SYNLETT
Spotlight 110

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

p-Toluenesulfonylmethyl Isocyanide (TosMIC)

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Introduction

p-Toluenesulfonylmethyl isocyanide (TosMIC) is one of the most versatile and widely applicable reagents in organic synthesis. The methylene group of TosMIC is highly activated (*p*Ka = 14) by the two electron-withdrawing substituents. Deprotonation of TosMIC has been achieved with an array of bases ranging from K_2CO_3 in MeOH to *n*-BuLi in THF. TosMIC is considered as a formaldehyde equivalent with reversible polarity. The reagent is a stable solid (mp 116–117 °C) that is commercially available, or can be prepared from *p*-toluenesulfonic acid[1] in a two-step process. Many heterocycles, such as oxazole, pyrrole, imidazole, thiazole and 1,3,4-triazole, can be synthesized from TosMIC.

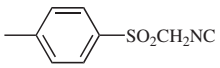
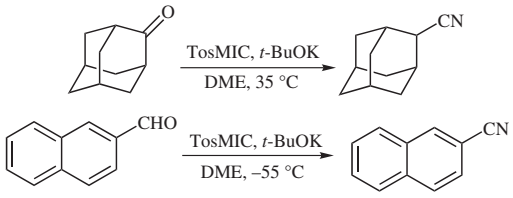


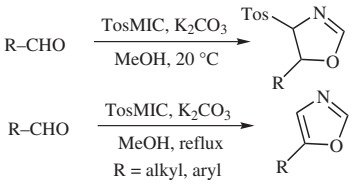
Figure 1

Abstracts

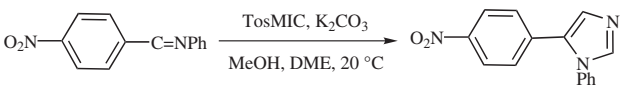
(A) Most ketones are converted in one operation into cyanides with TosMIC in the presence of potassium *tert*-butoxide in non-protic solvents (DME, DMSO).[2] The reductive cyanation of some aldehyde[3] was carried out at low temperature and needs addition of methanol.



(B) TosMIC on reaction with aldehyde in methanol at room temperature leads to oxazolene, where as oxazoles were formed at reflux temperature.[4] The addition of TosMIC to the aldehyde is followed by cyclization and subsequent elimination of the tosyl group to afford oxazole. Dhar et al. reported a modified oxazole synthesis using DBU in DME at 80 °C.[4b]



(C) Base-induced addition of TosMIC to aldimines in protic medium occurs with concomitant cyclization followed by elimination of *p*-toluenesulfonic acid to result in imidazoles.[5]



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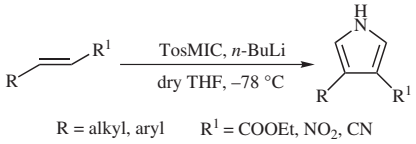
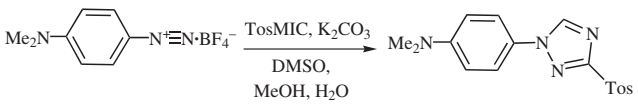
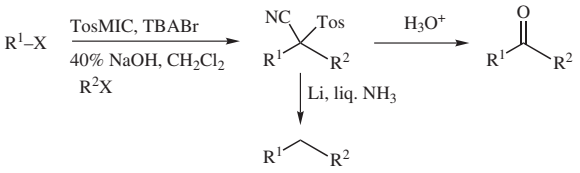
(D) Pyrroles[6] are obtained by base-induced addition of TosMIC to Michael acceptors. The ring closure between the isocyano and enolate carbons is followed by aromatization.



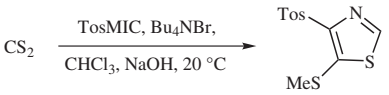
(E) TosMIC, on reaction with diazonium salts, results in 1,2,4-triazoles.[7] The TosMIC anion attacks the electrophilic β-nitrogen of the diazonium ion, then ring closure occurs.



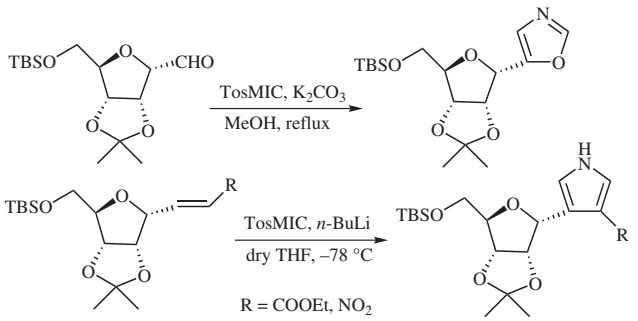
(F) Mono- and dialkylated TosMIC[8] were formed from corresponding alkyl halides under phase transfer conditions. Hydrolysis of dialkylated TosMIC leads to symmetrical and unsymmetrical ketones.[9] The reduction of mono and dialkylated TosMIC with Li in liquid NH_3 afforded the corresponding hydrocarbons.[10]



(G) Reaction of TosMIC with carbondisulfides under phase transfer conditions provides the tetrabutylammonium salt of thiazole, which can be converted to thiazole.[11]



(H) Recently, the synthesis of *C*-nucleosides by the TosMIC approach from sugar-derived aldehydes and other Michael acceptors was reported.[12]



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