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# EFFECTIVE CATALYTIC ASYMMETRIC SYNTHESIS OF R-(-)-PANTOLACTONE WITH POLYMER SUPPORTED CHIRAL PYRROLIDINEPHOSPHINE-RHODIUM COMPLEXES[1)]

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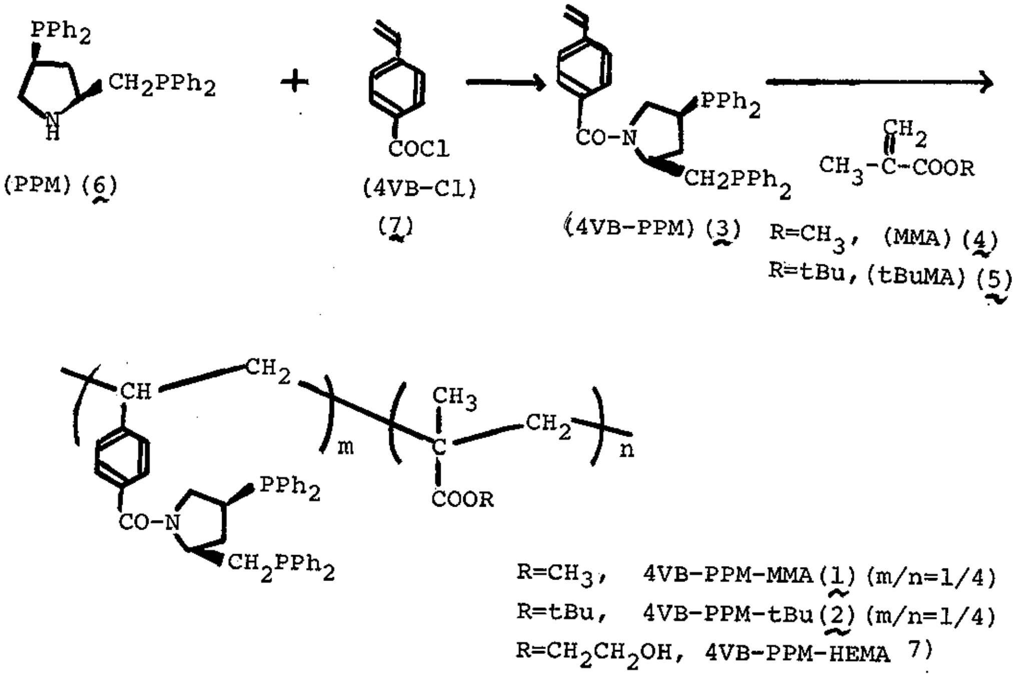
The syntheses of new polymer supported chiral pyrrolidinephosphine ligands; 4VB-PPM-MMA (1) and 4VB-PPM-tBuMA (2) and their application to the asymmetric hydrogenation of ketopantolactone were described. Thus, 4VB-PPM-MMA-Rh and 4VB-PPM-tBuMA-Rh gave R-(-)-pantolactone in 73.4 and 75.7% optical yield respectively.

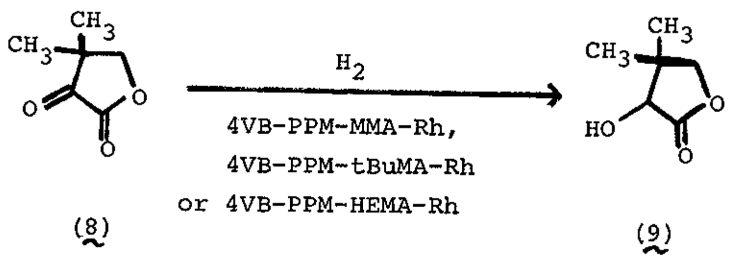
Homogeneous catalytic asymmetric hydrogenations[2)] with chiral phosphine rhodium catalysts have recently been proven to be practically useful for the preparation of chiral α-amino acids[3)], pantolactone[4)] and α-methylsuccinic acid[5)]. However, in these hydrogenations, chiral ligand-rhodium catalysts could not be reused because of their difficult separation from the reaction mixture. To overcome this difficulty, the polymer supported chiral catalysts have been investigated especially for the preparation of chiral α-amino acids[6,7)] and α-methylsuccinic acid[7)].

We wish to describe here the syntheses of new polymer supported pyrrolidinephosphine-ligands and their application to the catalytic asymmetric hydrogenation of ketopantolactone to R-(-)-pantolactone, the key compound for the preparation of biologically important pantothenic acid, pantetheine and coenzyme A.

Scheme I.



Scheme II.



As shown in Scheme I, new polymer supported pyrrolidinephosphines [8] (4VB-PPM-MMA (1) and 4VB-PPM-tBuMA (2)) were synthesized by the copolymerization of (2S,4S)-N-(4-vinylbenzoyl)-4-diphenylphosphino-2-diphenylphosphinomethylpyrrolidine (4VB-PPM) (3)[7] with methyl methacrylate (MMA) (4) or T-butyl methacrylate (tBuMA) (5) in benzene under reflux in the presence of azobisisobutylonitrile. The compositions (4VB-PPM/MMA and 4VB-PPM/tBuMA=1/4) of the polymerized products (1 and 2) were determined by elemental and spectral analyses.

In a typical experiment, the asymmetric hydrogenation of ketopantolactone (8) (5.0 mmole) was run in benzene under initial hydrogen pressure of 50 atm at 50°C for 45 h in the presence of the catalyst which was prepared in situ from 2 (0.06 mmole) and $[Rh(1,5\text{-cyclooctadiene})Cl]_2$ (0.025 mmole). After filteration of the reaction mixture to remove the catalyst followed by removal of the solvent, the residure was distilled to give R-(-)-pantolactone, bp 104°C (5 mmHg), $[\alpha]_D^{20}$ -38.4° (c 2.152, $H_2O$) (75.7% optical yield) in an almost quantitative chemical yield.

Table I indicated clearly that 4VB-PPM-MMA-Rh and 4VB-PPM-tBuMA-Rh were more effective than 4VB-PPM-HEMA-Rh mainly because the latter catalyst has the hydroxyl group in it, and also neutral catalysts gave the better optical yields than the cationic species.

Further investigations on polymer supported pyrrolidinephosphine complex catalysts are actively under way.

Table I. Asymmetric hydrogenation of ketopantolactone[a)]

| Chiral reagent | Solvent | Conversion[d)] (%) | Opt.y. (%) | (conf.)[b)] |
|---|---|---|---|---|
| 4VB-PPM-HEMA-Rh | benzene | 85 | 15.8 | (R) |
| 4VB-PPM-MMA-Rh | benzene | 100 | 73.4 | (R) |
| 4VB-PPM-MMA-Rh$^+$ | benzene | 100 | 29.2 | (R) |
| 4VB-PPM-tBuMA-Rh | benzene | 100 | 75.7 | (R) |
| 4VB-PPM-tBuMA-Rh | THF | 100 | 74.4 | (R) |
| BZPPM-Rh | benzene | 100 | 78.5[c)] | (R) |
| BZPPM-Rh$^+$ | benzene | 100 | 57.6 | (R) |

a) All hydrogenations were run with 5 mmole of substrate, 0.025 mmole of $[Rh(COD)Cl]_2$ and 0.06 mmole of bisphosphine in 5 ml of solvent at 50°C for 45 h under an initial hydrogen pressure of 50 atm.

b) Calculated on the basis of the reported value for optically pure R-9; $[\alpha]_D^{25}$-50.7°(c 2.05, $H_2O$)(E.T.Stiller, S.A.Harris, J.Finkelstein, J.C.Keresztesy and K.Folkers, J.Am.Chem.Soc., 62, 1785 (1940).

c) Data from ref. 4.

d) Vpc analysis.

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8 Satisfactory spectral and analytical data were obtained for these compounds.

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