

SYNLETT Spotlight 373

Potassium *tert*-Butoxide

Compiled by Yong Wang

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

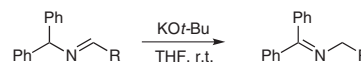
Introduction

Potassium *tert*-butoxide (KO*t*-Bu, mp 256–258 °C), recognized as one of the most commercially available and versatile alkoxide bases in organic synthesis, has attracted increasing attention in recent years, and many excellent examples promoted by KO*t*-Bu, such as alkylations, intramolecular aldol condensations, Michael additions, ketone cleavages, oxidations and rearrangement reactions

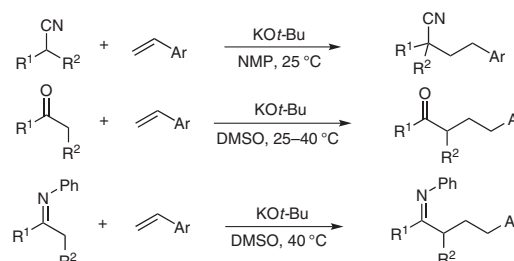
have been reported.¹ As to its continued popularity, the reason may partly be ascribed to the fact that its base strength is highly dependent on the choice of reaction solvent. The range from the strongest to the weakest is listed as follows: KO*t*-Bu in DMSO, neat KO*t*-Bu, KO*t*-Bu in toluene or in THF, and KO*t*-Bu in *t*-BuOH. Moreover, potassium *tert*-butoxide also serves as an efficient and powerful base in transition-metal-catalyzed couplings like Suzuki and Buchwald–Hartwig reactions, etc.²

Abstracts

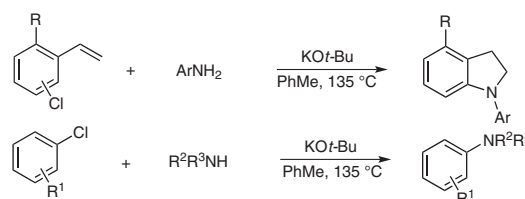
(A) With a catalytic amount of potassium *tert*-butoxide, Cainelli and co-workers have found that the synthesis of primary amine derivatives could successfully be achieved via a rapid 1,3-prototropic rearrangement of *N*-diphenylmethanimines.³ Moreover, this mild protocol for transamination can also be applied for aliphatic and aromatic aldimines.



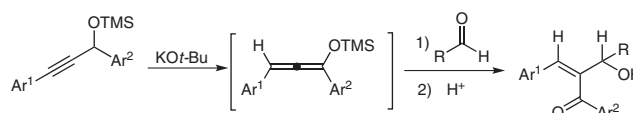
(B) Knochel and co-workers⁴ have developed a new and efficient synthetic method for the addition of various carbonyl compounds (nitriles, ketones, and imines) to styrenes in the presence of potassium *tert*-butoxide. The desired products could be obtained in good to excellent yields. It is important to mention that the combination of potassium *tert*-butoxide with polar solvents, dimethyl sulfoxide or *N*-methylpyrrolidinone allows the reaction to proceed in mild conditions.



(C) Beller et al.⁵ have disclosed a transition-metal-free amination of aryl chlorides in the presence of KO*t*-Bu, which probably proceeds via the formation of an aryne intermediate. It is interesting that the aliphatic and aromatic amines could react with *ortho*- and *meta*-chlorostyrene without palladium to give *N*-substituted 2,3-dihydroindoles in good yields. In addition, the intermolecular aminations of aryl chlorides with primary and secondary amines could also react smoothly, albeit only *meta*-substituted anilines were obtained.



(D) Yoshizawa et al.⁶ presented highly reactive 1,3-diaryl-2-propynyl trimethylsilyl ethers, which could easily isomerize into the corresponding siloxyallenes using a catalytic amount of potassium *tert*-butoxide under mild conditions. The obtained intermediates could react in situ with various aldehydes to afford selective β -branched Morita–Baylis–Hillman-type adducts in an one-pot reaction after acid treatment.



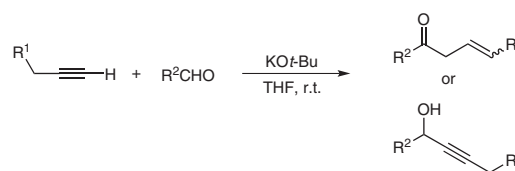
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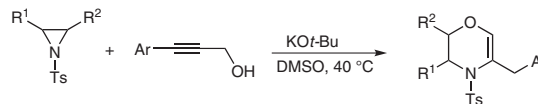
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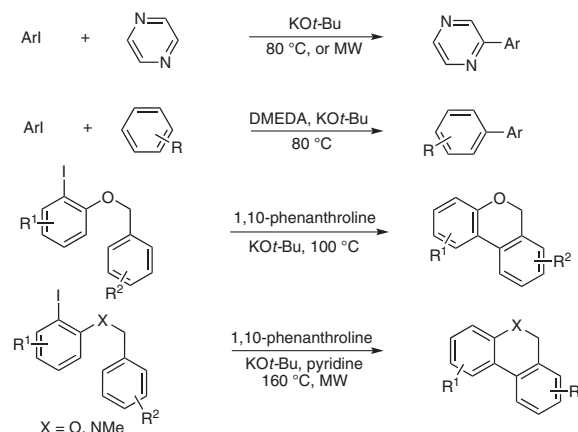
(E) Tu and co-workers⁷ have developed a concise and transition-metal-free method for the coupling of alkynes and aldehydes. The β,γ -unsaturated enones could be obtained in moderate to good yields in THF in the presence of potassium *tert*-butoxide at room temperature. However, the reaction of aliphatic aldehydes led to low yields of the desired products.



(F) An efficient and unprecedented synthetic route to dihydroxazine derivatives was developed by Zhou and co-workers,⁸ which underwent tandem ring-opening/closing reactions of *N*-Ts aziridines and aryl propargyl alcohols. It was interesting that *KOt*-Bu was found to be an effective promoting reagent for this transformation. This strategy offers an efficient protocol for the construction of six-membered ring systems under mild conditions.



(G) Instead of the employment of highly versatile and noble metals in the catalytic arylation reactions, Itami and co-workers reported for the first time that the coupling between electron-deficient nitrogen-containing heterocycles and iodoarenes could be smoothly promoted by *KOt*-Bu alone.⁹ Later on, the research groups of Shi,¹⁰ Hayashi,¹¹ Lei,¹² and Charette¹³ have reported subsequently on the construction of biaryl compounds from unactivated aromatic rings by the direct C–H activation with a combination of organocatalyst and *KOt*-Bu. In addition, the mechanism of these transition-metal-free couplings was also interpreted by Studer and Curran recently.¹⁴ It was believed that these base-promoted couplings would have a much broader application in organic synthesis.



References

- (1) (a) Pearson, D. E.; Buehler, C. A. *Chem. Rev.* **1974**, *74*, 45. (b) Friestad, G. K.; Branchaud, B. P. In *Handbook of Reagents for Organic Synthesis: Acidic and Basic Reagents*; Reich, H. J.; Rigby, J. H., Eds.; Wiley: New York, **1999**, 290–296.
- (2) Selected literatures for the use of *KOt*-Bu as a versatile base in metal-catalyzed reactions: (a) Singh, R.; Viciu, M. S.; Kramareva, N.; Navarro, O.; Nolan, S. P. *Org. Lett.* **2005**, *7*, 1829. (b) Li, J.; Cui, M.; Yu, A.; Wu, Y. *J. Organomet. Chem.* **2007**, *692*, 3732. (c) Blank, B.; Madalska, M.; Kempe, R. *Chem. Eur. J.* **2009**, *15*, 3790.
- (3) Cainelli, G.; Giacomini, D.; Trerè, A.; Boyd, P. P. *J. Org. Chem.* **1996**, *61*, 5134.
- (4) Rodriguez, A. L.; Bunlaksanusorn, T.; Knochel, P. *Org. Lett.* **2000**, *2*, 3285.
- (5) Beller, M.; Breindl, C.; Riermeier, T. H.; Tillack, A. *J. Org. Chem.* **2001**, *66*, 1403.
- (6) Yoshizawa, K.; Shioiri, T. *Tetrahedron Lett.* **2006**, *47*, 757.
- (7) Wang, S.; Tu, Y.; Wang, M. *Tetrahedron Lett.* **2006**, *47*, 8621.
- (8) Wang, L.; Liu, Q.; Wang, D.; Li, X.; Han, X.; Xiao, W.; Zhou, Y. *Org. Lett.* **2009**, *11*, 1119.
- (9) (a) Yanagisawa, S.; Ueda, K.; Taniguchi, T.; Itami, K. *Org. Lett.* **2008**, *10*, 4673. (b) Yanagisawa, S.; Itami, K. *ChemCatChem* **2011**, *3*, 827.
- (10) Sun, C.; Li, H.; Yu, D.; Yu, M.; Zhou, X.; Lu, X.; Huang, K.; Zheng, S.; Li, B.; Shi, Z. *Nat. Chem.* **2010**, *2*, 1044.
- (11) Shirakawa, E.; Itoh, K.; Higashino, T.; Hayashi, T. *J. Am. Chem. Soc.* **2010**, *132*, 15537.
- (12) Liu, W.; Cao, H.; Zhang, H.; Zhang, H.; Chung, K. H.; He, C.; Wang, H.; Kwong, F. Y.; Lei, A. *J. Am. Chem. Soc.* **2010**, *132*, 16737.
- (13) Roman, D. S.; Takahashi, Y.; Charette, A. B. *Org. Lett.* **2011**, *13*, 3242.
- (14) Studer, A.; Curran, D. P. *Angew. Chem. Int. Ed.* **2011**, *50*, 5018.