Catalytic Asymmetric Hydrogenation employing a Soluble, Optically Active, Rhodium Complex

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ENZYMIC CATALYSIS in the formation of organic compounds in nature provides the most efficient and stereospecific examples of catalytic asymmetric synthesis. Readily obtainable catalysts approaching the efficiency of enzymic processes would be highly desirable and would have obvious advantages over asymmetric syntheses requiring asymmetric reagents.

A few examples of non-enzymic catalytic asymmetric synthesis have been reported.[1] Optically active polymers have been employed as catalysts.[2]

We report a method for catalytic asymmetric hydrogenation employing as catalyst (or correctly as catalyst precursor) a soluble rhodium complex which contains optically active tertiary phosphine ligands. This approach has the advantage that the structure of the catalyst ligands can be varied according to the particular unsaturated substrate in order to achieve maximum asymmetric yield.

The only related studies have apparently been concerned with polymerizations with various optically active metal–ligand catalysts.[3]

Rhodium complexes of the type RhL_3Cl_3 (L = tertiary phosphine) can be converted into active homogeneous hydrogenation catalysts by dissolving in a benzene–ethanol (1 : 1 v/v) solvent system containing triethylamine (3·5 moles per mole of rhodium complex) and pressurizing with hydrogen gas.[4a] The hydrogenations were carried out in a Hoke bomb equipped with a pressure gauge and thermocouple at an initial pressure of 300—400 lb. in^{-2} and temperatures ranging from 25—80°. In all cases, the bomb was checked before and after a hydrogenation with an oct-1-ene solution in order to ensure that the bomb itself was catalytically inactive (*i.e.*, no rhodium metal deposition had occurred). The structure of the catalyst obtained from these Rh^{III} complexes may be of the type reported by Wilkinson and his co-workers[4b] for the homogeneous hydrogenation system obtained from chlorotris(triphenylphosphine)rhodium and hydrogen.

A sample of optically active (−)-methylpropylphenylphosphine (69% optical purity)[5b] was prepared by use of the reaction sequence outlined by Mislow and Korpiun, and added to a methanolic solution of rhodium trichloride trihydrate to give trichlorotris(methylpropylphenylphosphine)-rhodium (Ia),† m.p. 212—216°, $[\alpha]^{25}$ − 56° (benzene–ethanol, 1 : 1).

Hydrogenation of α-phenylacrylic acid (IIa) at 60°

$$RhCl_3L_3$$

(Ia) L = $\overset{*}{P}PhMePr^i$

(Ib) L = $PhP(CH_2\cdot\overset{*}{C}HMeEt)_2$

$$R\text{–}C(CO_2H)=CH_2 \xrightarrow[H_2]{RhCl_3L_3} R\text{–}\overset{*}{C}H(CO_2H)\cdot CH_3$$

(IIa) R = Ph (IIIa) R = Ph

(IIb) R = $HO_2C\cdot CH_2$ (IIIb) R = $HO_2C\cdot CH_2$

with (Ia) as catalyst (0·15 mole%) yielded

† A satisfactory analysis was obtained for this compound.

optically active hydratropic acid (IIIa), $[\alpha]_D^{25}$ + 12·2° (ethanol). This corresponds to 15% optical purity.[7] The method of work-up easily removes the catalyst, but even if it fails, the optically active catalyst would contribute only a maximum of 4% error in the observed rotation. Optically active hydratropic acid was found to be stable to racemization under the hydrogenation conditions and during work-up. The remarkable catalytic effect can best be demonstrated by the calculation that from one mole of optically active catalyst, we are generating about 100 moles of (+)-hydratropic acid.

Hydrogenation of itaconic acid (IIb) at 25° and at 60° with (Ia) as catalyst yielded methylsuccinic acid (IIIb) of 3% optical purity.

A smaller asymmetric effect was observed when the asymmetry was in the alkyl group rather than on the phosphorus. For example, hydrogenation of α-phenylacrylic acid (IIa) with (Ib)† as catalyst gave hydratropic acid of ~1% optical purity.

The inherent generality of this method offers almost unlimited opportunities for matching substrates with catalysts in a rational manner and we are hopeful that our current effort will result in real progress towards complete stereospecificity.

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