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ASYMMETRIC HOMOGENEOUS HYDROGENATION WITH PHOSPHINE-RHODIUM COMPLEXES CHIRAL BOTH AT PHOSPHORUS AND CARBON

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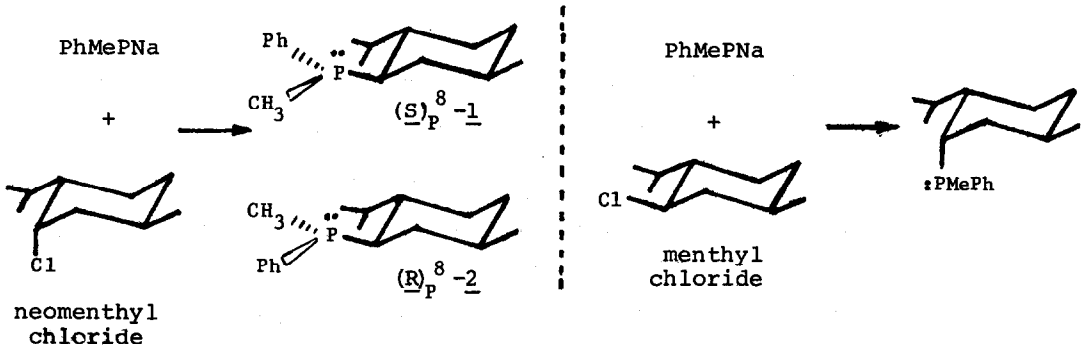
Previous rhodium homogeneous asymmetric hydrogenation catalysts have had the chirality of their phosphine ligands centered either at phosphorus[1,2] or carbon[3,4] but not both[5]. We now report the synthesis of a set of phosphines which are chiral at both phosphorus and carbon. Treatment of sodium methylphenylphosphide with purified ℓ-neomenthyl chloride[6] (THF, 20°) gave a mixture of ℓ-menthylmethylphenylphosphines 1 and 2 epimeric at phosphorus. The yield was 35% based on recovered methylphenylphosphine, but only 15% based on neomenthyl chloride due to elimination of HCl (trans diaxial C-3 chlorine and C-4 hydrogen). This mixture was converted to the air stable phosphine oxides which were separated (silica gel, 20:80 acetone:hexanes) and then reduced (phenylsilane) to regenerate the individual phosphines MMPP 1 and 2 with retention of configuration[7] (^{31}PNMR, 1 δ+32.0, from 1-oxide, δ-35.0 and 2 δ+34.9 from 2-oxide, δ-36.3*). The configuration at phosphorus in 1 and 2 is unknown at this time.[8] Under the mildest practical conditions of the phenylsilane reduction (5 days, 70°) 1 was stereochemically stable but 2 was epimerized at phosphorus to the extent of 13-25%; at 120° a 70:30 equilibrium mixture of epimers 1 and 2 was obtained. The ℓ-neomenthylmethylphenylphosphine oxides (3-oxide, δ-38.1 and 4-oxide, δ-35.3*) were synthesized separately by the same method starting with purified ℓ-menthyl chloride. Reduction with phenylsilane was more difficult (100°, 28 days) and gave extensive epimerization resulting in an approximate 50:50 mixture of the phosphines (3 and 4, δ+36.4 and +35.9*). These were not separable via their oxides and other methods of purification are under study.



In a typical case the homogeneous hydrogenation catalyst was prepared in 20 ml of 1:1 v:v ethanol-benzene from 20 μmoles of $[Rh(COD)Cl]_2$ and 0.3 mmoles of phosphine 1 or 2. The catalyst was prereduced (1 hr 40 psig). Triethylamine (0.3 mmoles) and substrate (0.3 mmoles) were added and the reaction stirred under H_2 (24-48 hrs, 30°). The asymmetric reductions ranged from 13 to 70% e.e. for the five substrates as shown in Table 1. The stereoselectivity of the reactions using the catalyst made from 1 should be correct since 1 was enantiomerically pure. However 2 was contaminated with 13-25% of 1 which catalyzed the formation of the enantiomeric product. Although we know the stereoselectivity of the catalyst made from 1, we cannot correct these results because of possible differences in rates of reductions, possible formation of mixed complexes and because excess phosphine was used.

Catalysts made from 1 and 2 gave enantiomeric products with (E)-β-methylcinnamic and atropic acids. Thus it appears that the stereochemistry at phosphorus, rather than at carbon, controls the configuration of the product. Both catalysts made from 1 and 2 give greater stereoselectivities than that made from ℓ-menthyldiphenylphosphine (MDPP)[2b]. However the catalyst made from impure 2 has comparable stereoselectivity for these substrates to that made from ℓ-neomenthyldiphenylphosphine (NDPP)[2]. The catalyst made from 2 has a lower stereoselectivity than Knowles catalyst (o-anisylcyclohexylmethylphosphine, ACMP) for α-acetylaminocinnamic acid but higher stereoselectivities for the other substrates listed in Table 1. Further comparisons are obtained by referring to the Morrison, Masler, Neuberg review.[4]

TABLE 1

Asymmetric Hydrogenation of α,β-unsaturated Carboxylic Acids with Rhodium(I)-MMPP Catalyst[a]

Olefin Substrate	MMPP[a] Phosphine	Synthetic Yield[b] (%)	Asym. Syn.[c] (%e.e.)
atropic acid	1[d]	46.6	13.5(R)
	2[e]	73.3	27.5(S)
(E)-β-methylcinnamic acid	1[d]	98.7	67.1(R)
	2[e]	92.4	70.6(S)
(E)-α-methylcinnamic acid	2[f]	70.4	61.4(R)
α-acetaminocinnamic acid	2[f]	80.0	43.7(R)
itaconic acid	2[f]	53.9	52.1(S)

a) MMPP = ℓ-menthylmethylphenylphosphine.

b) The synthetic yield was determined on the distilled acid fraction for liquids and on the crude acid fraction for solids.

c) The data are uncorrected and represent the actual asymmetric induction observed in the products. The configurations and percent enantiomeric excess (% e.e.) were determined on the basis of reported values for the optically pure compounds as follows: (S)-hydratropic acid, $[\alpha]_D^{20}$ + 81.1° (C 3.108 EtOH), H. S. Raper, J. Chem. Soc., 123, 2557 (1923); (S)-3-phenylbutanoic acid, $[\alpha]_D^{25}$ + 52.3° (C_6H_6), A. M. Weidler & G. Bergson, Acta Chem. Scand., 18, 1483 (1964); (S)-2-methyl-3-phenylpropanoic acid, $[\alpha]_D^{21}$ + 17.87° (C 5.034 EtOH), J. Kenyon, H. Phillips & V. P. Pittman, J. Chem. Soc., 1072 (1935); (S)-N-acetylphenylalanine, $[\alpha]_D^{26}$ + 46.0° (C 1 EtOH)[3a]; (R)-α-methylsuccinic acid, $[\alpha]_D^{20}$ + 16.88° (C 2.16 EtOH), E. Berner and R. Leonardsen, Justus Liebigs Ann. Chem., 538, 1 (1939).

d) By ^{31}P NMR analysis MMPP 1 is 98% 1 and 2% 2.

e) By ^{31}P NMR analysis MMPP 2 is 87% 2 and 13% 1.

f) By ^{31}P NMR analysis this sample of MMPP 2 is 75% 2 and 25% 1.

REFERENCES AND FOOTNOTES

*The ^{31}P NMR heteronoise decoupled spectra are recorded at 40.5 MHz with respect to external phosphoric acid in C_6D_6 solvent on XL-100 instrument.

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