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## Asymmetric Hydrogenation in Aqueous–Organic Two-phase Solvent Systems Using Rhodium Complexes of Sulphonated Phosphines

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Enamides (3)—(6) have been hydrogenated with enantiomeric excesses up to 88% in aqueous-organic two-phase solvent systems by rhodium complexes of sulphonated chiral bisphosphines.

One of the central problems in homogeneous catalysis is the separation of products from catalysts. One solution to this problem involves the attachment of a normally soluble catalyst







- $(3), R^1 = Ph, R^2 = H, R^3 = Me$
- (4),  $R^1 = Ph$ ,  $R^2 = R^3 = Me$ (5),  $R^1 = R^3 = Ph$ ,  $R^2 = H$

(6) 
$$R^1 = AcO \longrightarrow R^2 = H, R^3 = Me$$
  
MeO

to an insoluble support.<sup>1</sup> A quite different approach has involved the use of metal complexes of water-soluble ligands<sup>2-5</sup> such as sulphonated triarylphosphines.

Following earlier studies on the synthesis of asymmetric water-soluble diphosphines and their use in enantioselective hydrogenation in water,<sup>6,7</sup> we report herein the effectiveness

Table 1. Reduction of enamides (3)-(6).<sup>a</sup>

Ligand	Substrate	Solvent	$P(H_2)/atm.$	% E.e.
(1)	(3)	H <sub>2</sub> O-AcOEt	1	35
(1)	(3)	H <sub>2</sub> O-AcOEt <sup>b</sup>	1	37
(1)	(3)	H <sub>2</sub> O-AcOEt	5	21
(1)	(3)	H <sub>2</sub> O-AcOEt <sup>c</sup>	1	38
(1)	(3)	H <sub>2</sub> O-AcOEt <sup>d</sup>	1	42
(1)	(4)	H <sub>2</sub> O-AcOEt	1	19
(1)	(4)	H <sub>2</sub> O-AcOEt <sup>b</sup>	1	23
(1)	(4)	H <sub>2</sub> O-CH <sub>2</sub> Cl <sub>2</sub>	1	16
(1)	(4)	$H_{2}O-C_{6}H_{6}$	1	12
(1)	(6)	H <sub>2</sub> O-AcOEt	1	37
(2)	(3)	$H_2O-AcOEt$	10	88
(2)	(4)	H <sub>2</sub> O-AcOEt	5	82
(2)	(4)	H <sub>2</sub> O-AcOEt <sup>b</sup>	5	86
(2)	(4)	H <sub>2</sub> O-CH <sub>2</sub> Cl <sub>2</sub>	10	72
(2)	(4)	$H_2O-C_6H_6$	10	82
(2)	(5)	H <sub>2</sub> O-AcOEt	10	86
(2)	(6)	H <sub>2</sub> O-AcOEt	10	88

<sup>a</sup> Conditions: 25 °C, [substrate] = 1 M, [substrate]: [ligand]: [Rh] = 100:1, 1:1; 10 ml H<sub>2</sub>O, 10 ml organic solvent; all amino-acids obtained are (S) for (1) and (R) for (2). <sup>b</sup> Catalyst re-used. <sup>c</sup> KPF<sub>6</sub> added; [Rh]/[KPF<sub>6</sub>] = 1. <sup>d</sup> (1) is a mixture of di-, tri-, and tetra-sulphonated phosphines;  $[\alpha]_D^{25} + 29.4^{\circ}$  (c 1, H<sub>2</sub>O).

of rhodium complexes of sulphonated chiral phosphines as catalysts for the enantioselective hydrogenation in aqueousorganic two-phase solvent systems.<sup>8</sup> We used in hydrogenation tetrasulphonated cyclobutanediop (1) $\frac{1}{\alpha}$  27.41° (c 1,  $H_2O$ ;  $\delta$  (<sup>31</sup>P) (downfield from  $H_3PO_4$ ) 6.6 p.p.m. ( $H_2SO_4$ ) and sulphonated chiraphos (2) $\frac{1}{\alpha} = -98.2^{\circ}$  (c 1.1, H<sub>2</sub>O);  $\delta$  $(^{31}P)$  16.25 and 15.75 (H<sub>2</sub>SO<sub>4</sub>), corresponding respectively to disulphonated -PPh2 and monosulphonated -PPh2 (75% trisulphonated and 25% tetrasulphonated phosphine)}; they were obtained by sulphonation of the corresponding phosphines<sup>8</sup> [the diphosphine (2 mmol) was added to 30% SO<sub>3</sub> in  $H_2SO_4$  (10 ml); after 24 h, the solution was poured into ice (30 g) and neutralised with concentrated sodium hydroxide; after addition of methanol (200 ml) and separation of the sodium sulphate, evaporation of the solvent gave the sulphonated diphosphine]. The results reported in Table 1 show that the comples  $[RH(cod)Cl]_2^+$  –(1) or (2) (cod = cyclo-octa-1,5diene) is an effective catalyst precursor for the enantioselective hydrogenation of enamides (3)-(6) in aqueous-organic two-phase solvent systems. Sulphonated chiraphos (2) is the most efficient ligand, giving enantiomeric excesses (e.e.) up to 88%; this enantioselectivity, a little lower than obtained with (S,S)-chiraphos in ethanol,<sup>9</sup> did not decrease on recycling the catalyst. Sulphonated cyclobutanediop (1) gave a lower e.e.

[35% in H<sub>2</sub>O–AcOEt for enamide (3) vs. 91% using the non-sulphonated ligand in ethanol<sup>10</sup>]; this decrease in enantioselectivity using water as a solvent has already been found for 1,4-diphosphines.<sup>6</sup> In this case, the degree of sulphonation or the addition of KPF<sub>6</sub> has no influence on the enantioselectivity.

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<sup>&</sup>lt;sup>†</sup> Abbreviations: cyclobutanediop = (S, S)-1,2-bis(diphenylphosphinomethyl)cyclobutane; chiraphos = (S, S)-2,3-bis(diphenylphosphino)butane.