

# Stereochemistry at the Phosphorus Atom during Palladium-catalysed Formation of Carbon–Phosphorus Bonds and Mechanistic Implications

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The reaction of (*R*)-(+)-isopropyl methylphosphinate (**5**) with bromobenzene in the presence of Pd<sup>0</sup> catalyst and triethylamine to afford (*S*)-(–)-isopropyl methylphenylphosphinate (**6**) proceeds with complete retention of configuration *via* a front-sided attack by phenylpalladium bromide on the phosphorus nucleophile.

Recently, it has been shown that aryl- and alkenyl-phosphonates,<sup>1</sup> arylphenylphosphinates,<sup>2</sup> alkylarylphosphinates,<sup>3</sup> alkylarylphenylphosphine oxides,<sup>4</sup> alkenylmethyl- and alkenylaryl-phosphinates,<sup>5</sup> as well as alkenyldiphenyl- and alkenylbenzylphenyl-phosphine oxides<sup>6</sup> can be synthesised *via* palladium-catalysed formation of carbon–phosphorus bonds. Moreover, benzoxaphosphacycloalkane derivatives<sup>7</sup> and α-methylenephospholactones<sup>8</sup> have also been synthesized *via* an intramolecular version of this palladium-catalysed route. The formation of the carbon–phosphorus bond is assumed to occur *via* the pathway depicted in Scheme 1.<sup>2</sup> The palladium(0) species undergoes oxidative addition with aryl bromide to give the arylpalladium complex (**1**). Attack of the phosphorus nucleophile (**2**) at the arylpalladium complex in the presence of triethylamine results in the elimination of hydrogen bromide to give the intermediate (**3**) which then undergoes reductive elimination to afford the final product (**4**) and regenerate the Pd<sup>0</sup> species. However, the reaction mode of (**1**) with (**2**) remained unclear in this mechanism. We have therefore studied the stereochemistry of the carbon–phospho-

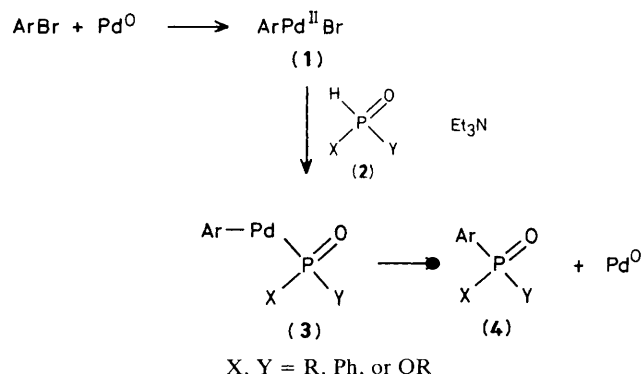
rus bond formation in this type of process in order to shed light on the reaction mechanism involved.

(*R*)-(+)-Isopropyl methylphosphinate (**5**) {[α]<sub>D</sub><sup>25</sup> +32.32°, lit.,<sup>9</sup> (*R*)-(+), [α]<sub>D</sub><sup>27</sup> +32.25°} (100% optical purity), which was prepared according to known procedures,<sup>9–11</sup> on treatment with bromobenzene in the presence of a catalytic amount of tetrakis(triphenylphosphine)palladium and triethylamine at 90°C, afforded (*S*)-(–)-isopropyl methylphenylphosphinate (**6**) in 93% optical purity {[α]<sub>D</sub><sup>10</sup> –50.26°, lit.,<sup>11</sup> (*R*)-(+), [α]<sub>D</sub><sup>25</sup> +35.7°, 66% optical purity} and in 88% yield (Scheme 2). This clearly demonstrates that the palladium-catalysed formation of carbon–phosphorus bonds occurs with complete retention of configuration at the chiral phosphorus atom.

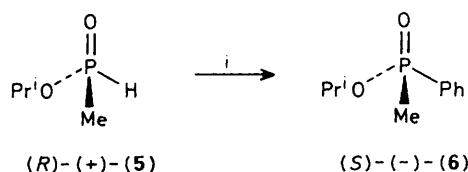
If the reductive elimination with formation of the carbon–phosphorus bond from intermediate (**3**) in Scheme 1 is assumed to occur in a mode akin to that of the carbon–carbon bond formation which is known to proceed with retention of configuration,<sup>12</sup> then this indicates that attack of the phosphorus nucleophile (**2**) at the arylpalladium complex also takes place with retention of configuration. Consequently, it can be assumed that the reaction of (*R*)-(**5**) with the arylpalladium complex occurs by a front-sided replacement of hydrogen in (*R*)-(**5**), presumably *via* its trico-ordinated tautomer (*R*)-(**5a**).† In other words, the lone electron pair of (*R*)-(**5a**) attacks the Pd atom in the arylpalladium complex, thus facilitating the loss of a proton from (*R*)-(**5a**) and a bromide ion from the arylpalladium complex with the aid of triethylamine; this results in the formation of triethylamine hydrobromide and an intermediate of type (**3**). Reductive elimination then takes place to yield the final product (**6**).

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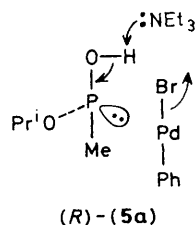
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Scheme 1. Phosphine ligands are omitted for clarity.



Scheme 2. Reagents and conditions: i, PhBr, Pd(PPh<sub>3</sub>)<sub>4</sub> (5 mol %), Et<sub>3</sub>N, 90°C, 0.5 h.



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† It has been reported that the hydrogen in optically active isopropyl methylphosphinate underwent exchange with deuterium in MeOD with retention of configuration *via* a front-sided attack, see ref. 10.