The Asymmetric Synthesis of Hydratropic Acid and Amino-acids by Homogeneous Catalytic Hydrogenation

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Summary A new optically active diphosphine–rhodium(I) catalytic system has been used in several asymmetric reductions giving optical yields of up to 72%.

THE first asymmetric reduction of ethylenic compounds using chiral rhodium complexes has been recently described.[1–3] We now report a new catalytic system for the asymmetric reduction of unsaturated prochiral acids giving the highest optical yields so far obtained in homogeneous asymmetric catalysis.

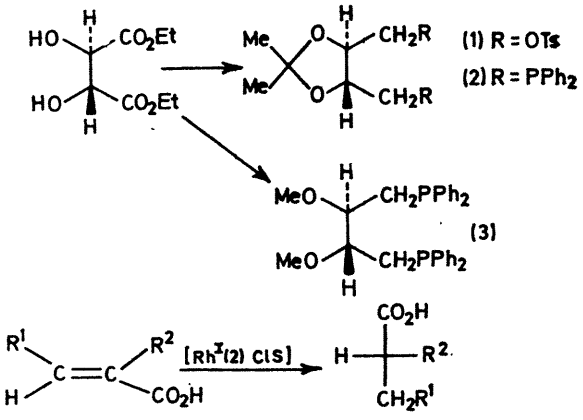
We have prepared *in situ* complexes represented as [Rh^{I}(P–P)ClS], where P–P is a chiral diphosphine and S the solvent. These complexes are prepared by adding 2 mol of the diphosphine to a benzene–ethanol solution of [Rh(cyclo-octene)$_2$Cl]$_2$. These solutions catalyse the hydrogenation of ethylenic compounds at room temperature and atmospheric pressure. We have studied the use of the asymmetric diphosphine (**2**), m.p. 87°, $[\alpha]_D^{22}$ −12·3° (*c* 4·57, C_6H_6), which is prepared from (+)-ethyl tartrate. The PPh_2 groups are introduced by treating the ditosylate[4] (**1**) with sodium diphenyl phosphide.

Reduction of atropic acid (**4**) (3mM) in the presence of the rhodium complex [R^1(**2**)ClS] (0·1 mM) and triethylamine (0·3 mM) in benzene–ethanol (1 : 2) gives quantitatively (*S*)-hydratropic acid (**5**) with an optical purity of 63%. The asymmetric reduction of (**4**) has been previously described[1] using an optically active phosphine [P*Me(Ph)Pr]–rhodium complex to give an optical purity of 28%.

Hydrogenation of the methyl ester of (**4**) in the presence of our catalyst produces methyl hydratropate of low optical purity (7%), but having the (*R*)-configuration.

α-Acetamidocinnamic acid (**6**) (50 mM) is reduced quantitatively and rapidly in the presence of 0·1 mM of the complex [Rh(**2**)ClS] to give (*R*)-*N*-acetylphenylalanine (**7**) with an optical yield of 72%, the chemical yield being 95%. α-Phenylacetamidoacrylic acid[5] (**8**) is also reduced to (*R*)-*N*-phenylacetylalanine (**9**) which, after hydrolysis, yields (*R*)-alanine (**10**) with an optical purity of 68%.

The optical rotations of the isolated compounds were measured without recrystallization in order to avoid alteration of the enantiomeric purity.†



(**4**) R^1 = H, R^2 = Ph
(**5**) R^1 = H, R^2 = Ph
(**6**) R^1 = Ph, R^2 = NHAc
(**7**) R^1 = Ph, R^2 = NHAc
(**8**) R^1 = H, R^2 = $NHCOCH_2Ph$
(**9**) R^1 = H, R^2 = $NHCOCH_2Ph$

The high stereoselectivity observed can probably be ascribed to the conformational rigidity of the diphosphine chelating the rhodium, together with the participation of the acid function of the substrates.

We are investigating the use of other asymmetric diphosphines, such as (**3**), $[\alpha]_D$ + 4·0° (*c* 2·45, C_6H_6), and the application of these reductions to the asymmetric synthesis of other amino-acids.

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† Optical yields are calculated from the specific rotations of the pure enantiomers which are reported in the literature: ref. 6 for (**5**); ref. 7 for (**7**); ref. 8 for (**10**).

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