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REVERSAL OF CHIRALITY INDUCED BY ORTHO-METHOXYL SUBSTITUTION OF ARYLPHOSPHINE LIGANDS IN RHODIUM-CATALYSED ASYMMETRIC HYDROGENATION

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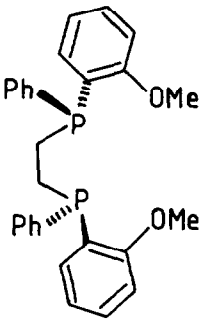
Abstract: o-Methoxyl substitution in DIOP(2) causes a reversal of configuration in asymmetric homogeneous hydrogenation of enamides.

Many diverse types of optically active biphosphine have been applied to asymmetric hydrogenation. The most common structure has a chiral chain of two or four atoms linking two diphenylphosphine groups, so that the active rhodium catalyst contains a 5- or 7-membered chelate ring. There is one example[1] of a chelating biphosphine (1) which is asymmetric at phosphorus, and this is highly effective in the reduction of Z-dehydroamino acids, giving optical yields in excess of 90%. The o-methoxyl group in (1) is essential for high stereoselectivity and in related monophosphines other ortho-substituents are much less effective.[1] In the present work we describe the consequences of o-methoxyl substitution in DIOP[2] (2) the most widely used asymmetric biphosphine.



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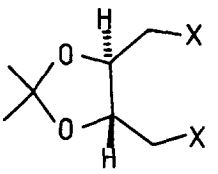
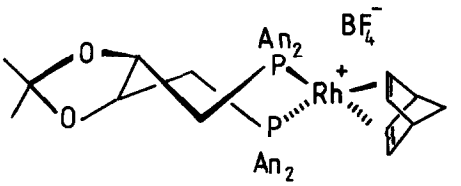


2 x = PPh_2

3 x = OTs

4 x = $P(oC_6H_4OMe)_2$



5 An = oC_6H_4OMe

The reaction of ditosylate (3)[3] with potassium di-o-anisylphosphide in dioxan (20°C, 10 min; anion formed by cleavage of tri-o-anisylphosphine in situ) gave, after recrystallisation from methanol analytically pure R-PAMPOP (4) (31%, m.p. 148-9°, $[\alpha]_{20}^{D}$ =-27.16 (0.6, $CHCl_3$)). This was converted into the rhodium norbornadiene complex (5) by conventional methods. The proton n.m.r. spectrum of (5) in CD_2Cl_2 showed two separate pairs of diastereotopic O-methyl groups, δ 3.64, 3.97 p.p.m., indicating a fixed conformation in which one pair is weakly co-ordinated to rhodium, as in the analogous cyclooctadiene complex of (1).[4] One pair of ortho-protons is at unusually low field and the other at rather high field, δ 6.56, 9.15 p.p.m. with broadening at ambient temperature.

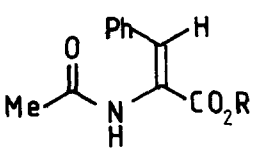
Complex (5) catalyses the hydrogenation of several unsaturated acids and esters and

results are recorded in the TABLE, along with comparable data obtained using (2). The former reacts more slowly, and reduction was normally carried out by stirring a solution of catalyst and substrate overnight under hydrogen. Complete hydrogenation was obtained in all cases save that of atropic acid, which was recovered unchanged, although a bright red colour indicated complexation of the substrate.

TABLE

Substrate	Optical yield [a]	Analysis	Optical yield, (2) [a,5]
6a	31 S	GLC [b]	81 R
6b	71 S	GLC [b]	55 R
7a	66 S	rotation [c]	70 R
7b	88 S	rotation [c]	38 R
8	22 S	rotation [c]	5 R
9a	8 S	GLC [b]	73 R
9b	57 S	GLC [b]	60 R
10a	0	NMR [d]	7 S
10b	—	—	63 R
11	37 R	NMR [d]	—

[a] Conditions for (4): catalyst: substrate 1:100, MeOH, 20°, pH_2 = 1 atm, conditions for (2) as described in the original papers standardised to the R-configuration of phosphine. [b] S-N-behenylvaline tert-butylamide 4% on Chromosorb G AW-DCMS. [c] Perkin-Elmer 241 dilute solution in MeOH or $CHCl_3$. [d] Eu(hfc)$_3$, 1.5 equiv. in CCl_4.



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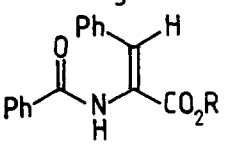

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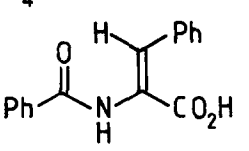

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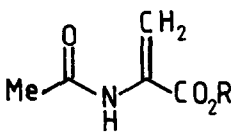

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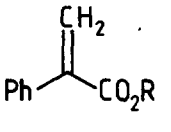

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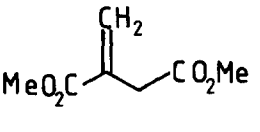

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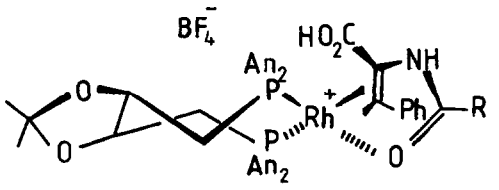
6,7,9,10; a) R = H, b) R = Me

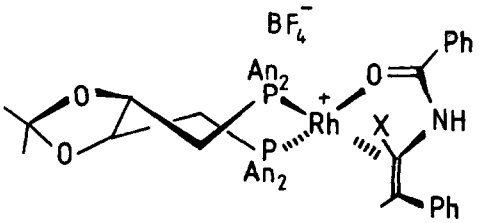
Thus PAMPOP reduces Z dehydroamino acids in the opposite stereochemical sense to DIOP, its ring-alkylated derivatives and a range of its carbocyclic analogues. [5,6] It gives higher optical yields with esters than with acids, at variance with the normal trend, [6] and thereby ruling out the possibility of intracomplex hydrogen-bonding between carboxylic acid and methoxyl-group. Dimethyl itaconate (11) is normally a poor substrate in asymmetric hydrogenation[7] and this is the best optical yield yet reported.

Phosphorus-31 NMR studies give some insight into the reaction mechanism. Complex (5) (δ 11.8 p.p.m J_{RhP} = 157 Hz) reacts slowly with hydrogen in MeOH (1 ml, 0.03M, 120 mins) to

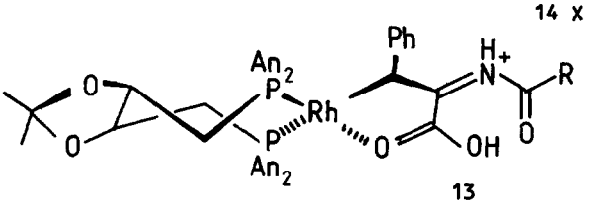
give a yellow solvent adduct (δ 43.4, J_{RhP} = 203 Hz). This reacts at low temperatures with (6a) to give a single species (12a) (δ, 40.9, δ_2 3.9 p.p.m.; J_{RhP_1} = 152, J_{RhP_2} = 134, J_{PP} = 56 Hz). On warming to 250K this isomerises to a second species (13a) which is the major component (60%) at equilibrium (δ, 30.3, δ_2 -2.6 p.p.m.; J_{RhP_1} = 147, J_{RhP_2} = 125, $J_{P_1P_2}$ = 32 Hz). Under hydrogen (c. 500 mm, 250K) both species disappear simultaneously, suggesting that the equilibration rate exceeds the rate of hydrogenation. A closely related pair of complexes is formed from (6b). With (7a) or its carbon-13 labelled analogues,[8] the major species at equilibrium is (12b) (65%) together with (13b)(15%) and a new species (14)(20%). ^{13}C chemical shifts and ^{31}P - ^{13}C coupling constants[8] establish that (12b) and (14) are conventional enamide complexes with bound olefin and amide, and free carboxyl groups. In (13b), however, the amide is free and the carboxyl group bound to rhodium. In addition, there is a coupling constant of 42 Hz between C_1 and P_2, which is uniquely consistent with a σ-benzyl complex.[9] Rhodium alkyls are normally unstable and the ready accessibility of (13) under catalytic conditions presents intriguing possibilities for further study.



12 a) R = Me b) R = Ph



14 X = CO_2H



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