Practical Synthesis of $N$-Substituted Cyanamides as N-C-N Building Blocks for Heterocycle Synthesis

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A variety of carboxamidoximes (2), prepared from carbonitriles with NH$_2$OH, could react with benzenesulfonyl chlorides (TsCl or o-NsCl) and DIPEA to form $N$-substituted cyanamides (3) in very good yields. The benzenesulfonyl chloride promoted Tiemann rearrangement of carboxamidoximes (2) is readily amenable for the synthesis of a wide variety of cyanamide derivatives in multi-gram scales from carbonitriles.\textsuperscript{1} Acidic hydrolysis of the $N$-substituted cyanamides (3) afforded the corresponding $N$-monosubstituted ureas (4) in good yields. The preparation of the $N$-monosubstituted ureas (4) could also be accomplished in a one-pot fashion effectively from carbonitriles (2) with comparable yields.\textsuperscript{2} $N$-Alkyl-$N'$-arylguanidines (5) could be obtained from the reaction of $N$-arylcyanamides (3) with various primary and secondary alkylamines, under the catalysis of Cul and Xantphos in DMF. This methodology provides a direct access to versatile $N,N'$-disubstituted guanidine derivatives (5) from previously described $N$-arylcyanamides (3).\textsuperscript{3} The application of $N$-substituted cyanamides (3) toward the synthesis of various heterocycles, including benzimidazoles, benzoxazoles, and quinazolinones, has also been demonstrated.

References

