Pergamon

Tetrahedron Letters, Vol. 37, No. 27, pp. 4713-4716, 1996

0040-4039/96 $15.00 + 0.00

PII: S0040-4039(96)00948-3

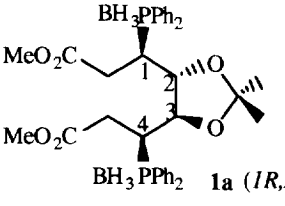
Diastereoselective Synthesis of Diphosphines, Effect of their Configuration in Asymmetric Catalysis

Pascal Pellon*, Celine Le Goaster and Loic Toupet#

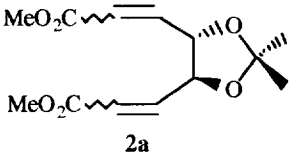
Laboratoire de Synthèse Organique, associé au CNRS. Université de Rennes 1, avenue du général Leclerc, 35042 Rennes Cedex, France.
Groupe Matière Condensée et Matériaux, associé au CNRS. Université de Rennes 1, avenue du general Leclerc, 35042 Rennes Cedex, France.

***Abstract** : The addition of diphenylphosphine-borane complex on the activated diene **2b** (prepared from D-mannitol), led to the three diastereomeric diphosphines **1b, 3** and **4**. Effect of the configuration of those diphosphines was observed in the catalytic α-acetamidoacrylic acid hydrogenation*. Copyright © 1996 Elsevier Science Ltd

Chiral diphosphines[1] are ligands of choice for a wide range of enantioselective transition metal-catalysed processes. The ligand configurations may have an impact on the complex shape, and consequently on the enantioselectivity of the reaction. Recently, we have described the synthesis of the chiral diphosphine-borane complex **1a**[2].



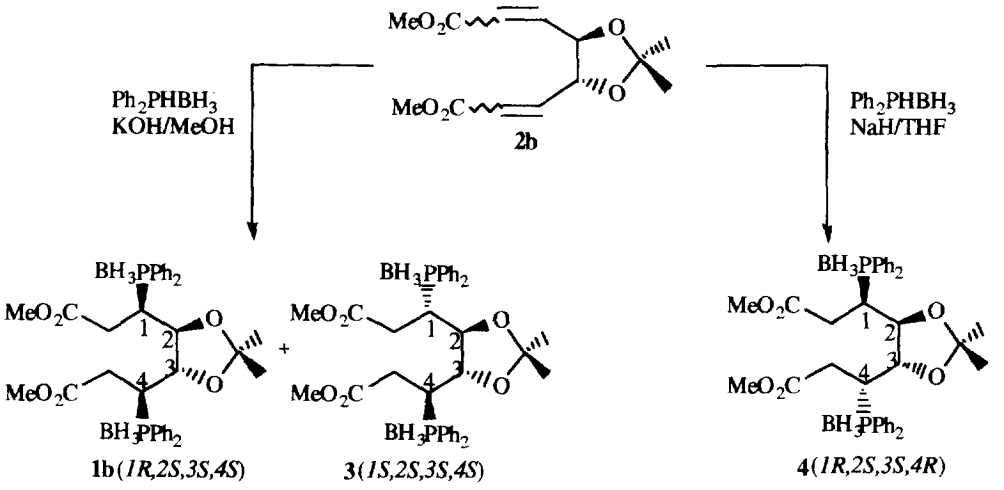
1a (*1R,2R,3R,4S*)



2a

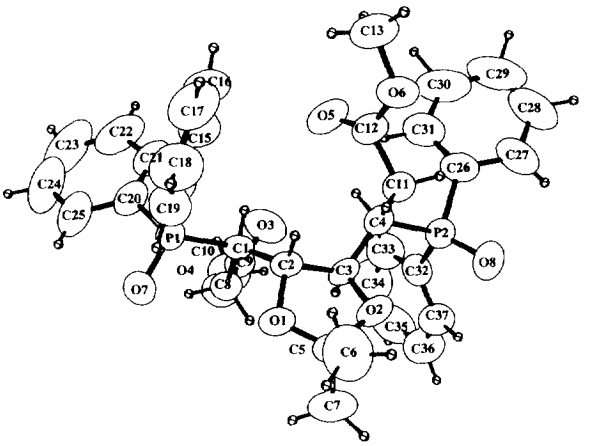
We report herein the synthesis of three diastereomers of **1a**, with different configurations at C_1, C_2, C_3 and C_4. Those diastereomers, with similar structure to DIOP, have been used as ligand in asymmetric catalysis in order to study their stereoselectivity. The synthesis of **1a** was achieved by addition of diphenylphosphide-borane complex on the activated diene **2a** which was synthesized from (*2R, 3R*)-diethyl tartrate[2]. The diene **2b**, enantiomer of **2a**, could be prepared by a cheaper method proposed by Takamo and coll.[3], from D-mannitol. For this reason, we have chosen to use the diene **2b** as precursor (Kagan had also prepared the (+) DIOP and dimethyl DIOP from D-mannitol[4]).

Depending on the reaction conditions, the addition of the diphenylphosphine-borane complex on the diene **2b** led to the formation of the three diastereomers : **1b**, **3**, **4**.



Complex **1b** has been prepared, *in anhydrous conditions*, using a catalytic amount of KOH in methanol[2]. The mixture of **1b** and **3** was synthesized from a stoichiometric amount of KOH in methanol. Complex **1b**, less soluble, precipitated at first, and complex **3** crystallized when the complex **1b** has been filtrated. So products **1b** and **3** could be separated by filtration (with a purity superior at 90%) and were purified by recrystallization[5]. Complex **4** was prepared using NaH in tetrahydrofuran[6].

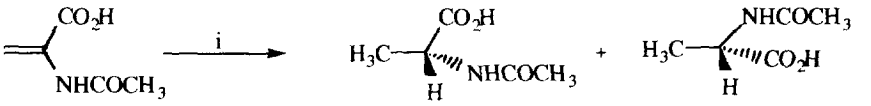
The stereochemistry of **4** was established by X-ray structure of the oxidized form, because of the bad crystallization of the borane complex. The stereochemistry of **3** was deduced from NMR comparison with the spectra of **1b** and **4**.



Perspective drawing of the molecule in the crystal structure of the oxidized form of 4 with selected bonds distances (Å)[7] *C_1-C_2 1.501; P_1-O_7 1.484; C_1-P_1 1.835; C_1-C_8 1.53; C_4-C_3 1.508; P_2-O_8 1.471; C_4-P_2 1.833; C_4-C_{11} 1.527.*

In a previous paper[8], the phosphine-borane decomplexation was realized during catalyst formation. We decided here to isolate the three free diphosphines in order to have a better control on the catalyst synthesis. So, the boronato group was removed with one equivalent of DABCO at 40 °C, during 4 hours[9].

Then, we investigated the effect of the configurations of the ligand in α-acetamidoacrylic acid catalysed hydrogenation. The results are reported in table 1.



i : H_2 / 20 °C / MeOH / catalyst 5 *R* 5 *S*

Table 1: Asymmetric hydrogenation of α-acetamidoacrylic acid :

ENTRY	LIGAND	TIME	YIELD	PRODUCT 5	ee
1	*1R,2S,3S,4S*:**1b**	60 min	81%	R	80%
2	*1S,2S,3S,4S*::**3**	90 min	81%	R	69%
3	*1R,2S,3S,4R* :**4**	60 min	90%	S	24%
4	(+) DIOP	a	a	S	72%
5	dimethyl DIOP	a	a	R	70%

conditions : catalyst prepared in situ from $(RhClCOD)_2$ and diphosphine; Substrat/Rh=40; optical purities are calculated from the value of the optically pure N-acetyl-(R)-alanine, (Litt.[10] $[\alpha]_D^{20}$ *+66.5 (c 2, H_2O))*[11] *; a : see reference 4.*

This work demonstrated that the configuration at C_1 and C_4 of the phosphines **1b**, **3** and **4** has an important effect on the enantioselectivity of the catalyst (entry 1 and 3). Our current investigations are directed toward the studies of those phosphines in different catalytic reactions.

References and notes

1. Noyori R., *Asymmetric Catalysis in Organic Synthesis* ; John Wiley and Sons ; New-York, **1994.**
   Kagan H.B., C. R. Acad. Sci., **1996**, *322*, serie IIb, 131.
   Imamoto T., Tsuruta H., Wada Y., Masuda H., Yamaguchi K., *Tetrahedron Lett.*, **1995**, *36*, 8271.
   Kless A., Kadyrov R., Börner A., Holz J., Kagan H.B., *Tetrahedron Lett.*, **1995**, *36*, 4601.
2. Gourdel Y., Pellon P., Toupet L., Le Corre M., *Tetrahedron Lett.*, **1994**, *35*, 1197.
3. Takamo S., Kurotaki A., Ogasawara T., *Synthesis* , **1987**, 1075.
   Takamo S., Kurotaki A., Ogasawara T., Takahashi M., *Synthesis*, **1986**, 403.
4. Kagan H.B. and al., Bull. Soc. Chim. Belg., **1979**, *11*, 923.
5. **Compound 1b and 3**[12] **:** to a solution of the diene **2b** (1.53 g, 5.6 mmol) and Ph_2PHBH_3 (2.24 g, 11.2 mmol) in 7.6 mL of methanol was added at 0 °C a solution of 1N KOH in MeOH (11.2 mL, 11.2 mmol). The reaction was vigorously stirred, and after 15 min, a white precipitate appeared. One hour later, the precipitate was recovered and dried under reduced pressure. Product **1b** : m = 1.7 g - yield = 46%. The second precipitate was recovered one hour later. Product **3** : m = 0.5 g yield = 13.5%. The total yield of this reaction is about 59%.
   product **1b**:: $[\alpha]_D^{20}$ +10.6 (c 1, $CHCl_3$) enantiomer of **1a** : see reference 2.

product **3**: mp = 128-129 °C; $[\alpha]_D^{20}$ -5.5 (c 0.49, $CHCl_3$). ^1H NMR δ (ppm) : 0.7 (s, 6H); 1.0 (m, 6H); 2.6 (m, 4H); 3.5 (m, 2H); 3.6 (s, 6H); 4.3 (m, 2H); 7.3-8.5 (m, 20H). ^{31}P NMR δ (ppm) : 24.8 . ^{13}C NMR δ (ppm) : 26.6 (CH_3); 33.4 (CH_2); 34.7 (d, $^1J_{C-P}$ = 33.5 Hz, CH); 52.5 (CH_3); 80.4 (CH); 110.1 (Cq); 133.6-128.0 ($C_{aromatics}$); 172.0 (CO). Anal. Calcd for $C_{37}H_{46}O_6B_2P_2$: C, 66.14; H, 6.91; P, 8.94. Found : C, 66.31; H, 6.74; P, 8.91.

6. **Compound 4 :** to a solution of Ph_2PHBH_3 (3g, 15 mmol) in dry THF (35 mL) cooled to -30 °C, was rapidly added NaH in mineral oil (60%) (0.59 g, 15 mmol). After keeping this temperature during 30 min, diene **2b** (2g, 7.4 mmol) was dropped to the solution. The temperature was slowly elevated to room temperature. After stirring during 2 hours, the reaction mixture was hydrolysed at 0 °C, by 1N HCl, and extracted with CH_2Cl_2 . The organic layer was separated, washed with H_2O, and dried (Na_2SO_4). The product, 2.5 g of a white solid, was isolated by recrystallization in EtOH. Yield : 50%.; mp = 165-166 °C; $[\alpha]_D^{20}$ +61.5 (c 0.51, $CHCl_3$).^1H NMR δ (ppm) : 0.9 (m, 6H); 1.2 (s, 6H); 2.5 (m, 4H); 3.5 (s, 6H); 3.6 (m, 2H); 3.7 (d, $^3J_{H-H}$ = 6 Hz, 2H); 7.8-7.9 (m, 20H). ^{31}P NMR δ (ppm) : 30.9. ^{13}C NMR δ (ppm) : 26.3 (CH_3); 28.6 (CH_2); 29.0 (d, $^1J_{C-P}$ = 22 Hz, CH); 52.5 (CH_3); 74.5 (CH); 107.6 (Cq); 133.9-126.0 (C aromatics); 172.4 (CO). Anal. Calcd for $C_{37}H_{46}O_6P_2$: C, 66.14; H, 6.91; P, 8.94. Found : C, 66.24; H, 6.86; P, 9.24.

7. The X-ray analysis of the oxidized form of **4** : $P_2O_8C_{37}H_{40}$: Mr = 780.8. triclinic, P1, a = 9.983 (2), b = 10.038 (8); c = 12.395 (9) Å, V = 1043 (1)$Å^{-3}$, Z = 1, D_X = 1.243 $mg.m^{-3}$, (MoKα) = 0.70926 Å, μ = 1.547 cm^{-1}, F(000) = 414, T = 293 K, final R = 0.055 for 2583 observations.

8. Brisset H., Gourdel Y., Pellon P., Le Corre M., *Tetrahedron lett.*, **1994**, *34*, 4523.

9. **Decomplexation of the diphosphine-borane complex** (general procedure) : a mixture of DABCO (0.168 g, 1.49 mmol) in 20 mL of toluene, was dried by azeotropic distillation (around 10 mL of toluene). The diphosphine-borane complex (0.74 mmol) was then added to the solution, and the mixture was kept at 40 °C during 4 hours. The solvent was removed under reduced pressure, and the residual oil was chromatographed on silica gel with toluene/ether (95/5) as eluent.
From **1b** : *1R,2S,3S,4S* : ^1H NMR δ (ppm) : 1.4 (s, 3H); 1.5 (s, 3H); 2.4-2.6 (m, 4H); 3.3 (m, 2H); 3.5 (s, 3H); 3.6 (s, 3H); 4.1 (m, 1H); 4.3 (m, 1H); 7.2-7.6 (m, 20H). ^{31}P NMR δ (ppm): - 6.7 and -11.8. ^{13}C NMR δ (ppm) : 27.3 and 27.0 (CH_3); 33.4 and 33.0 (CH); 35.6 and 31.9 (CH_2); 51.7 (CH_3); 79.8 and 78.4 (CH); 108.7 (Cq); 136.2-127.9 ($C_{aromatics}$); 173.3 and 172.9 (CO).
From **3** : *1S,2S,3S,4S* : ^1H NMR δ (ppm) : 1.5 (s, 6H); 2.4 (m, 4H); 3.4 (m, 2H); 3.5 (s, 6H); 4.4 (d,$^3J_{H-H}$ = 9 Hz, 2H); 7.2-7.6 (m, 20H). ^{31}P NMR δ (ppm) : -12.7. ^{13}C NMR δ (ppm) : 27.5 (CH_3); 33.2 (d, $^1J_{C-P}$ = 27 Hz , CH); 33.3 (CH_2); 51.7 (CH_3); 79.5 (CH); 108.9 (Cq); 137.9-125.3 ($C_{aromatics}$); 173,0 (CO).
From **4** : *1R,2S,3S,4R* : ^1H NMR δ (ppm) : 1.3 (s, 6H); 2.2-2.5 (m, 4H); 3.3 (s, 6H); 3.4 (m, 2H); 3.8 (m, 2H); 7.2-7.7 (m, 20H). ^{31}P NMR δ (ppm) : -4.7. ^{13}C NMR δ (ppm) : 26.8 (CH_3); 32.0 (d, $^1J_{C-P}$ = 36 Hz, CH); 32.1 (CH_2); 51.7 (CH_3); 78.2 (CH); 108.2 (Cq); 125.3-137.8 ($C_{aromatics}$); 173.0 (CO).

10. Birbaum S.M., Levintov L., Kingsley R.B, Greenstein J.P., *J. Biol. Chem.*, **1952**, *194*, 455.

11. **General procedure for asymmetric catalysis** : a mixture of $(RhCODCl)_2$ (0.0014 mmol), of ligand (0.030 mmol), and of α-acetamidoacrylic acid (1.120 mmol) in 2.6 mL of MeOH in the hydrogenation flask, was stirred under hydrogen atmospher during the appropriate time. The solution was evaporated to dryness. The residue was dissolved in water and separated from the insoluble catalyst by filtration. Evaporation to dryness afforded the N-acetyl alanine.

12. All reactions were carried out under a nitrogen atmospher. Toluene and tetrahydrofuran were distillated over Na before use and methanol over CaO. ^1H , ^{13}C and ^{31}P NMR were performed on a Brucker AC 300 spectrometer, in deuteriochloroform, using the solvent as internal reference. Optical rotations were recorded on Perkin Elmer 241 MC polarimeter. Melting points were determined on a Kofler hot stage apparatus. Silica gel (70-230 mesh) for column chromatography was purchased from Merck.

(*Received in France* 1 *April* 1996; *accepted* 14 *May* 1996)