



# Palladium-tetraphosphine catalysed allylic substitution in water

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**Abstract**—The *cis,cis,cis*-1,2,3,4-tetrakis(diphenylphosphinomethyl)cyclopentane/[PdCl(C<sub>3</sub>H<sub>5</sub>)<sub>2</sub>] system catalyses allylic amination in water with very high substrate/catalyst ratio in good yields. A turnover number of 980 000 can be obtained for the addition of dipropylamine to allyl acetate in the presence of this catalyst. © 2001 Elsevier Science Ltd. All rights reserved.

Palladium allylic substitution is probably the most widely employed palladium methodology in organic synthesis.<sup>1</sup> The use of water as solvent for organic synthesis is very attractive for environmental, economical and safety reasons. A few years ago, Genet et al. and Sinou et al. reported an efficient method for performing the allylic substitution<sup>2,3</sup> in water. They employed palladium complexes associated with sulfonated phosphine ligands<sup>4</sup> in a two-phase aqueous–organic medium. Recently, Kobayashi et al. and Sinou et al. reported that palladium-catalysed alkylation also occurred in water in the presence of non-water-soluble ligands, but the addition of surfactants such as cetyltrimethylammonium bromide was required.<sup>5,6</sup>

However, these procedures suffer from high catalyst loading and some of them from high temperatures and long reaction times. Moreover, few results have been obtained so far for allylic amination in water.

The nature of the phosphine ligand on complexes has a tremendous influence on the stability of the catalysts and on the rate of catalysed reactions. In order to find more stable and more efficient palladium catalysts, we have decided to study the influence of the new tetrapodal phosphine ligand, *cis,cis,cis*-1,2,3,4-tetrakis(diphenylphosphinomethyl)cyclopentane or Tedicyp **1** (Fig. 1),<sup>7</sup> in which the four diphenylphosphinoalkyl groups are stereospecifically bound to the same face of the cyclopentane ring, in several catalysed reactions.

We have reported recently that the complex formed by association of **1** with [PdCl(C<sub>3</sub>H<sub>5</sub>)<sub>2</sub>] is an extremely efficient catalyst for allylic amination.<sup>8</sup> For example, a

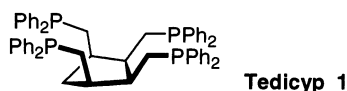
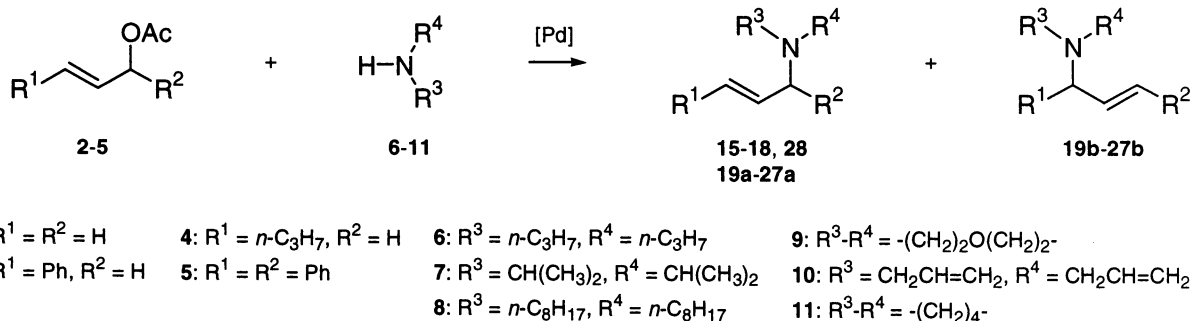


Figure 1.



Scheme 1.

**Keywords:** tetraphosphine; palladium; water; allylic amination; allylamine; allylacetate.

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**Table 1.** Palladium catalysed allylic alkylation of secondary amines **6–11** in water<sup>10</sup>

| Allyl acetate | Nucleophile | Product (major isomer) | Ratio a/b | Ratio substrate/catalyst | Yield (%)           |
|---------------|-------------|------------------------|-----------|--------------------------|---------------------|
| <b>2</b>      | <b>6</b>    | <b>15</b>              | —         | 1 000 000                | 98 <sup>a,d,f</sup> |
| <b>2</b>      | <b>7</b>    | <b>16</b>              | —         | 1000                     | 97 <sup>b</sup>     |
| <b>2</b>      | <b>8</b>    | <b>17</b>              | —         | 100 000                  | 80 <sup>c,d</sup>   |
| <b>2</b>      | <b>9</b>    | <b>18</b>              | —         | 100 000                  | 96 <sup>b,d</sup>   |
| <b>3</b>      | <b>10</b>   | <b>19a</b>             | 99/1      | 10 000                   | 100 <sup>a,e</sup>  |
| <b>3</b>      | <b>8</b>    | <b>20a</b>             | 100/0     | 10 000                   | 100 <sup>a,d</sup>  |
| <b>3</b>      | <b>9</b>    | <b>21a</b>             | 85/15     | 10 000                   | 62 <sup>b</sup>     |
| <b>3</b>      | <b>11</b>   | <b>22a</b>             | 84/16     | 10 000                   | 97 <sup>b</sup>     |
| <b>4</b>      | <b>6</b>    | <b>23a</b>             | 99/1      | 1000                     | 85 <sup>a</sup>     |
| <b>4</b>      | <b>10</b>   | <b>24a</b>             | 98/2      | 1000                     | 85 <sup>a,e</sup>   |
| <b>4</b>      | <b>8</b>    | <b>25a</b>             | 100/0     | 1000                     | 97 <sup>b</sup>     |
| <b>4</b>      | <b>11</b>   | <b>26a</b>             | 95/5      | 1000                     | 95 <sup>a</sup>     |
| <b>4</b>      | <b>9</b>    | <b>27a</b>             | 98/2      | 1000                     | 91 <sup>b</sup>     |
| <b>5</b>      | <b>6</b>    | <b>28</b>              | —         | 100                      | 45 <sup>b</sup>     |

Conditions: catalyst: [Pd(C<sub>3</sub>H<sub>5</sub>)Cl]<sub>2</sub>/1 1/2,<sup>9</sup> H<sub>2</sub>O, 25°C, 20 h.

<sup>a</sup> Allyl acetate: 1 equiv., amine: 2 equiv.

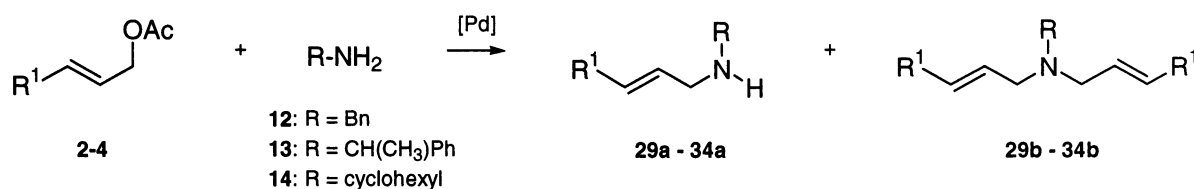
<sup>b</sup> Allyl acetate: 2 equiv., amine: 1 equiv., K<sub>2</sub>CO<sub>3</sub>: 1 equiv.

<sup>c</sup> Water saturated with NaCl.

<sup>d</sup> 55°C.

<sup>e</sup> 40 h.

<sup>f</sup> 240 h.

**Scheme 2.**

TON (turnover number) of 680 000 for the addition of dipropylamine **6** to allyl acetate **2** had been obtained when the reaction was conducted in THF. In this paper we wish to describe the results obtained in water for the catalysed allylic amination using **1** as a ligand. We could expect that if a small amount of this complex is soluble in the reaction mixture when water is used as the solvent, and if this catalyst is water-stable, some addition product should be observed.

First, we tried with the substrates which were the most reactive when the reaction was performed in THF: addition of dipropylamine **6** to allyl acetate **2**. Surprisingly, we observed that the reaction rate was in fact slightly higher in water than in THF. The complex formed by association of Tedicyp and [PdCl(C<sub>3</sub>H<sub>5</sub>)]<sub>2</sub> seemed to be very water-stable. A conversion of 98% (Scheme 1, Table 1) was observed when a substrate/catalyst ratio of 1 000 000 was used. In THF the conversion was 68% in the same conditions. Moreover, this reaction was carried out in the absence of surfactants. In the presence of cetyltrimethylammonium bromide a slower reaction rate and a lower conversion was obtained. A similar tendency was observed for the alkylation of morpholine **9** by allyl acetate **2**. In the presence of 0.001% catalyst, the conversion was 96% in water and 57% in THF. On the other hand, an amine with long alkyl groups such as dioctylamine **8** led to a

much slower reaction rate in water than in THF: **4** and 99% yields were observed, respectively. However, if this reaction was conducted in brine instead of water the conversion rose to 80%. With primary amines, we obtained mixtures of monoalkylation and dialkylation products (Scheme 2, Table 2). Benzylamine **12** led to the dialkylation product **29b** in 96% conversion and 95% selectivity in the presence of 0.001% catalyst. The alkylation rate of phenylethylamine **13** and cyclohexylamine **14** is slower but a high selectivity in favour of the dialkylation products **30b** and **31b** was observed.

Next we tried to evaluate the scope and limitations of Tedicyp–palladium complex for this reaction, so we investigated the allylation of amines with substituted allyl acetates. We noted good regio- and stereoselectivity for the amination of cinnamyl acetate **3** in favour of the linear *E* isomer. When we used cinnamyl acetate **3** in the presence of 0.1% catalyst, high yields and high selectivity were obtained for the alkylation of dioctylamine **8** and diallylamine **10**. The regioselectivity of the addition of cyclic amines **9** and **11** was slightly lower; 15% and 16% of the branched products **21b** and **22b** were obtained. High selectivity was also observed for the addition of **6**, **8**, **9** and **10** to (*E*)-hex-2-en-1-yl acetate **4**, however, 5% of the branched isomer was obtained with pyrrolidine **11**. A similar selectivity was observed in THF. Much lower TON was observed in the course of

**Table 2.** Palladium catalysed allylic alkylation of primary amines **12–14** in water

| Allyl acetate | Nucleophile | Product (major isomer) | Ratio a/b         | Ratio substrate/catalyst | Yield (%)         |
|---------------|-------------|------------------------|-------------------|--------------------------|-------------------|
| <b>2</b>      | <b>12</b>   | <b>29b</b>             | 5/95              | 100 000                  | 96 <sup>b,c</sup> |
| <b>2</b>      | <b>13</b>   | <b>30b</b>             | 3/97              | 1000                     | 96 <sup>b</sup>   |
| <b>2</b>      | <b>14</b>   | <b>31b</b>             | 1/99              | 1000                     | 100 <sup>b</sup>  |
| <b>3</b>      | <b>12</b>   | <b>32a</b>             | 99/1 <sup>d</sup> | 1000                     | 96 <sup>a</sup>   |
| <b>3</b>      | <b>14</b>   | <b>33a</b>             | 99/1 <sup>d</sup> | 1000                     | 87 <sup>a</sup>   |
| <b>4</b>      | <b>14</b>   | <b>34a</b>             | 7/93              | 1000                     | 94 <sup>b</sup>   |

Conditions: catalyst: [Pd(C<sub>3</sub>H<sub>5</sub>)Cl]<sub>2</sub>/1 1/2,<sup>9</sup> H<sub>2</sub>O, 25°C, 20 h. For <sup>a,b</sup> see Table 1.

<sup>c</sup> 55°C.

<sup>d</sup> For compounds **32** and **33**, 4% of the branched isomer of the mono addition product was also observed.

the amination of hindered 3-acetoxy-1,3-diphenyl-1-propene **5**.

In conclusion, the Tedicyp–palladium complex obtained by addition of Tedicyp to [Pd(C<sub>3</sub>H<sub>5</sub>)Cl]<sub>2</sub> provides a convenient catalyst for the allylic amination reaction in water. This catalyst seems to be very water-stable. This stability probably comes from the presence of the four diphenylphosphinoalkyl groups stereospecifically bound to the same face of the cyclopentane ring. All four phosphines probably cannot bind at the same time to the same palladium centre, but the presence of these four phosphines on the ligand close to the metal centre along with steric factors seems to increase the coordination of the ligand to the palladium complex. In the presence of this catalyst the allylic substitution reaction can be performed in water with as little as 0.0001% catalyst. This procedure represents an environmentally friendly method for the preparation of allylic compounds. Further applications of this ligand will be reported in due course.

### Acknowledgements

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- The *cis,cis,cis*-1,2,3,4-tetrakis(diphenylphosphinomethyl)-cyclopentane/[PdCl(C<sub>3</sub>H<sub>5</sub>)<sub>2</sub>]<sub>2</sub> complex was prepared by stirring under argon the tetraphosphine **1**<sup>8</sup> (14 mg, 16.2×10<sup>-3</sup> mmol) with [PdCl(C<sub>3</sub>H<sub>5</sub>)<sub>2</sub>]<sub>2</sub> (3 mg, 8.1×10<sup>-3</sup> mmol) in THF (10 mL) for 10 minutes at room temperature followed by evaporation of the solvent. <sup>31</sup>P NMR (162 MHz, CDCl<sub>3</sub>) δ 25 (w=80 Hz), 19.4 (w=110 Hz); <sup>31</sup>P NMR (162 MHz, H<sub>2</sub>O–pyrrolidine) δ 14 (w=600 Hz).
- As a typical experiment the reaction of (*E*)-hex-2-en-1-yl acetate **4** (0.33 g, 2.3 mmol) and diethylamine **8** (1.4 mL, 4.6 mmol) at 50°C for 20 h in distilled water (2 mL) in the presence of the Tedicyp–palladium complex (2.3×10<sup>-3</sup> mmol) under argon affords the corresponding addition product **25a** after addition of an NaOH solution, extraction with ether, drying over MgSO<sub>4</sub>, evaporation and filtration on silica gel (ether/pentane: 1/9) in 97% (0.718 g) isolated yield.