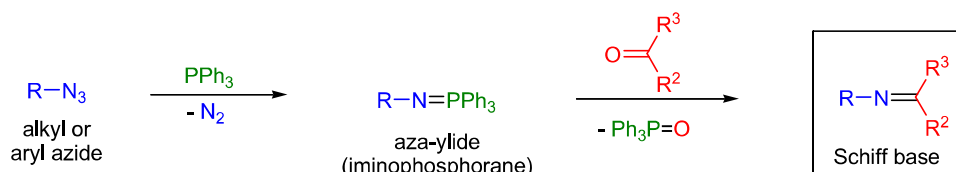


## AZA-WITTIG REACTION

(References are on page 539)

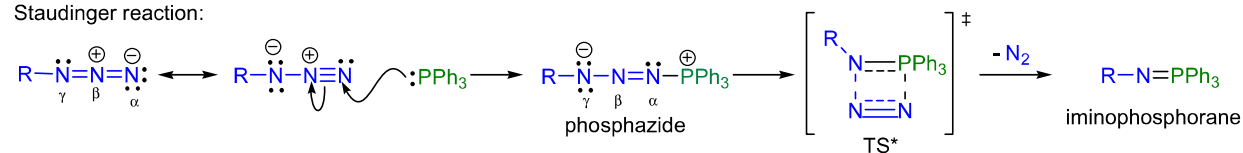
**Importance:**[Seminal Publications<sup>1</sup>; Reviews<sup>2-11</sup>; Theoretical Studies<sup>12-17</sup>]

In 1919, H. Staudinger and J. Meyer prepared PhN=PPh<sub>3</sub>, an aza-ylide which was the first example of an aza-Wittig reagent.<sup>1</sup> By definition an ylide is "a substance in which a carbanion is attached directly to a heteroatom carrying a substantial degree of positive charge and in which the positive charge is created by the sigma bonding of substituents to the heteroatom".<sup>4</sup> The reaction of aza-ylides (iminophosphoranes) with various carbonyl compounds is called the *aza-Wittig reaction*. The product of the reaction is a Schiff base. Just as in the regular *Wittig reaction*, the by-product is triphenylphosphine oxide. Over the last decade, the *aza-Wittig* methodology has received considerable attention because of its utility in the synthesis of C=N double bond containing compounds, in particular, nitrogen heterocycles. The *intramolecular aza-Wittig reaction* is a powerful tool for the synthesis of 5-, 6-, 7-, and 8 membered heterocycles.

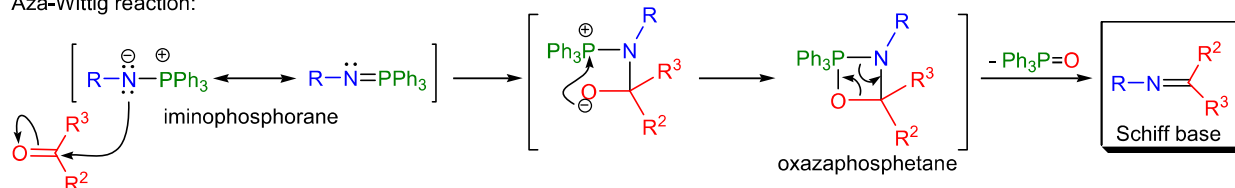
**Mechanism:** <sup>18,15</sup>

In the first step, the triphenylphosphine reacts with an alkyl azide to form an iminophosphorane with loss of nitrogen (*Staudinger reaction*). In the second step, the nucleophilic nitrogen of the iminophosphorane attacks the carbonyl group to form a four-membered intermediate (oxazaphosphetane) from which the product Schiff base and the by-product triphenylphosphine oxide are released.

Staudinger reaction:



Aza-Wittig reaction:

**Synthetic Applications:**

The solid phase synthesis of *trisubstituted guanidines* was achieved in the research group of D.H. Drewery by utilizing the *aza-Wittig reaction*. The reaction of solid-supported alkyl iminophosphorane and aryl or alkyl isothiocyanates afforded carbodiimides, which upon treatment with primary or secondary amines provided the trisubstituted guanidines.<sup>19</sup>

