speculations seem not yet to be justified.

## References

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