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PALLADIUM-CATALYZED ASYMMETRIC HYDROESTERIFICATION OF α-METHYLSTYRENE BY THE USE OF CHIRAL DIBENZOPHOSPHOLES AS LIGANDS

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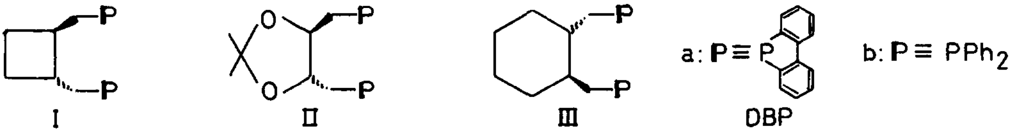
Asymmetric carbonylation is a useful reaction for the syntheses of optically active carbonyl compounds some of which could be intermediates for medicines and perfumes. We have reported[1] that a diphosphine (IIa) , analogous to (-)-Diop, which has the 5*H*-dibenzophospholyl group (DBP) in place of the diphenylphosphino group of (-)-Diop (IIb) is an extremely efficient chiral ligand for the rhodium-catalyzed asymmetric hydroformylation of styrene or butenes. Subsequently, we have also found that another DBP derivative, Ia, has higher asymmetric induction ability in the hydroformylation than the diphenylphosphino analogue, Ib.[2] Even by the use of Ia and IIa, however, the optical yield with a vinylidene-type olefin, α-methylstyrene, was very poor, and the highest value was less than 3%.



I   II   III   DBP

Recently, Consiglio, *et al*.[3-6] have investigated the asymmetric hydroesterification of olefins in detail by the use of palladium-IIb catalyst in order to search for the optimum reaction conditions for high optical yields. Their reports encouraged us to apply the chiral dibenzophospholes, Ia, IIa, and IIIa,[2] to the palladium-catalyzed asymmetric hydroesterification of α-methylstyrene.

Table 1 shows that Ia and IIa are more effective chiral ligands than Ib and IIb. When Ia, Ib, IIa, or IIb was used, the prefered configuration of the product was independent of the ligands, and was always *S*. This fact forms a striking contrast to rhodium complex-catalyzed asymmetric hydroformylation[2] where Ia and IIa have a tendency to give the opposite antipode to the one obtained with Ib and IIb, respectively. On the other hand, IIIa gave the product with lower optical purity and with opposite configuration in the hydroesterification of α-methylstyrene in comparison with the case in which IIIb[2] was used. These results may be ascribed to that the catalyst species bearing Ia, Ib, IIa, or IIb as chiral ligand forms a similar diastereomeric key intermediate with the substrate, while the structures of the key intermediates bearing IIIa and IIIb seem to be entirely different from each other because of the conformational flexibility of the six-membered ring.

It is reported[5] that, in order to achieve a higher optical yield in asymmetric hydroesterification catalyzed by the palladium-IIb system, the phosphorus/Pd ratio must be kept at one or less, and that the carbon monoxide pressure must be maintained as highly as possible — *e.g.*, up to 700 atm — during the reaction. However, by the use of Ia or IIa, an optical yield higher than 40% was readily attained even under a relatively low pressure, and the values were independent of the P/Pd ratio between 0.8 and 2. Moreover, *tert*-butyl 3-phenylbutanoate (IV) with $[\alpha]_D$ of +20.1° (benzene, c 11.75) was obtained by agitating 0.02 mol of α-methylstyrene, 0.03 mol of *tert*-butyl alcohol, 8 ml of benzene, 0.1 mmol of $PdCl_2(PhCN)_2$, and 0.042 mmol of IIa at 100°C under 238 — 236 atm of CO for 94 h (at 8% conversion). The optical rotation value corresponds to the optical purity of 69% (the highest value that has ever been attained[5] in catalytic asymmetric carbonylation) on the basis that independently prepared IV with $[\alpha]_D$ of +13.65° gave 3-phenylbutanoic acid[7] of 46.9% optical purity through saponification.

As the asymmetric hydroesterification of α-methylstyrene derivatives could be an alternative route to optically active 3-arylbutanoic acids, *i.e.*, a series of non-steroidal anti-inflammatory drugs,[8] search for the optimum conditions of the reaction is now under way.

Table 1. Palladium-catalyzed asymmetric hydroesterification of α-methylstyrene

Phosphine	P/Pd (atom)	Time (h)	Conversion(%)	Esters (%)	Isopropyl 3-phenylbutanoate/esters(%)	Configuration	Optical purity(%)*
Ia	2	45	68	98	97	S	40
	0.8	85	66	97	97	S	40
Ib	2	17	66	97	99	S	9.3
IIa	4	113	24	77	98	S	43
	2	21	33	91	89	S	44
	0.8	41	27	88	74	S	42
IIb(Diop)	2	19	83	99	99	S	8.9
IIIa	2	162	53	94	97	S	7.3
IIIb	2	42	23	81	92	R	22

α-Methylstyrene 0.023 mol, CO 240—220 atm at reaction temperature (100°C), isopropyl alcohol 11.5 ml, $PdCl_2(PhCN)_2$ 0.115 mmol. *Determined on the basis that isopropyl 3-phenylbutanoate of α_D +3.94° was reported to be of 14.2% optical purity in Ref.3.

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