Preparation of New Chiral Peralkyldiphosphines as Efficient Ligands for Catalytic Asymmetric Hydrogenation of α-Dicarbonyl Compounds

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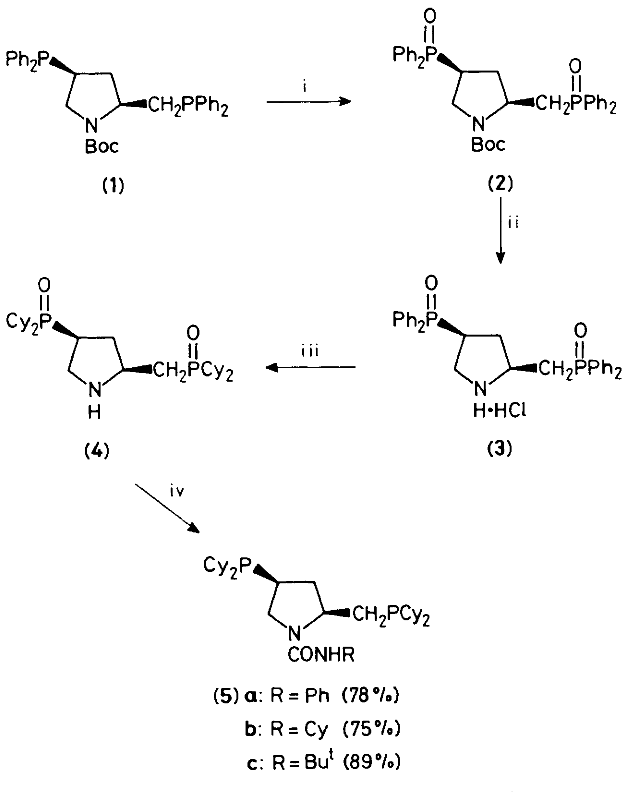
New chiral peralkyldiphosphines (**5**) containing a pyrrolidine ring have been prepared by a new method, which is widely applicable to transformation of known chiral diphosphines into the corresponding cyclohexyl analogues; asymmetric hydrogenation of α-dicarbonyl compounds catalysed by rhodium complexes of (**5**) proceeds smoothly under mild conditions (1 atm H_2; 35 °C) to give moderate optical yields.

There are only a limited number of reports on the catalytic asymmetric hydrogenation of ketones compared to that of olefins.[1] One reason seems to be that few efficient catalysts are available; ketones are not reduced with classical Wilkinson catalysts. Recently we have found that rhodium(I) peralkyldiphosphine complexes show high catalytic activity for hydrogenation of various kinds of ketones.[2] As the first example of optically active peralkyldiphosphines which may be used in the catalytic asymmetric hydrogenation of prochiral ketones we have prepared the ligand Rdiop [2,3-*O*-isopropylidene-2,3-dihydroxy-1,4-bis(dialkylphosphino)-butane] and showed that its rhodium(I) complexes are effective catalysts for asymmetric hydrogenation of ketones.[3] We now report the preparation of the new chiral peralkyldi-

Table 1. Physical properties of the chiral peralkyldiphosphines (**5**).

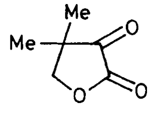
Compound	M.p. (t/°C)	I.r.(ν/cm^{-1}) ν(NH)	ν(CO)	Amide	$^{31}P\{^1H\}$ N.m.r.[a] $\delta(CHCl_3)$	$[\alpha]_D^{21}(C_6H_6)$
(**5a**)	212—212.5	3300	1645	1535	+6.9(s), −11.1(s)	−30.4° (c 0.68)
(**5b**)	192.5—194	3260	1615	1540	+5.6(s), −11.6(s)	−13.9° (c 0.96)
(**5c**)	166—168	3290	1625	1530	+6.4(s), −12.3(s)	−13.3° (c 1.62)

[a] In p.p.m. from external H_3PO_4; downfield is positive.

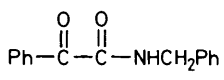


Cy = cyclohexyl; Boc = t-butoxycarbonyl

Scheme 1. *Reagents:* i, 10% H_2O_2, acetone, 85% yield; ii, 25% HCl, MeOH, 86% yield; iii, H_2, Rh–Al_2O_3, then NaOH, 73% yield; iv, $HSiCl_3$, NEt_3, then RNCO.



(A)



(B)

Table 2. Asymmetric hydrogenation of α-dicarbonyl compounds catalysed by Rh–(**5**) complexes.[a]

Substrate	Ligand	$t_{1/2}$/min[b]	% Enantiomeric excess[c] (Confign.)
(A)	(**5a**)	26	41(S)
	(**5b**)	23	50(S)
	(**5c**)	16	62(S)
	(**5c**)[d]	20	66(S)
(B)	(**5a**)	19	35(R)
	(**5b**)	20	41(R)
	(**5c**)	25	47(R)

[a] All reactions were carried out with [substrate] = 0.5 M, [Rh] = 2.5 mM (0.5 mol %) under atmospheric pressure of hydrogen at 35 °C in tetrahydrofuran unless otherwise stated. The catalyst precursors were prepared *in situ* from $[Rh(C_8H_{14})_2Cl]_2$ and 2.2 equiv. of (**5**). [b] Times required for 50% conversion. [c] Optical yields were determined on the basis of the maximum rotations of the pure enantiomers: D-pantoyl lactone, $[\alpha]_D^{25}$ −50.7° (c 2.05, H_2O);[8] (S)-N-benzylmandelamide, $[\alpha]_D^{25}$ + 79.9° (c 1.09, $CHCl_3$).[3c] [d] Benzene was used as a solvent.

phosphines (**5**) containing a pyrrolidine ring by a new method (Scheme 1),† which may be widely applicable to the transformation of known chiral aryldiphosphines into the corresponding cyclohexyl analogues. Optically active diphosphines containing a pyrrolidine ring are known to be excellent ligands for asymmetric catalysis and show a much higher degree of asymmetric induction in the hydrogenation of dehydroamino-acid derivatives than diop.[4,5] The diphosphines (**5**) prepared here are thus expected to be more efficient ligands in asymmetric hydrogenation of ketones than Rdiop.

Conventional methods [reaction between the alkali metal dialkylphosphide and the corresponding chiral bis-toluene-p-sulphonate], could not be used for the preparation of (**5**) (or Rdiop[3a]). Attempts to convert the pyrrolidine derivative (**1**) into the cyclohexyl analogue by direct hydrogenation of the diphenylphosphino groups failed. We hoped to prepare the cyclohexyl compounds (**5**)[5] *via* hydrogenation of diphenylphosphinoyl groups to give dicyclohexylphosphinoyl groups.[6] Oxidation of (**1**) with 10% hydrogen peroxide in ice-cooled acetone proceeded smoothly during 2 h to give the P,P'-dioxide (**2**), m.p. 227—230 °C, $[\alpha]_D^{21}$ −12.6 ° (c 1.18, benzene). Removal of the Boc group by treating (**2**) with methanolic hydrogen chloride at 0 °C gave the bis-diphenylphosphinoyl compound (**3**), m.p. 268—270 °C, $[\alpha]_D^{21}$ + 5.9 ° (c 2.69, MeOH), which was hydrogenated to provide the cyclohexyl analogue. The hydrogenation was somewhat sluggish, and Rh–Al_2O_3 was the most satisfactory catalyst. The bis-diphenylphosphinoyl compound (**3**) was hydrogenated in methanol with hydrogen (130 atm) at 150 °C for 2 days over 5% Rh–Al_2O_3. After neutralisation and recrystallisation from $CHCl_3$–Et_2O the bis-dicyclohexylphosphinoyl analogue (**4**) was isolated as colourless crystals containing 2 moles of solvating chloroform, m.p. 215—215.5 °C, $[\alpha]_D^{21}$ −11.4 ° (c 2.30, benzene). Reduction of the phosphine oxide was achieved by refluxing (**4**) with $HSiCl_3$–NEt_3 in acetonitrile under nitrogen for 2 h and followed by treatment with 25% NaOH.[7] The resulting oily product, N-unsubstituted diphosphine, without purification, was transformed into the crystalline product (**5**) by reaction with the appropriate isocyanate in CH_2Cl_2 at room temperature for 2 h. Compounds (**5a**—**c**) were isolated in good yields as colourless crystals after recrystallisation from ethanol and their physical properties are listed in Table 1. Two singlet $^{31}P\{^1H\}$ n.m.r. signals for each diphosphine indicate that the diphosphines (**5**) are optically pure and that racemisation did not occur during their preparation.

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† All new compounds, (**2**)—(**5**), gave satisfactory spectroscopic data and elemental analyses.

As expected, the rhodium(I) complexes of (**5**) showed high catalytic activity for hydrogenation of ketones. As shown in Table 2 α-dicarbonyl compounds were hydrogenated smoothly under atmospheric pressure of hydrogen at 35 °C to give the corresponding optically active α-hydroxy carbonyl compounds in moderate optical yields.

The present findings may provide a general method of conversion of known chiral diphosphines into the corresponding cyclohexyl analogues leading to more efficient chiral ligands for ketone hydrogenation.

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