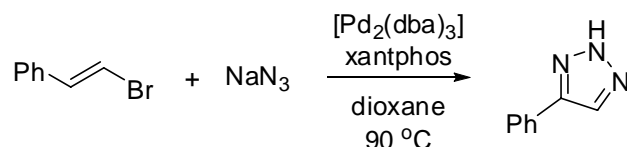


Palladium-Catalysed Synthesis of 1,2,3-Triazoles

1,2,3-Triazoles display a wide spectrum of biological activity and are commonly found in pharmaceuticals. They are conventionally formed by the Huisgen dipolar cycloaddition of alkynes with organic azides.¹

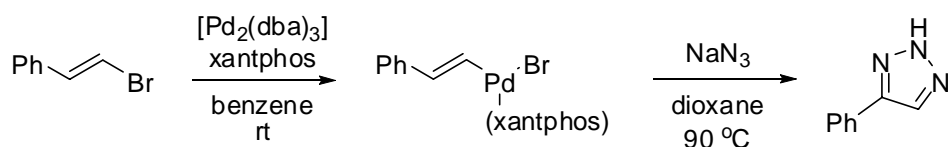
The coupling of an azide with an alkenyl halide under palladium-catalysis conditions led to the formation of 1,2,3-triazoles (Scheme 1).²



Scheme 1

The reaction worked well for many aromatic alkenyl bromides. For alkyl-triazoles, more forcing conditions were required (DMSO, 110 °C).

Oxidative addition of palladium to the C-Br bond has been proven; since the same intermediate can be generated by Buchwald's procedure.³ This intermediate goes on to form the triazole under standard conditions (Scheme 2).

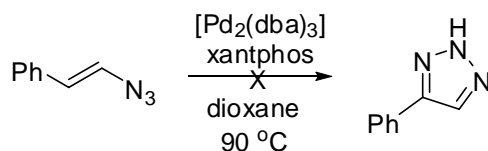


Scheme 2

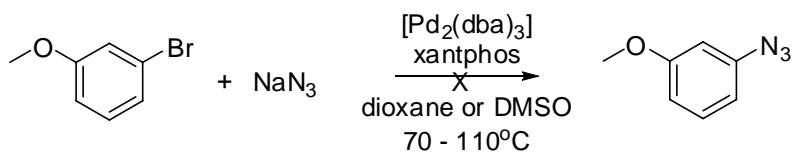
Two reaction pathways were postulated:

- (a) Substitution of bromine by azide, reductive elimination then Pd-promoted 1,5-electrocyclisation and subsequent tautomerisation.
- (b) [3+2] cycloaddition of azide anion with the vinylpalladium complex, beta-elimination and reductive elimination.

Mechanism (a) was disproved (Schemes 3 and 4).



Scheme 3



Scheme 4

Hence a mechanism involving the formation of a vinyl azide via a reductive elimination process probably was not occurring, suggesting mechanism (b) was operating.

References

1. Huisgen, R. (1961). "Cenetary Lecture - 1,3-Dipolar Cycloadditions". *Proceedings of the Chemical Society of London*: 357.
2. *Angew. Chem. Int. Ed.* **2006**, 45, 6893-6896.
3. *Organometallics*, **2006**, 25, 82.