Journal of Organometallic Chemistry, 253 (1983) 249–252
Elsevier Sequoia S.A., Lausanne – Printed in The Netherlands

1,4:3,6-DIANHYDRO-2,5-DIDEOXY-2,5-BIS(DIPHENYLPHOSPHINO)-L-IDITOL. A NEW CHIRAL LIGAND FOR ASYMMETRIC HYDROGENATION WITH RHODIUM COMPLEXES AS CATALYSTS

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(Received March 29th, 1983)

Summary

A new chiral 1,4-diphosphine, 1,4 : 3,6-dianhydro-2,5-dideoxy-2,5-bis(diphenylphosphino)-L-iditol, has been prepared from D-mannitol. Rhodium complexes of this ligand are asymmetric homogeneous hydrogenation catalysts for dehydroamino acids, giving (*S*)-amino acids in 21–58% optical yields.

Introduction

The effectiveness of chiral hydrogenation catalysts formed from bis(tertiary phosphines) involving PPh_2 groups is believed to be due to restriction of the rhodium containing chelate ring to one conformation by a barrier to inversion, so that a "rigid" phosphine and consequently a fixed phenyl group orientation are present [1]. This prompted us to prepare a new ligand of this type with a well defined conformation, starting from D-mannitol, an inexpensive, readily available material.

Results and discussion

D-Mannitol (**1**) was converted into 1,4 : 3,6-dianhydro-D-mannitol (**2**) in the presence of concentrated hydrochloric acid in 28% yield [2]. Treatment of **2** with *p*-toluenesulfonyl chloride in dry pyridine afforded 1,4 : 3,6-dianhydro-2,5-di-*O*-(*p*-toluenesulfonyl)-D-mannitol **3**. Nucleophilic displacement of the *p*-toluene sulfonate groups of **3** with PPh_2^- gave **4**.

The phosphine **4** formed in the reaction of the ditosylate with Ph_2P^- was expected to posses *diexo* substituents at C(2,5) (L-iditol configuration). The substitution reactions of 1,4 : 3,6-dianhydro-2,5-di-*O*-mesyl- and -di-*O*-tosylhexitols have been discussed in several papers [3,4]. A general rule has been postulated, according to which only leaving groups situated in the *endo* positions on the cis fused

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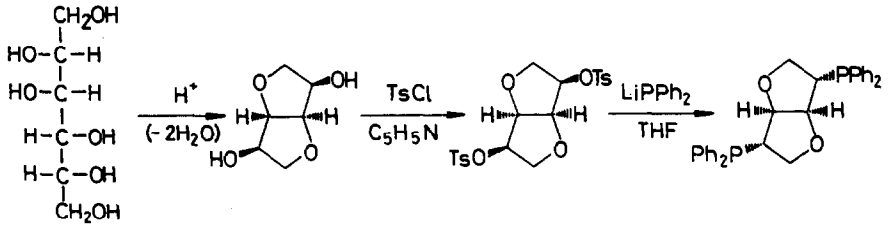
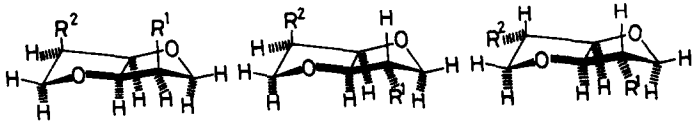
tetrahydrofuran rings are replaced by nucleophiles, because in these cases nucleophilic attack may come from the relatively unhindered *exo* positions. Unexpectedly,



1 2 3 4

however, in the reaction of 1,4 : 3,6-dianhydro-2,5-di-*O*-mesyl-D-mannitol with NaI, two diiodo compounds **5**, having structures **B** and **C** ($R^1 = R^2 = I$), were formed [4]. Accordingly both of the structures **B** and **C** ($R^1 = R^2 = PPh_2$) must also be considered for the phosphine **4**. However, the presence of only one singlet in the ^{31}P NMR



A B C

of **4** makes it very likely that the asymmetric **B** configuration can be exluded. This conclusion is supported by the ^{13}C NMR spectrum of **4**. For C_2 symmetry of structure **C** the C(1,6) and C(2,5) as well as the C(3,4) atom pairs would have identical chemical shifts in these isomers, and consistently only three groups of lines appear in the ^{13}C NMR of **4** (Table 1). A similar argument supports structure **A** for the dianhydro mannitol **2** ($R^1 = R^2 = OH$) and the ditosylate **3** ($R^1 = R^2 = OTs$).

The chiral diphosphine **4** was tried as ligand for the homogeneous catalytic hydrogenation of (acylamino)cinnamic acid derivatives with rhodium complexes as catalysts (Table 2). Only moderate optical yields were achieved showing that the configuration of this new phosphine is not very well suited for the formation of a rhodium chelate ring required for an efficient catalyst. The data also show the

TABLE 1

CARBON-13 NMR CHEMICAL SHIFTS OF 1,4:3,6-DIANHYDROHEXITOLS AND THEIR DERIVATIVES

Compound	Configuration	Carbon-13 signal (ppm) from $(CH_3)_4Si$					
		C(1)	C(2)	C(3)	C(4)	C(5)	C(6)
2	**A**	73.9	73.9	83.0	83.0	73.9	73.9
3	**A**	70.0	78.2	80.0	80.0	78.2	70.0
4	**C**	71.2 [a]	44.4 [b]	87.6 [c]	87.6 [c]	44.4 [b]	71.2 [a]
5 [d]	**C**	77.6	26.5	88.5	88.5	26.5	77.6
5 [d]	**B**	78.1	26.9	89.2	83.8	21.7	76.6

[a] d, J(PCC) 21.5 Hz. [b] d, J(PC) 11.5 Hz. [c] dd, J(PCC) 24 Hz, J(PCCC) 2.5 Hz. [d] Data taken from ref. 4.

TABLE 2

ASYMMETRIC HYDROGENATION OF *E*-PhCH=C(NHCOR')COOR [a]

R'	R	Catalyst	Solvent	H_2 pressure (bar)	Optical yield (%)
Me	H	$[Rh(NBD)Cl]_2$ + 4	MeOH/PhH (1/1)	1	58
		$[Rh(NBD)Cl]_2$ + 4	MeOH/PhH (1/1)	35	31
		$[Rh(NBD)_2]BF_4$ + 4	MeOH	1	54
Me	Me	$[Rh(NBD)Cl]_2$ + 4	MeOH/PhH (1/1)	1	43
		$[Rh(NBD)Cl]_2$ + 4	MeOH/PhH (1/1)	35	21
		$[Rh(NBD)_2]BF_4$ + 4	MeOH	1	37
Ph	H	$[Rh(NBD)Cl]_2$ + 4	MeOH/PhH (1/1)	1	38

[a] Reaction conditions: 2.5 mmol substrate, substrate/Rh/P = 50/1/2.2, 10 ml of solvent, 25°C, 24 h.

profound influence of the hydrogen pressure on optical yields. This inverse dependence of optical yield on hydrogen pressure is in good agreement with the mechanism of asymmetric hydrogenation suggested by Halpern [5].

In all these hydrogenations the (*S*)-enantiomer was formed in excess. Further experiments are in progress to clarify the properties of **4** in various complexes.

Experimental

The ^1H NMR spectra were recorded in $CDCl_3$ with TMS as internal standard on a Tesla Mode BS 487 C spectrometer, and the ^{13}C NMR spectra in $CDCl_3$ at 20 MHz and ^{31}P NMR spectra in $CDCl_3$ at 32.1 MHz on a Varian CFT-20 spectrometer. Mass spectra were recorded with a JEOLCO MS 01 SG-2 spectrometer at 75 eV. The optical rotations of the products were measured on a Schmidt Haensch LM visual polarimeter.

1,4 : 3,6-Dianhydro-D-mannitol (2)

A solution of the commercially available D-mannitol (100 g, 0.549 mol) in 500 ml of conc. hydrochloric acid was refluxed for 72 h. The dark solution was then concentrated in vacuo to a syrup, which was dissolved in 250 ml of water. The solvent was again evaporated off to remove HCl. The residue was fractionally distilled and the fraction collected at 135–145°C/11 mmHg was recrystallized from ethyl acetate to yield 22.1 g (27%) of **2**: m.p. 86–87°C; $[\alpha]_D^{20}$ +60.9° (*c* 2.1, $CHCl_3$). Found: C, 48.83; H, 6.99. $C_6H_{10}O_4$ calcd.: C, 49.33; H, 6.85%.

1,4 : 3,6-Dianhydro-2,5-di-O-(p-toluenesulfonyl)-D-mannitol (3)

To a solution of **2** (7.3 g, 0.05 mol) in 100 ml of dry pyridine cooled in a ice bath was added 27 g (0.15 mol) of recrystallized *p*-toluenesulphonyl chloride. The mixture was stirred at 0°C for 4 h. The solution was kept overnight at +5°C. The solution was then added to 500 ml of a mixture of ice and water with stirring. The precipitated **3** was filtered off and dissolved in 150 ml of $CHCl_3$. The $CHCl_3$ solution was washed successively with 1 *N* hydrochloric acid, then with water, and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the residue was recrystallized from EtOH to yield 14.5 g (64%) of pure **3**: m.p. 83°C;

$[\alpha]_D^{20}$ +94.3° (*c* 2.04, $CHCl_3$); ^1H NMR 2.38 (s, $2CH_3$); 3.75 (m, $2CH_2$); 4.40 (m, 2CH); 4.81 (m, 2CHO); 7.28 (d, *J* 8 Hz), 7.74 (d, *J* 8 Hz) (aromatic protons). Found: C, 52.89; H, 5.04. $C_{20}H_{22}O_8S_2$ calcd.: C, 52.87; H, 4.84%.

1,4 : 3,6-Dianhydro-2,5-dideoxy-2,5-bis(diphenylphosphino)-L-iditol (4)

To a solution of $LiPPh_2$ prepared from 9.7 g (0.044 mol) of $ClPPh_2$ with 0.77 g (0.110 mol) of Li in 60 ml of THF at 0°C under Ar was slowly added a 60 ml THF solution of **3** (0.020 mol). After stirring for 1 h at 25°C the solvent was evaporated under vacuum. The residue was treated with 60 ml of deoxygenated water and the aqueous mixture was extracted with $CHCl_3$. The organic layer was dried over $MgSO_4$ and chromatographed on a silicagel column using $CHCl_3$ as eluent. After crystallization in EtOH under Ar, stereochemically pure **4** was obtained as white needles 3.4 g, 35%, m.p. 110–112°C; $[\alpha]_D^{20}$ +32.8° (*c* 5.0, $CHCl_3$).

Mass spectrum: M^+, $m/e = 482$ (100%); $[M - P(C_6H_5)_2]^+$ 297 (42%); $[(C_6H_5)_2P]^+$ 185 (62%); $[C_{12}H_8P]^+$ 183 (65%); $[C_6H_5P]^+$ 108 (23%).

^1H NMR 3.05 (m, $2CH_2$), 3.37–4.25 (m, 2CH), 4.38 (m, 2CHO), 7.12–7.62 (m, aromatic protons).

^{31}P NMR 14.6 ppm (s), upfield from external 85% H_3PO_4. Found: C, 74.47; H, 5.82; P, 12.37. $C_{30}H_{28}O_2P_2$ calcd.: C, 74.71; H, 5.81; P, 12.84%.

Hydrogenation experiments

The rhodium complex and the appropiate amount of phosphine were dissolved in MeOH or MeOH/PhH under Ar. In the case of $[Rh(NBD)Cl]_2$ + **4** the solution was prehydrogenated for 40 min at room temperature. Hydrogenations were performed in a glass reactor at atmospheric pressure in 20 ml stainless steel autoclaves at 35 bar under the conditions specified in Table 2. Products were worked up as previously described [6].

References

1 M.D. Fryzuk and B.J. Bosnich, J. Am. Chem. Soc., 99 (1977) 6262; 100 (1978) 5491.

2 R. Montgomery and L.F. Wiggins, J. Chem. Soc., (1948) 2204.

3 (a) R.C. Hockett, H.G. Fletcher Jr., E.L. Sheffield and R.M. Goepp Jr., J. Am. Chem. Soc., 68 (1946) 927; (b) L.F. Wiggins and D.J.C. Wood, J. Chem. Soc., (1951) 1180; (c) A.C. Cope and T.Y. Shen, J. Am. Chem. Soc., 78 (1966) 3177, 5912.

4 P. Sohár, G. Medgyes and I. Kuszmann, Org. Magn. Res., 11 (1978) 357.

5 A.S.C. Chan, J.J. Pluth and J. Halpern, J. Am. Chem. Soc., 102 (1980) 5952.

6 J. Bakos, I. Tóth and L. Markó, J. Org. Chem., 46 (1981) 5427.