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A new chiral diphosphine ligand and its asymmetric induction in catalytic hydroformylation of olefins

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Abstract

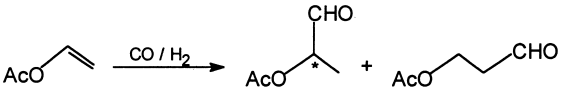
A new chiral ligand, 1,6-anhydro-2,4-bis(diphenylphosphino)pyranose (ABDPP), was prepared from D-glucose. The ligand was used to prepare a chiral rhodium catalyst system for asymmetric hydroformylation of olefins. For vinyl acetate, the catalytic hydroformylation gave rather high yield (96%), high enantioselectivity (92% ee), and high regioselectivity ($b/n = 95/5$). But for styrene and norbornene, the results were not so good. The rather high sterioselectivity in the hydroformylation of vinyl acetate is explained in terms of the hydrogen bonding between OH group in the ligand molecule and the carbonyl group of vinyl acetate.

Keywords: Chiral diphosphine; Asymmetric hydroformylation; Rhodium catalyst

1. Introduction

Hydroformylation is one of the most important methods for the functionalization of olefins and is a very powerful synthetic tool for the preparation of fine chemicals. The demand of pharmaceutical and agrochemical industries for enantiomerically pure compounds appears to be remarkably increasing [1]. Asymmetric hydroformylation is used to produce many optically active aldehydes as synthetic intermediates for the production of pharmacologically active molecules. For examples, some chiral aldehydes prepared by asymmetric hydroformylation of simple olefins can be conveniently transformed into optically active α-amino acids. A series of functionalized 2-arylpropanoic acids, which are optically active non-steroidal anti-inflammatory agents, can be prepared by asymmetric hydroformylation of aryl olefins.

Asymmetric hydroformylation is a great challenge to chemists because the catalytic reactions need not only the enantioselectivity but also the regioselectivity. The following is a typical example:



It can be seen that asymmetric hydroformylation is much more difficult than asymmetric hydrogenation. Many chiral diphosphines, such as DIOP, CHIRAPHOS, BINAP, which are very good for asymmetric hydrogenation, but not very suitable for asymmetric hydroformylation [2–6].

In 1980s, the best results in asymmetric hydroformylation were achieved with the $PtCl_2$[(S, S)-BPPM]–$SnCl_2$ system [7], which gave high selectivity to aldehydes and high enantiometic excesses (60–80% ee) although the brenched to normal

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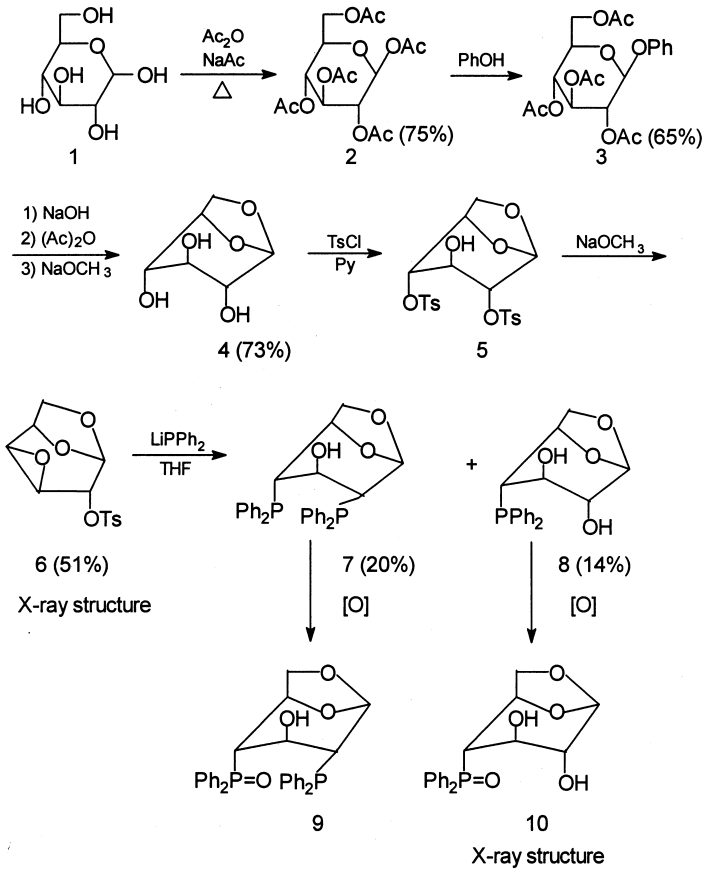
ratios were low ($b/n \sim 29/71$–$37/63$). The undesirable side reaction of product racemization could be avoided by carrying out the catalytic reaction in the presence of triethyl orthoformate as the solvent, which can convert aldehydes to corresponding acetals, which are unsusceptible to racemization. Introduction of two dibenzophosphole groups instead of four phenyl groups in BPPM molecule resulted in a considerable increase of the *b*/*n* ratio while maintaining a quite good enantioselectivity (ee>96%, $b/n = 77/23$) but the reaction rate was very low [8]. The breakthrough was reported in 1993. The Rh–BINAPHOS catalytic system was used for asymmetric hydroformylation of a variety of olefins resulting in very high enantioselectivities (73–95% ee) and very high regioselectivities (85/12 to 98/2 of *b*/*n*) [9]. So far, the phosphine–phosphite, such as BINAPHOS, ligands are most promising for asymmetric hydroformylation [10]. But their synthesis is rather complicated, and their separation from the catalytic reaction system for reuse is a big problem. In order to achieve both high enantio and high regio-selectivity in hydroformylation of olefins, searching some appropriate chiral ligands is essential, although this is a challenging subject.

In this paper, the synthesis of a new chiral diphosphine derived from D-glucose and its rather high chiral induction in the asymmetric hydroformylation of vinyl acetate are reported [11,12]. Scheme 1 gives the synthetic steps. Then catalytic experiments of asymmetric hydroformylation reactions are described,



Scheme 1.

and finally the experimental results are present and discussed.

2. Experimental

2.1. Preparation of 1,6-dehydro-β-D-glucose (4)

In a 500 ml round bottom flask, 43.0 g (1.1 mol) NaOH was dissolved in 333 ml water. Then 55.1 g (0.13 mol) β-phenyl-tetraacetyl-D-glucoside (**3**) was added. The solution was refluxed in an oil bath for more than 20 h. After cooling, it was neutralized with 45.5 g (0.46 mol) concentrated sulfuric acid diluted with ice of same volume. The solution was concentrated on a rotary evaporator, then extracted with 250 ml 95% boiling ethanol, filtered, and the filter cake was washed with 50 ml hot ethanol twice. The combined ethanol solution was concentrated and acetylized with 150 ml acetic acid anhydride. Then the mixture was heated at 100°C in an oil bath for 1 h. The excess acetic acid anhydride was decomposed with 13 ml water. Acetic acid was removed under reduced pressure. Then the mixture was extracted with 200 ml chloroform. The salt suspended in the solution was washed off with water. The chloroform was removed under vacuum, then 15 ml 95% ethanol was added to the residue. After 8–10 h, white solid was obtained with vacuum filtration. The mother liquid was concentrated, and 10 ml ether was added. After crystallizing in fridge, more solid was obtained. The combined solid was triturated in 40 ml 0°C ether. White solid 1,6-anhydro-2,3,4-triacetyl-β-D-glucose 27.5 g (0.087 mol) was obtained after suction filtration. Yield: 73%, m.p.: 107–109°C (lit. m.p.: 108–109°C). Elemental anal.: C 49.80%, H 5.52%; Calc.: C 50.0%, H 5.56%.

The above product 25 g was dissolved in 250 ml methanol. Sodium (0.25 g, 0.011 mol) in 25 ml methanol was added to it. After 15–20 min at room temperature, the solution was neutralized with acidic ion-exchange resin, then treated with 5 g active carbon. White product **4** (13.4 g, 0.083 mol) was obtained after filtration, rotary evaporation, and recrystallization in methanol. Yield: >95%, m.p.: 172–174°C. Elemental anal.: C 44.46%, H 6.24%; Calc.: C 44.44%, H 6.11%. ^{1}H NMR (DMSO, TMS): δ 5.20 (s, 1H), 4.35 (d, 1H), 3.90 (d, 1H), 3.60 (d, 1H), 3.50 (m, 2H), 3.20 (d, 1H), 3.35 (s, 3H).

2.2. Preparation of 1,6:3,4-dianhydro-2-p-toluenesulfonato-β-D-pyranose (6)

In a 50 ml round bottom flask, 2.0 g (0.012 mol) 1,6-dehydro-β-D-glucose was dissolved in 10 ml dry pyridine. Then the solution was cooled to about 0°C, and the solution of 5.0 g (0.026 mol) TsCl in 10 ml pyridine and 20 ml chloroform was added dropwise. The solution was stirred at room temperature for 2–3 days. Then 3 ml water was added, the organic layer was separated, and washed with water, 5% diluted sulfuric acid, water several times, then dried over Na_2SO_4. Sticky oil was obtained after rotary evaporation. Pure product was obtained after recrystallization in acetone–ether several times. M.p.: 118–120°C. Elemental anal.: C 51.2%, H 4.82%; Calc.: C 51.05%, H 4.71%.

The above sticky oil can be used directly to prepare 1,6:3,4-dianhydro-2-*p*-toluenesulfonato-pyranose, which was dissolved it in 30 ml chloroform, then a solution of 1 g sodium in 20 ml anhydrous methanol was added. The solution was allowed to sit overnight after shaking. The precipitate was dissolved in 5 ml water. The organic layer was separated. The water layer was extracted with chloroform one more time. The combined organic layer was dried over Na_2SO_4, concentrated under vacuum. White needle crystals (**6**) 1.8 g (0.061 mol, yield 51%) were obtained after recrystallization in anhydrous methanol. M.p.: 150–151°C. $[\alpha]_D^{18}$ −37° ($c = 1.0$, chloroform). Elemental anal.: C 52.45%, H 4.67%; Calc.: C 52.35%, H 4.70%. ^{1}H NMR ($CDCl_3$, TMS): δ 7.38–7.85 (dd, 4H), 5.17 (s, 1H), 4.85 (dd, 1H), 4.38 (s, 1H), 3.93 (d, 1H), 3.61 (dd, 1H), 3.49 (m, 1H), 3.12 (dd, 1H), 2.46 (s, 3H). MS (FB) M^+ +3, 301 (60%). IR (KBr pallet) ν 2989, 2968, 2903, 1597, 1493, 1464, 1180, 1128 cm^{-1}.

2.3. Preparation of 1,6:3,4-dianhydro-2-p-toluenesulfonato-β-D-pyranogalactose (6) via tri-p-toluenesulfonato-glucose

To a 50 ml round bottom flask was added 2.0 g (0.012 mol) 1,6-dehydroglucose and 10 ml dry pyridine. A solution of 10.0 g (0.051 mol) TsCl in 15 ml pyridine and 20 ml chloroform was added dropwise with stirring. After reacting at room temperature for two days, the flask was warmed for 1–2 h. To

this 3 ml water was added with stirring after cooling. Water layer was removed, and the organic layer was washed with water, 5% diluted sulfuric acid, water several times, then dried over Na_2SO_4. A sticky residue was obtained after rotary evaporation. 1,6-Dehydro-2,3,3-tri(*p*-toluenesulfonato)-pyranose was obtained after recrystallization 3–4 times in acetone–ether. M.p.: 101–103°C. Elemental anal.: C 51.73%, H 4.45%; Calc.: C 51.91%, H 4.52%.

The sticky residue can be used directly to prepare 1,6:3,4-dianhydro-2-*p*-toluenesulfonato-β-D-pyranose: after dissolving it in ethanol, excess $Ba(OH)_2$ in water–ethanol was added. After reacting at 90°C for 4–5 h, the solvent was removed under vacuum. Then it was extracted with chloroform three times, dried over Na_2SO_4, and the solvent was removed under vacuum. White crystals (**6**) 1.6 g (0.0054 mol, yield 45%) was obtained after recrystallization in anhydrous methanol.

2.4. Preparation of 1,6-anhydro-2,4-bis(diphenylphosphino)pyranose (**7**) and 1,6-anhydro-4-diphenylphosphinopyranose (**8**)

In a 100 ml three-neck flask fitted with dropping funnel, condenser and Schlenck N_2 system, 5.28 g (0.02 mol) triphenylphosphine was added. The system was flashed with N_2 three times, then 15 ml dry THF was added through a syringe. The system was cooled to about 0°C with an ice-water bath, then 0.28 g lithium stick was added with stirring. The ice-water bath was removed after the solution darkened. The reaction was continued for 4–5 h at room temperature. *t*-Butyl chloride of 1.9 g was added through the dropping funnel. After the boiling ceased, the system was cooled to −3 to −5°C with salt-ice bath, then a solution of 2.0 g (0.0067 mol) 1,6:3,4-dianhydro-2-*p*-toluenesulfonatopyranose in 10 ml THF was added dropwise. After 2 h, the ice bath was removed, and the reaction was continued at room temperature for 3–4 h. The ice-water bath was reapplied, and 20 ml deoxygenated water was added. The system was extracted with freshly purified ether twice under N_2. The extract was dried over Na_2SO_4 under N_2. A sticky oil was obtained after rotary evaporation. Chromatography was carried on a silica gel column protected with Ar, using CH_2Cl_2 as developing solvent, and the portions of $R_f = 4.0$ and $R_f = 0.23$ were collected.

Component of $R_f = 0.23$. The sticky liquid obtained after solvent removal was compound **8**, 0.15 g (yield 14%), ^{31}P NMR ($CDCl_3$, 85% H_3PO_4 internal standard): δ −14.23 ppm; ^{1}H NMR ($CDCl_3$, TMS internal standard): δ 7.30–7.90 ppm (m, 10H), 5.52 (s, 1H), 4.25 (d, 1H), 4.15 (d, 1H), 3.83 (d, 1H), 3.72 (m, 1H), 3.69 (s, 1H), 3.59 (m, 2H), 2.86 (s, 1H).

Since compound **8** was sensitive to the air, the sample soon became the oxide (**10**) and precipitated after the NMR test. Compound **10** is white crystalline, m.p.: 92–94°C; $[\alpha]_D^{18}$ −30 ($c = 1.0$, methanol); Elemental anal.: C 62.73%, H 5.47%; Calc.: C 62.43%, H 5.49%. ^{31}P NMR (DMSO, 85% H_3PO_4 internal standard): δ 30.70 ppm. ^{1}H NMR (DMSO, TMS): δ 7.5–8.0 ppm (m, 10H), 5.21 (s, 1H), 4.32 (dd, 1H), 4.20 (d, 1H), 3.85 (d, 1H), 3.60 (dd, 1H), 3.33 (s, 3H), 3.23 (s, 1H), 3.21 (d, 1H). IR (KBr pallet): ν 3277–3337, 3057, 2951, 2891, 1923, 1800, 1589, 1439, 1155, 1118 cm^{-1}; MSS (EI), M^+ 346 (30%). Its crystal cell parameters: monoclinic, $a = 11.575$, $b = 12.521$, $c = 11.573$, $\beta = 89.89$, space group $P2_1$(#4), $Z = 4$ [12].

Component of $R_f = 0.40$. 0.65 g (yield 20.0%) 1,6-dehydro-2,4-bis-(diphenylphosphino)pyranose (**7**) (white, snowflake-like solid) was obtained after rotary evaporation, m.p.: 125.0°C, $[\alpha]_D^{18}$ −62°C (C 1.2, chloroform). Elemental anal.: C 72.04%, H 5.56%; Calc.: C 72.29%, H 5.62%, ^{31}P NMR ($CDCl_3$, 85% H_3PO_4 internal standard): δ −13.85 ppm and −18.85 ppm. ^{1}H NMR ($CDCl_3$, TMS): δ 7.21–7.60 ppm (m, 20H), 5.35 (s, 1H), 4.38 (dd, 1H), 4.25 (d, 1H), 3.68 (m, 2H), 2.95 (m, 2H), 2.05 (s, 1H), IR (KBr pallet): ν 3412 (br, OH), 3051, 2960, 2893 (CH), 1600, 1479, 1433 (C=C), 1174, 1116 (COC); MS (EI), M^+ *m/e* 498 (15%).

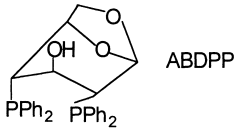
2.5. Asymmetric catalytic hydroformylation reaction

The reaction was carried out in 20 ml stainless steel reactor. Toluene was purified by distillation under N_2 or Ar. The olefin, catalyst (Rh–P), and solvent was added to the reactor, then filled with syngas ($CO/H_2 = 1/1$). The system was flushed with the syngas three times to remove the air inside. Then syngas was added until a selected pressure was reached, and the system was stirred under certain temperature. The pressure was dropping, indicating the reaction was proceeding.

After certain time, the reactor was cooled to room temperature, and the excess syngas was released. The component in the product was analyzed with GC. The conversion and *b*/*n* ratio of the aldehyde can be calculated from the GC data, or from the ^{1}H NMR integral. Product aldehyde can be obtained after distillation under reduced pressure. The ee value can be obtained by ^{1}H NMR with the help of chiral chemical shifting reagent. This method can be applied directly to the reaction mixture since the reagents and other products would not give any effect. The absolute configuration (R or S) was determined by the optical rotation.

3. Results and discussion

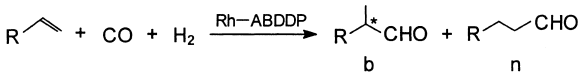
The new chiral diphosphine, ABDPP, prepared from D-glucose has some remarkable futures:



ABDPP

1. In the ligand molecule, the carbon atoms C(1), C(5) and C(6) with two oxygen atoms form a rigid five-membered ring.
2. Two diphenylphosphino groups are bonded directly to C(2) and C(4) in the pyranose moiety.
3. The −OH group bonded to C(3) is located between the four phenyl groups, but off their center.

This ligand was used to prepare a chiral rhodium catalyst for asymmetric hydroformylation of olefins.



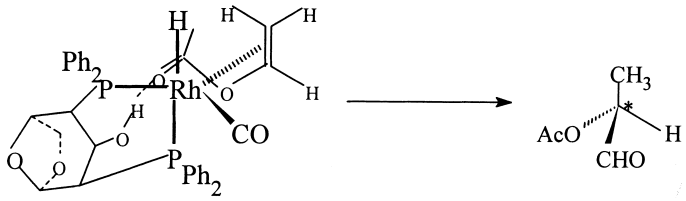
Experimental results are listed in Table 1. From the data in Table 1, it is can be seen that the chiral ligand ABDPP is very suitable for the asymmetric hydroformylation of vinyl acetate giving 92% ee and $b/n = 95/5$. However, ABDPP is not so good for the asymmetric hydroformylation of styrene and norborene.

Table 1
Asymmetric hydroformylation of olefins catalyzed by the chiral Rh–ABDPP catalyst[a]

Substrate	P/Rh	*T* (°C)	*t* (h)	Yield (%)	*b*/*n*	ee (%)
AcO	4	80	24	96	95/5	92
	2.5	80	24	95	93/7	86
	4	60	48	90	96/4	93
Ph	4	80	24	91	90/10	63
	4	60	48	80	89/11	68
	4	80	24	100	–	22
	4	60	48	89	–	25

[a] Other conditions: $[ClRh(cod)]_2$, 0.015 mmol; substrate, 1.0 ml; toluene, 5.0 ml; pressure, 6.0 MPa; $H_2/CO = 1/1$.

The rather high enantioselectivity (>90% ee) and regioselectivity ($b/n =\sim 95/5$) in the hydroformylation of vinyl acetate is explained in terms of the hydrogen bonding between OH group in the ligand molecule and the carbonyl group in the acetate. The following model proposed for the transition state of the asymmetric hydroformylation of vinyl acetate catalyzed by Rh–ABDPP system.



Acknowledgements

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