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

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**Introduction**

Tripotassium phosphate (potassium phosphate tribasic, K₃PO₄) is a strong inorganic base (pKₐ = 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.

**Abstracts**

Under microwave conditions secondary BOC amines can be deprotected in methanol using a catalytic amount of K₃PO₄·H₂O. This procedure is advantageous when the molecule is sensitive to acidic conditions or contains other carbonyl groups.¹

In the presence of anhydrous K₃PO₄ in the ionic liquid [BMIM]BF₄, 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 coupling³ between alkenyl triflates (Tf) and boronic acids is assisted by the presence of K₃PO₄ using dioxane as solvent. This base produces dramatic rate and yield enhancements.⁴

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The palladium-catalyzed cross-coupling between potassium cyclopropyl trifluoroborates (BF3K) and aryl bromides uses K3PO4 as an inexpensive, but effective base.5

Another palladium-catalyzed cross-coupling, the Sonogashira reaction6 between aryl bromides and terminal alkynes, has been shown to benefit from the use of K3PO4. The combination of K3PO4 in DMSO also assisted the deacetonation of 4-aryl-2-methylbut-3-yn-2-ol intermediates.7

K3PO4 is the optimum base in the ligand-free Heck reaction8 using 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 Cs2CO3 was thought crucial to its success, it has been found that K3PO4 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 K3PO4 in combination with the palladacycle of Bedford allows this coupling in high yields.14

Hartwig and co-workers have pursued the efficient α-arylation of amino acid derivatives. The weaker base K3PO4 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

(2) Xu, H.; Chen, Y. Molecules 2007, 12, 861.