Pergamon

Tetrahedron Letters 43 (2002) 4025–4028

TETRAHEDRON LETTERS

Totally diastereoselective synthesis of a new chiral quinoline diazaphospholidine ligand and its derivatives

Guillaume Delapierre, Mathieu Achard and Gérard Buono*

ENSSPICAM, UMR 6516 'Synthèse, Catalyse et Chiralité', Av. Escadrille Normandie Niemen, F-13397 Marseille Cedex 20, France

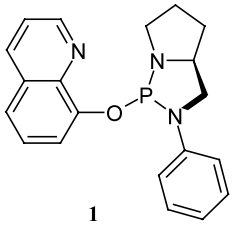
Received 8 April 2002; accepted 10 April 2002

Abstract—QUIPHOS-PN5, a new stable P,N ligand with a stereogenic phosphorus centre was synthesised in two steps from 8-bromoquinoline (61% yield). Its structure and its bidentate chelating ability was confirmed by the X-ray structure of a palladium(II) complex with this ligand. P(V) derivatives of QUIPHOS-PN5 were then easily obtained in excellent yields (85–100%).

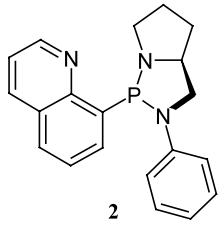
Chiral organophosphorus compounds found broad applications in asymmetric catalysis as ligands of transition metals[1] or as catalysts.[2] By adding a coordinating nitrogen atom to these structures, we obtained hybrid bidentate and unsymmetrical P,N ligands, interesting because of the different electronic properties of phosphorus and nitrogen atom which might enhance both the catalyst activity and the enantioselectivity.[3] Oxidised phosphorus ($P\lambda^5\sigma^4$) have demonstrated their efficiency, mainly as catalyst in asymmetric catalysis.[2,4]

We previously described the synthesis of QUIPHOS **1**, a stable P,N six-membered ring chelate ligand with a stereogenic phosphorus atom.[5] This ligand is efficient in asymmetric catalysis, associated to palladium in allylic alkylation (ee up to 85%)[6] and allylic amination (ee up 93%)[7] or to copper in Diels–Alder reaction (ee up to >98%)[8] and conjugate addition (ee up to 61%).[9]

To evaluate the electronic differentiation and the bite angle effects[10] of the P,N bidentate ligand in different asymmetric catalytic reactions catalysed by transition metal complexes, we report in this letter an efficient synthesis of **2**. This ligand, called QUIPHOS-PN5 is an analogue of **1** and is able to form five-membered ring chelate. Moreover, the stability of the ligand was expected to increase by replacing the hydrolysable P–O bond by a stable P–C one.



1



2

QUIPHOS-PN5 **2** was easily obtained in two steps from 8-bromoquinoline **3** in 61% overall yield (Scheme 1). 8-Lithioquinoline generated in situ with *sec*-butyllithium was trapped by chlorobis(dimethylamino)phosphine[11] to form 8-(bis(dimethylamino)phosphine)-quinoline **4**.[12] A totally diastereoselective exchange reaction between **4** and (*S*)-anilinomethylpyrrolidine[5] **5** afforded QUIPHOS-PN5 **2** characterised as the thermodynamic *anti*-diastereomer.[13]

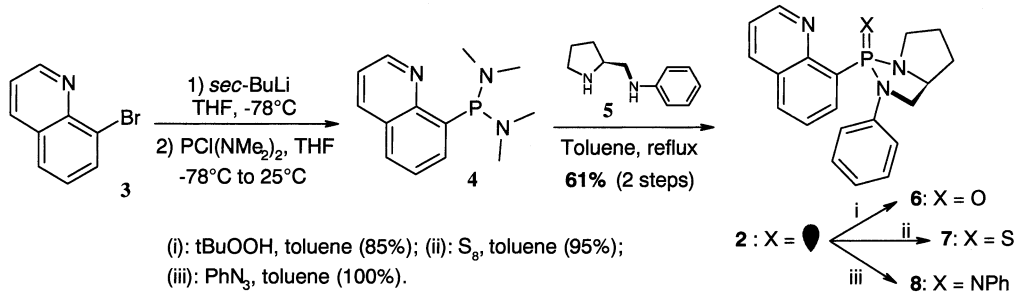
The chiral oxide diazaphospholidine **6** and the corresponding phosphine sulphide **7** were prepared, respectively, by action of *t*-butyl hydroperoxide and sulphur with **2** in 100 and 95% chemical yields. By the same way, the reaction of phenyl azide with **2** leads to the chiral iminodiazaphospholidine[14] **8** in 85% chemical yield. This new compound has two different basic amine sites closely positioned and may accept a proton between the nitrogens.

Complex **9** was obtained in quantitative yield by mixing an equimolar amount of $PdCl_2(CH_3CN)_2$ and ligand **2** in methylene chloride (Scheme 2). Crystallisation from toluene afforded **9** as pale brown crystals stable to air and moisture. X-Ray diffraction analysis confirms the chelating ability of ligand **2** towards palladium and the

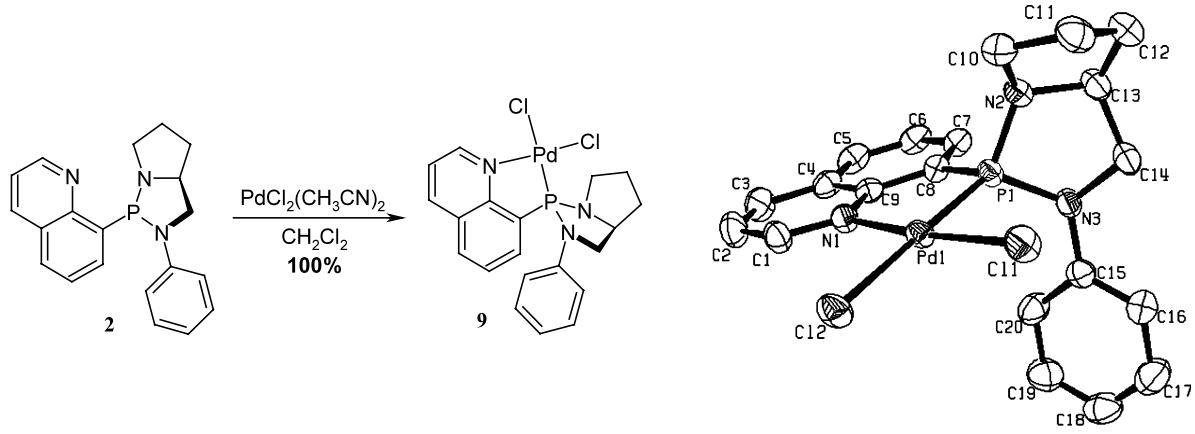
Keywords: chiral bidentate P,N ligand; phosphine oxide; phosphine sulphide; iminophosphorane; palladium complex.

* Corresponding author. Tel.: +33 (0) 491288681; fax: +33 (0) 491282742; e-mail: buono@spi-chim-u-3mrs.fr

0040-4039/02/$ - see front matter
PII: S0040-4039(02)00691-3



Scheme 1.



Scheme 2. Structure of **9**, showing labelling scheme. Selected bond distances (Å): Pd1–Cl1 = 2.30 (12), Pd1–Cl2 = 2.40 (12), Pd1–P1 = 2.18 (13), Pd1–N1 = 2.07 (3). Selected angle (°): P1–Pd1–N1 = 85.8. Selected dihedral angles (°): Cl2–Pd1–Cl1–P1 = 178.6, Cl2–Pd1–Cl1–N1 = −177.8.

S_p absolute configuration of the phosphorus ($\sigma^3\lambda^3$) atom.[15] A classical square planar geometry is observed for this Pd(II) complex (bite angle:[16] P1–Pd1–N1 = 85.8, Cl2–Pd1–Cl1–P1 = 178.6 and Cl2–Pd1–Cl1–N1 = −177.8°). Moreover, the Pd–Cl bond lengths are significantly different from one another, the chlorine atom *trans* to phosphorus displaying the expected longer distance (Pd1–Cl2 = 2.40 (12) Å) as compared to its partner *trans* to nitrogen (Pd1–Cl1 = 2.30 (12) Å). This is the expression of the higher *trans* influence of the phosphine ligand.[17]

In conclusion, we have reported the easy synthesis of a new stable chiral P,N ligand and three of its derivatives in good to excellent yields. The optimisation of the synthesis of the key intermediate **4** allows us to modify the nature of the chiral auxiliary. Applications of the four new compounds **2**, **6**–**8** as ligands or catalysts in asymmetric catalysis are in progress.

Experimental

8-(Bis(dimethylamino)phosphine)quinoline 4: Under argon, *sec*-BuLi (1.1N in hexanes, 8.7 mL, 9.61 mmol) was dropwise added to a cooled solution (−78°C) of 8-hydroxyquinoline (2 g, 9.61 mmol) in dry THF (25 mL). After stirring for 5 min, a solution of $ClP(NMe_2)_2$ (1.78 g, 11.54 mmol) in THF (2 mL) was added and the solution was allowed to warm to rt. After stirring 12 h at rt, the mixture was evaporated and the residue was taken up in a mixture of Et_2O (100 mL) and a solution of EDTA/0.5N NaOH (1:4.2, 20 mL). After stirring for 5 min, the two layers were separated. The organic layer was washed with water (2×10 mL), dried (Na_2SO_4), filtered and evaporated to give **4** as an orange oil (2.35 g) and enough pure for the synthesis of **2**, ^{1}H NMR ($CDCl_3$): δ (ppm, *J* Hz) 8.76 (dd, 1H, *J* 1.8, 3.9), 7.90 (dd, 1H, *J* 1.5, 8.1), 7.70 (ddd, 1H, *J* 1.8, 3.0, 7.2), 7.54 (dd, 1H, *J* 1.5, 8.1), 7.35 (dt, 1H, *J* 1.2, 6.9), 7.16 (dd, 1H, *J* 4.2, 8.1), 2.58 (d, 12H, *J* 9.9); ^{13}C NMR ($CDCl_3$): δ (ppm, *J* Hz) 149.0 (d, *J* 1.1), 148.8, 139.8 (d, *J* 12.1), 135.6 (d, *J* 1.7), 131.8 (d, *J* 5.2), 127.7 (d, *J* 1.7), 127.6 (d, *J* 1.1), 125.8, 120.4, 41.5 (d, *J* 17.8); ^{31}P NMR ($CDCl_3$): δ (ppm) 98.3.

(2*R*,5*S*)-3-Phenyl-2-(8-quinolyle)-1,3-diaza-2-phosphabicyclo-[3.3.0]-octane 2: A solution of (*S*)-anilinomethylpyrrolidine **5** (1.42 g, 8.08 mmol) and **4** (2 g, 8.08 mmol) in dry toluene (4 mL) was refluxed for 2 h under argon and then evaporated. The residue was taken up in dry Et_2O (13 mL), filtered and washed with Et_2O to give **2** as a white powder (1.63 g, 61% from **3**), mp 191°C, $[\alpha]_D^{20} = -486.5$ (*c* 0.5, CH_2Cl_2), ^{1}H NMR ($CDCl_3$): δ (ppm, *J* Hz) 8.80 (dd, 1H, *J* 1.2, 3.9), 7.92 (d, 1H, *J* 8.1), 7.57 (d, 1H, *J* 8.1), 7.23–7.36 (m, 1H), 7.18–7.23 (m, 2H), 7.01 (t, 2H, *J* 7.8), 6.72 (d, 2H, *J* 7.8), 6.57 (t, 1H, *J* 7.4), 3.78–3.86 (m, 1H), 3.55 (t, 1H, *J* 8.0), 3.19–3.39 (m, 2H), 3.02 (td, 1H, *J* 2.1, 8.6), 1.61–1.96 (m, 4H), ^{13}C NMR ($CDCl_3$): δ (ppm, *J* Hz)

149.9 (d, *J* 15.9), 149.7 (d, *J* 1.7), 147.0 (d, *J* 15.4), 139.2 (d, *J* 26.0), 136.0 (d, *J* 1.1), 130.4 (d, *J* 2.8), 129.0, 128.9 (d, *J* 1.2), 128.4 (d, *J* 1.1), 126.0, 121.0, 117.5, 115.2 (d, *J* 13.2), 63.9 (d, *J* 8.5), 53.8 (d, *J* 4.8), 52.4 (d, *J* 30.0), 30.5, 25.5 (d, *J* 6.0), ^{31}P NMR ($CDCl_3$): δ (ppm) 97.4. Anal. calcd for $C_{20}H_{20}N_3P$: C, 72.06; H, 6.05; N, 12.60. Found: C, 72.14; H, 6.09; N, 12.60%.

(2*R*,5*S*)-3-Phenyl-2-(8-quinolyle)-1,3-diaza-2-phosphabicyclo-[3.3.0]-octane-2-oxide 6: Under argon, *t*BuOOH (5.5N solution in toluene, 164 μL, 0.9 mmol) was carefully added to an ice cooled solution of **5** (0.301 g, 0.9 mmol) in dry toluene (10 mL). After stirring for 30 min at 0°C, the mixture was evaporated to give **6** as a brown solid (0.315 g, 100%), mp 193°C, $[\alpha]_D^{20} = -202$ (*c* 0.5, CH_2Cl_2), ^{1}H NMR ($CDCl_3$): δ (ppm, *J* Hz) 8.76 (dd, 1H, *J* 1.7, 4.3), 8.53 (ddd, 1H, *J* 1.5, 7.0, 15.6), 7.86 (td, 1H, *J* 2.0, 8.3), 7.69 (td, 1H, *J* 1.2, 8.3), 7.41 (ddd, 1H, *J* 3.0, 7.0, 8.0), 7.16 (dd, 1H, *J* 4.0, 8.0), 6.92–7.05 (m, 4H), 6.61 (tt, 1H, *J* 1.5, 6.8), 4.07–4.28 (m, 2H), 3.79–3.97 (m, 1H), 3.40–3.48 (m, 1H), 2.81–2.99 (m, 1H), 1.66–2.12 (m, 4H); ^{13}C NMR ($CDCl_3$): δ (ppm, *J* Hz) 150.5, 148.6, (d, *J* 5.7), 142.7 (d, *J* 7.2), 139.0 (d, *J* 8.4), 136.6 (d, *J* 1.9), 133.6–130.4 (d, *J* 162.5), 132.6 (d, *J* 3.0), 129.1, 128.6 (d, *J* 9.5), 126.1 (d, *J* 15.7), 121.56, 120.18, 116.2 (d, *J* 4.6), 60.0 (d, *J* 6.1), 50.1 (d, *J* 15.7), 45.8, 34.1, 27.0 (d, *J* 2.6); ^{31}P NMR ($CDCl_3$): δ (ppm) 27.7. Anal. calcd for $C_{20}H_{20}N_3OP$: C, 68.76; H, 5.77; N, 12.03. Found: C, 68.87; H, 5.77; N, 11.87%.

(2*R*,5*S*)-3-Phenyl-2-(8-quinolyle)-1,3-diaza-2-phosphabicyclo-[3.3.0]-octane-2-sulphide 7: Under argon at rt, sulphur (28.8 mg, 0.899 mmol) was added to a solution of **5** (0.3 g, 0.899 mmol) in dry toluene (10 mL). This solution was stirred for 30 min, then evaporated and the residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate, 3:2) to give **7** as a red-brown solid (312 mg, 95%), mp 220°C, $[\alpha]_D^{20} = +7.14$ (*c* 0.5, CH_2Cl_2), ^{1}H NMR ($CDCl_3$): δ (ppm, *J* Hz) 8.91 (ddd, 1H, *J* 1.5, 7.3, 20.2), 8.77 (dd, 1H, *J* 1.7, 4.0), 7.94 (td, 1H, *J* 2.0, 8.3), 7.77 (td, 1H, *J* 1.5, 8.0), 7.49 (td, 1H, *J* 3.0, 7.3), 7.20 (dd, 1H, *J* 8.3, 4.2), 6.91–7.04 (m, 4H), 6.62 (tt, 1H, *J* 1.2, 7.0), 4.30–4.55 (m, 1H), 4.18 (q, 1H, *J* 8.0), 3.95–4.14 (m, 1H), 3.44–3.54 (m, 1H), 2.73–2.92 (m, 1H), 1.62–2.19 (m, 4H); ^{13}C NMR ($CDCl_3$): δ (ppm, *J* Hz) 150.3, 147.5 (d, *J* 3.4), 142.7 (d, *J* 7.2), 140.7 (d, *J* 16.1), 136.8, 136.1–133.7 (d, *J* 124.9), 133.0 (d, *J* 3.0), 129.0, 128.6 (d, *J* 8.0), 126.0 (d, *J* 18.0), 121.6, 120.5, 116.6 (d, *J* 5.7), 62.2 (d, *J* 4.2), 52.5 (d, *J* 12.6), 46.8 (d, *J* 3.8), 33.8 (d, *J* 1.9), 27.4 (d, *J* 3.4), ^{31}P NMR ($CDCl_3$): δ (ppm) 75.9. Anal. calcd for $C_{20}H_{20}N_3PS$: C, 65.74; H, 5.52; N, 11.50. Found: C, 65.69; H, 5.47; N, 11.29%.

(2*R*,5*S*)-3-Phenyl-2-(8-quinolyle)-1,3-diaza-2-phosphabicyclo-[3.3.0]-octane-2-phenylimino 8: Under argon, phenyl azide (63 mg, 0.531 mmol) was added to an ice cooled solution of **5** (154 mg, 0.469 mmol) in toluene (5 mL). The solution was stirring at rt for 30 min, then at 60°C overnight. The solvent was evaporated and the residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate, 2:8) to afford **8** as a yellow solid (192 mg, 85%), mp 80°C, $[\alpha]_D^{20} = +3.5$ (*c* 0.5, CH_2Cl_2), ^{1}H NMR ($CDCl_3$): δ (ppm, *J* Hz) 8.86 (dd, 1H, *J* 1.7, 4.2), 8.71 (d, 1H, *J* 7.5), 8.40 (ddd, 1H, *J* 1.5, 7.0, 15.6), 8.13 (td, 1H, *J* 2.0, 8.3), 7.82 (td, 1H, *J* 1.2, 8.0), 7.48 (dd, 1H, *J* 2.2, 8.0), 7.43 (dd, 1H, *J* 4.2, 8.3), 7.11–7.22 (m, 3H), 7.0 (td, 2H, *J* 1.0, 7.3), 6.85 (m, 1H), 6.53 (td, 1H, *J* 1.0, 7.3), 6.34 (dt, 2H, *J* 0.7, 7.5), 4.17–4.38 (m, 1H), 3.12–3.30 (m, 1H), 2.81–3.03 (m, 3H), 1.38–1.70 (m, 4H), ^{13}C NMR ($CDCl_3$): δ (ppm, *J* Hz) 150.2, 148.8, 147.2 (d, *J* 7.2), 141.6, 138.1, 136.3 (d, *J* 6.9), 132.9–130.0 (d, *J* 148.7), 132.3 (d, *J* 3.0), 129.7, 129.4, 128.6 (d, *J* 9.9), 127.1, 126.9, 121.8 (d, *J* 3.0), 119.25 (d, *J* 6.9), 117.0, 112.9, 58.6 (d, *J* 3.8), 49.4, 47.3 (d, *J* 4.9), 30.6 (d, *J* 5.7), 25.6 (d, *J* 6.5), ^{31}P NMR ($CDCl_3$): δ (ppm) 18.2.

[$PdCl_2$(QUIPHOS-PN5)] 9: Under argon, **5** (55.39 mg, 0.166 mmol) was added to a solution of $PdCl_2(MeCN)_2$ (43.10 mg, 0.166 mmol) in dry dichloromethane (5 mL). The solution was stirred for 10 min, then evaporated to give **9** as a yellow solid (84.9 mg, 100%), mp 253°C, $[\alpha]_D^{20} = +180$ (*c* 0.1, CH_2Cl_2), ^{1}H NMR ($CDCl_3$): δ (ppm, *J* Hz) 10.45 (d, 1H, *J* 5.3), 8.51 (d, 1H, *J* 8.3), 8.06–8.18 (m, 2H), 7.66–7.80 (m, 2H), 7.09–7.12 (m, 4H), 6.91–6.99 (m, 1H), 4.25–4.46 (m, 2H), 3.78–4.10 (m, 2H), 2.99–3.17 (m, 1H), 2.31–2.52 (m, 1H), 1.95–2.21 (m, 3H), ^{31}P NMR ($CDCl_3$): δ (ppm) 103.3.

Acknowledgements

We thank Dr. Michel Giorgi for his kind assistance with X-ray analysis of compound **9**. We are grateful to CNRS for its financial support. M.A. acknowledges MENRT for a doctoral fellowship.

References

1. (a) Brunner, H.; Zeittlmer, W. *Handbook of Enantioselective Catalysis with Transition Metals*; VCH: Weinheim, 1993; Vol. I: Products and Catalysts and Vol. II: Ligands-References; (b) Kagan, H. B.; Sasaki, M. In *The Chemistry of Organophosphorus Compounds*; Hartley, F. R., Ed.; John Wiley and Sons: New York, 1990; pp. 51–102; (c) Ohkuma, T.; Katamura, M.; Noyori, R. In *Catalytic Asymmetric Synthesis*, 2nd ed.; Ojima, I., Ed.; Wiley-VCH: New York, 2000; Chapter 1.
2. (a) Buono, G.; Chiodi, O.; Wills, M. *Synlett* **1999**, 377–388; (b) Brunel, J. M.; Buono, G. In *New Aspects in Phosphorus Chemistry*, *Top. Curr. Chem.*; Majoral, J.-P., Ed.; Springer Verlag: Berlin, 2002; Vol. 220, pp. 79–105.
3. (a) Humphries, A. C.; Pfaltz, A. In *Stimulating Concepts in Chemistry*; Vögtle, F.; Stoddart, J. F.; Shibasaki, M., Eds.; Wiley-VCH: New York, 2000; pp. 89–103; (b) Helmchen, G.; Pfaltz, A. *Acc. Chem. Res.* **2000**, *33*, 336–345; (c) McCarthy, M.; Guiry, P. J. *Tetrahedron* **2001**, *57*, 3809–3844.
4. Denmark, S. E.; Stavenger, R. A. *Acc. Chem. Res.* **2000**, *33*, 432–440.
5. Brunel, J. M.; Constantieux, T.; Buono, G. *J. Org. Chem.* **1999**, *64*, 8940–8942.

6. Brunel, J. M.; Constantieux, T.; Labande, A.; Lubatti, F.; Buono, G. *Tetrahedron Lett*. **1997**, *38*, 5971–5974.
7. Constantieux, T.; Brunel, J. M.; Labande, A.; Buono, G. *Synlett* **1998**, 49–50.
8. Brunel, J. M.; Del Campo, B.; Buono, G. *Tetrahedron Lett*. **1998**, *39*, 9663–9666.
9. Delapierre, G.; Constantieux, T.; Brunel, J. M.; Buono, G. *Eur. J. Org. Chem*. **2000**, 2507–2511.
10. van Leeuwen, P. W. N. M.; Kamer, P. C. J.; Reek, J. N. H.; Dierkes, P. *Chem. Rev*. **2000**, *100*, 2741–2769.
11. King, R. B.; Masler, W. F. *J. Am. Chem. Soc*. **1977**, *99*, 4001–4008.
12. A preparation of this compound was previously reported without any characterisation of the product: Issleib, K.; Haftendorn, M. *Z. Anorg. Allg. Chem*. **1970**, *376*, 79–86.
13. ^{31}P NMR on the crude mixture gave only one signal at 97.4 ppm. The notations of the *syn* and *anti* diastereomers are according to the methylene substituent of the pyrrolidine ring with respect to the extracyclic quinoline group: Cros, P.; Buono, G.; Peiffer, G.; Denis, D.; Mortreux, A.; Petit, F. *New J. Chem*. **1987**, *11*, 573–579.
14. For a first iminodiazaphospholidines with a stereogenic phosphorus centre, see: Brunel, J. M.; Legrand, O.; Reymond, S.; Buono, G. *J. Am. Chem. Soc*. **1999**, *121*, 5807–5808.
15. Crystallographic data for the structure **9** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 180259. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44 (0) 1223-336033 or e-mail: deposit@ccdc.cam.ac.uk].
16. P2–Pd1–N7 = 91.3 (2) is the bite angle of QUIPHOS coordinated to cationic π-allyl palladium.[5]
17. For a review, see: Appleton, T. G.; Clark, H. C.; Manzer, L. E. *Coord. Chem. Rev*. **1973**, *10*, 335–342.