**SYNLETT Spotlight 339**

This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research.

**Tripotassium Phosphate: From Buffers to Organic Synthesis**

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**Introduction**

Tripotassium phosphate (potassium phosphate tribasic, \( \text{K}_3\text{PO}_4 \)) is a strong inorganic base (\( pK_a = 12.32 \) for the conjugate acid). It is non-toxic, very inexpensive, and available from many chemical supply companies. This chemical is used as a food additive or to form stable phosphate buffer solutions in water. However, it is soluble in organic solvents (both in polar and nonpolar), and thus has been used as an alternative non-nucleophilic base in several reactions.

The choice of base in an organic reaction depends on various factors. In several cases, a super strong base like \( n-\text{BuLi} \) is not needed for the deprotonation and chemists rely on weaker organic amines or inorganic salts. Organic amines (e.g., triethylamine, pyridine) are usually foul smelling liquids soluble in most solvents, but can cause problems with nucleophilic attack or coordination to metals. Inorganic salts used in organic synthesis include \( \text{K}_2\text{CO}_3 \) and \( \text{Cs}_2\text{CO}_3 \), although the former is only soluble in polar solvents and the latter is very expensive and can be moisture-sensitive. \( \text{K}_3\text{PO}_4 \) is slightly hygroscopic, but its melting point is 1380 °C so it can be easily heated to remove water without decomposition.

**Abstracts**

Under microwave conditions secondary BOC amines can be deprotected in methanol using a catalytic amount of \( \text{K}_3\text{PO}_4 \cdot \text{H}_2\text{O} \). This procedure is advantageous when the molecule is sensitive to acidic conditions or contains other carbonyl groups.\(^1\)

In the presence of anhydrous \( \text{K}_3\text{PO}_4 \) in the ionic liquid \([\text{BMIM}]\text{BF}_4\), phenol mesylates (Ms) are deprotected to form the phenolate anion, which can undergo further nucleophilic aromatic substitutions (SNAr) to form diaryl ethers.\(^2\)

The Suzuki coupling\(^3\) between alkenyl triflates (Tf) and boronic acids is assisted by the presence of \( \text{K}_3\text{PO}_4 \) using dioxane as solvent. This base produces dramatic rate and yield enhancements.\(^4\)
The palladium-catalyzed cross-coupling between potassium cyclopropyl trifluoroborates ($\text{BF}_3\text{K}$) and aryl bromides uses $\text{K}_3\text{PO}_4$ as an inexpensive, but effective base.\(^5\)

Another palladium-catalyzed cross-coupling, the Sonogashira reaction\(^6\) between aryl bromides and terminal alkynes, has been shown to benefit from the use of $\text{K}_3\text{PO}_4$. The combination of $\text{K}_3\text{PO}_4$ in DMSO also assisted the deacetonation of 4-aryl-2-methylbut-3-yn-2-ol intermediates.\(^7\)

$\text{K}_3\text{PO}_4$ is the optimum base in the ligand-free Heck reaction\(^8\) using $\text{Pd(OAc)}_2$ in $N,N$-dimethylacetamide (DMA). The catalytic coupling of aryl bromides to olefins using these conditions has turnover numbers (TON) of up to 38500.\(^9\)

Aryl ethers can be formed by the copper-catalyzed Ullmann reaction.\(^10\) Although $\text{Cs}_2\text{CO}_3$ was thought crucial to its success, it has been found that $\text{K}_3\text{PO}_4$ in DMF is an excellent alternative for the formation of diaryl ethers (including heteroaromatic) and aryl alkyl ethers.\(^11\)

Buchwald and co-workers have developed a catalytic method to couple amines to aryl chlorides. The use of phosphate in 1,2-dimethoxyethane showed great versatility in the C–N cross-coupling.\(^12\)

When aryl halides are coupled to organostannanes (Stille reaction)\(^13\) the choice of base is important, especially with aryl chlorides as substrates. The use of $\text{K}_3\text{PO}_4$ in combination with the palladacycle of Bedford allows this coupling in high yields.\(^14\)

Hartwig and co-workers have pursued the efficient $\alpha$-arylation of amino acid derivatives. The weaker base $\text{K}_3\text{PO}_4$ can deprotonate the C–H of $N$-(diphenylmethylene)glycinate and allows the formation of the enolate, which is then coupled to aryl halides in good yield.\(^15\)

References