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LETTERS

## Synthesis of 4-(2-diphenylphosphino-1-naphthyl)-2-phenylquinazoline; a potential P–N chelating ligand for asymmetric catalysis

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### Abstract

We describe a multistep synthesis leading in a good yield to the title compound. The biaryl linkage was formed in a Pd-catalysed coupling of 2-phenyl-4-chloroquinazoline with 2-methoxy-1-naphthylboronic acid. A further metal-catalysed reaction gave the formation of the naphthylphosphorus bond allowing us to obtain the required phosphonimine ligand **1** as the racemate. © 1999 Elsevier Science Ltd. All rights reserved.

*Keywords:* quinazoline; coupling reactions; biaryls; ligands.

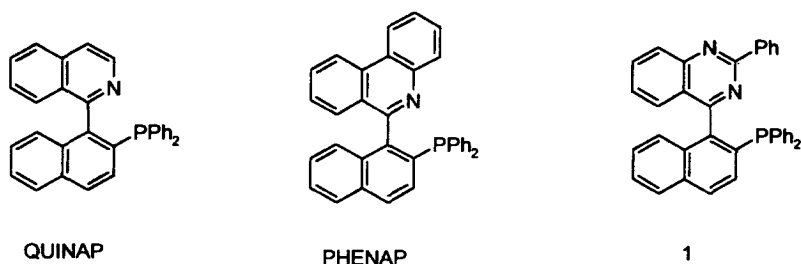
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Many recent asymmetric syntheses have been based on atropisomerically chiral ligands such as BINAP and related compounds.<sup>1</sup>

Recently, the synthesis of axially chiral P–N chelates, representative of a novel class of ligands, has been developed by the group of Brown.<sup>2</sup> The isoquinoline moiety has been used as a ‘building block’ for the synthesis of various chiral phosphinamine ligands. The best known, 1-(2-diphenylphosphino-1-naphthyl)isoquinoline (QUINAP) was applied with success in catalytic asymmetric hydroborations<sup>3</sup> and allylic alkylations.<sup>4</sup> A phenanthridine analogue of QUINAP, named PHENAP, has been also synthesised<sup>2d</sup> and its catalytic activity studied.<sup>5</sup> More recently a new chiral phosphinamine based on the 3,6-dimethylpyrazine has been reported,<sup>6</sup> but to date no atropisomerically chiral P–N chelating ligand bearing a benzodiazine moiety has been described.

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We report here, starting from the commercial 2-phenyl-4-chloroquinazoline, the synthesis of the 4-(2-diphenylphosphino-1-naphthyl)-2-phenylquinazoline **1**.<sup>7a</sup>

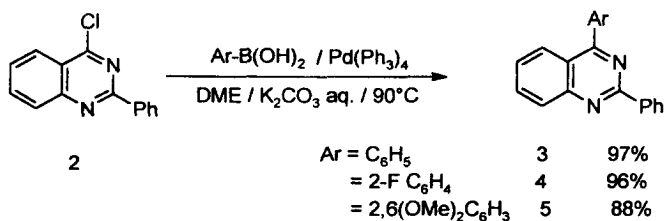
In such an atropisomeric phosphinamine, bearing a benzodiazine moiety, the presence of two nitrogen atoms in the diazine ring modifies the basicity of the nitrogen donor atom, which becomes considerably different from that of QUINAP or PHENAP. Such a variation of basicity could induce an alteration of the reactivity and of the ee in asymmetric catalysis. Otherwise, it could be interesting to appreciate the role of a bulky substituent such as a phenyl group on the *ortho* position of the chelating nitrogen.

The synthetic route chosen for the preparation of **1** involved a cross-coupling reaction for the biaryl linkage and a metal-catalysed reaction for the formation of the naphthylphosphorus bond.

Thus the synthesis of ligand **1** was dependent on the successful construction of the C–C bond between the naphthyl group and the quinazoline. The palladium-catalysed condensation of arylboronic acids was an efficient tool for asymmetrical biaryl constructions; generally aryl bromides or iodides are preferred because of their superior activity.

In a first step, we have tested the Pd-catalysed reaction of various boronic acids with the commercial 4-chloro-2-phenylquinazoline **2**.

It could be noted that compound **2** was sufficiently activated towards Pd-catalysed coupling reactions to give the expected biaryls in high yields (Scheme 1).

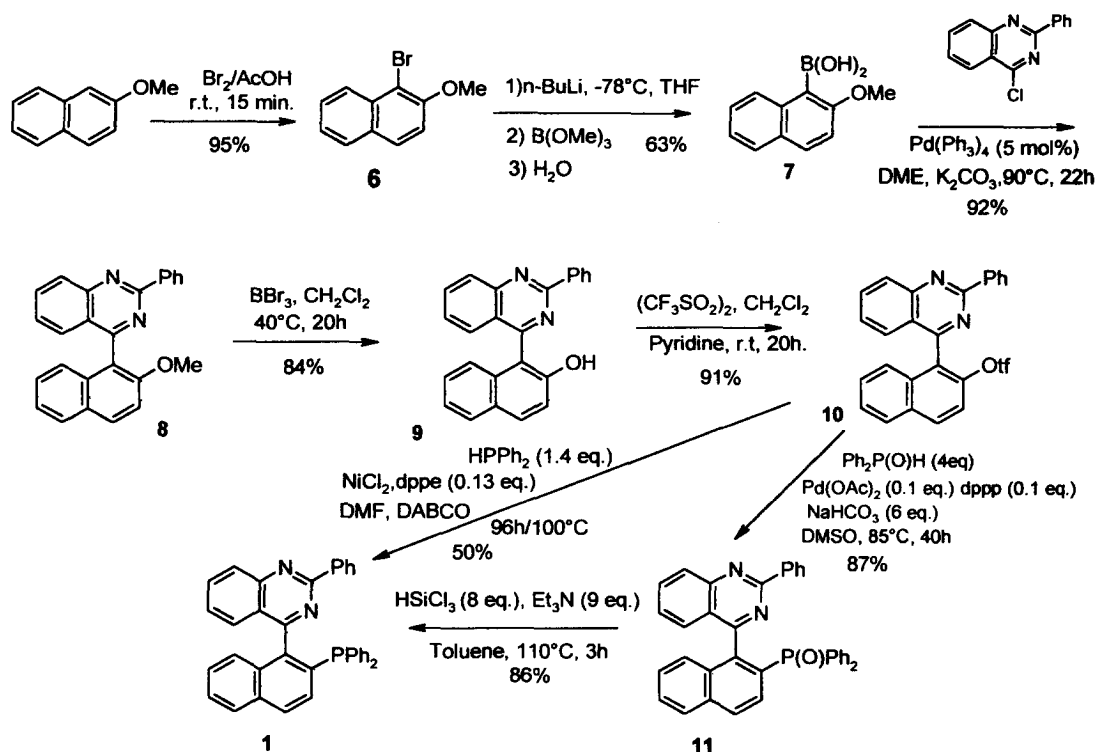


Scheme 1.

The overall synthetic route of **1** is given in Scheme 2. 2-Methoxy-1-naphthylboronic acid **7** was prepared from 1-bromo-2-methoxynaphthalene **6** via a lithiated derivative according to the procedure of Brown and co-workers.<sup>2b</sup> The cross-coupling reaction between compounds **2** and **7** has been performed under Suzuki's conditions to give the expected biaryl **8** in high yield. The demethylation of the ether **8** was performed with BBr<sub>3</sub> to give the phenol **9** in good yield. The reaction of **9** at room temperature with trifluoromethane sulfonic anhydride in the presence of pyridine gave the triflate **10** in 87% yield.

The P–N ligand **1**<sup>7b</sup> was obtained from triflate **10** either by a metal-catalysed reaction with diphenylphosphine oxide in DMSO<sup>8</sup> followed by reduction with trichlorosilane and triethylamine (overall yield 71%) or, by adapting the procedure of Cai,<sup>9</sup> by a nickel-catalysed reaction with diphenylphosphine in 50% yield.

In conclusion, starting from the boronic acid **8**, we have prepared a new axially chiral phosphinamine **1** in five steps with an overall yield of 53% or in four steps in a lower yield 35%. The resolution via



Scheme 2.

fractional crystallisation of diastereomeric palladium salts is in progress and further work is directed towards syntheses of various new diphenylphosphinonaphthylquinazolines with structural variation.

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- (a) Gautheron Chapoulaud, V. PhD Thesis, 1998, Rouen. (b) Key data: (**1**) pale yellow solid mp 220–222°C; found: C, 83.97; H, 5.08; N, 5.15. C<sub>36</sub>H<sub>25</sub>N<sub>2</sub>P requires C, 83.70; H, 4.88; N, 5.42; IR (KBr)  $\nu$  3056, 1567, 1541, 1487, 1436, 1338, 1024, 708, 695 cm<sup>-1</sup>; <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>):  $\delta$  8.19 (m, 3H), 7.99–7.86 (m, 3H), 7.55–7.16 (m, 19H); <sup>31</sup>P NMR (50.65 MHz, CDCl<sub>3</sub>):  $\delta$  -15.2.
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