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Remarking
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Green Approach in the Synthesis of Heterocyclic Compounds From α-Tosyloxyketones and α, β-Ditosyloxyketones

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Abstract

α-Tosyloxyketones and α, β-ditosyloxyketones are important precursors thereby providing green and superior alternative to large number of heterocyclic syntheses that make the use of highly lachrymatory bromo analogs.

Keywords: α-Tosyloxyketones, α, β-ditosyloxyketones, HTIB and Heterocyclic Compounds.

Introduction

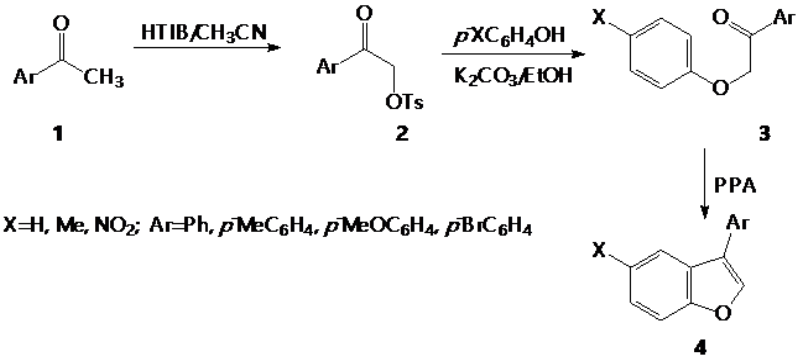
The concept of Green Chemistry incorporates a new approach[1-6] to the synthesis, processing and application of chemical substances in such a manner as to reduce threats to human health and environment. Since one of the twelve principles of green chemistry is that the synthetic methods should be designed to use and generate substances that possess little or no toxicity to human health and the environment, the present paper is a review article that emphasize on the route for the synthesis of heterocycles which involve little or no toxic chemical substances.

Objective

The objective of the review article is to highlights the synthesis of five membered heterocycles from monotosyloxy and ditosyloxycarbonyl compounds which are less toxic as compared to their bromo analogoues. Moreover the various enlisted cases of synthesis of heterocycles also provide the opportunity to study the comparative behaviour of α-Tosyloxyketones and α, β-ditosyloxyketones with their bromo analogues.

α-Tosyloxycarbonyl compounds are important precursors for the synthesis of a number of heterocyclics. Infect the studies involving α-Tosyloxyketones have offered a superior alternative to the large number of existing syntheses that make the use of highly lachrymatory α -haloketones in the conventional approach. The approach of using α-tosyloxyketones as intermediate has distinct advantage that it not only avoids the use of highly toxic α –haloketones, but also provides a direct one step synthesis of various heterocycles.

α –Aryloxyketones **3**, obtained by the reaction of α –tosyloxyacetophenones with phenols, undergo cyclization to benzofurans (**4**) by using the standard conditions (**Scheme-1**).[7]



Scheme-1

2-(α-Tosyloxy) acylphenylbenzoates (**6**) are cyclized to coumarin-3-onedimethylacetals (**7**) by using KOH in methanol. Acid hydrolysis of **7** affords the corresponding coumarin-3-ones (**8**) (**Scheme-2**).[8]

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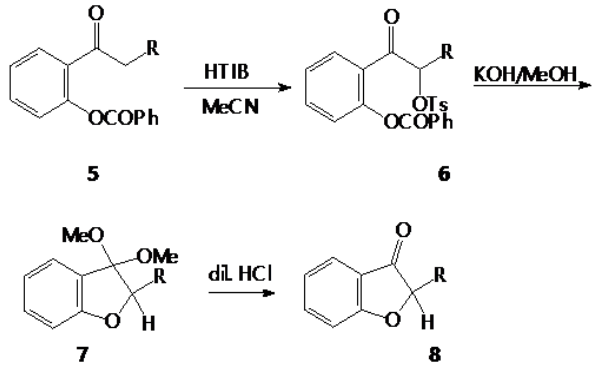
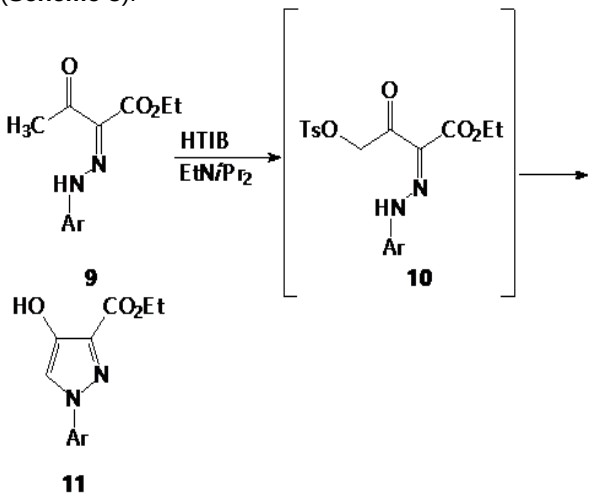


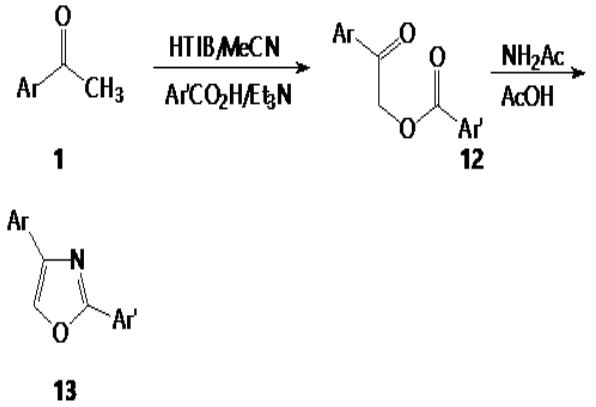
Scheme-2

Pyrazoles **11** are synthesized by the oxidation of arylhydrazones with HTIB. The reaction was carried out in one pot in the presence of diisopropylethylamine.In the intermediate α-tosyloxycompounds (generated in situ), the intramolecular participation of amino group displaces the tosyloxy group to produce the cyclized products (**Scheme-3**).[9]



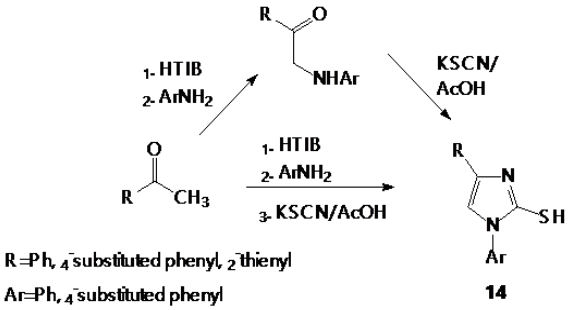
Scheme-3

α-Aryloxyacetophenones (**12**), which are obtained by the oxidation of **1** with HTIB by treatment with *p*-substituted benzoic acids, are cyclized to oxazoles (**13**) (**Scheme-4**).[7]



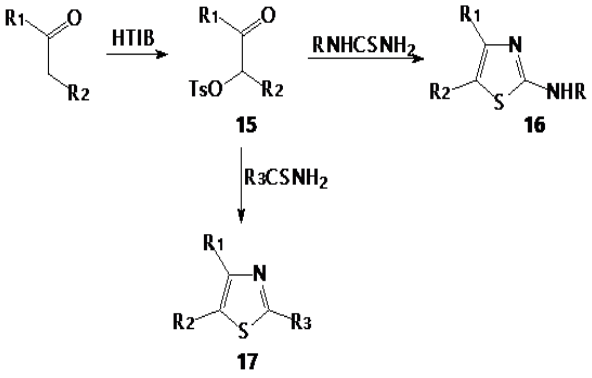
Scheme-4

HTIB mediated method has been successfully used for the synthesis of 2-mercaptoimidazoles. The method offers a superior alternative to the most widely used Marckwald's synthesis.[10] The method is also applicable to the synthesis of 4-(2-thienyl)imidazoles(**14**, R=2-thienyl) (**Scheme-5**).[11]



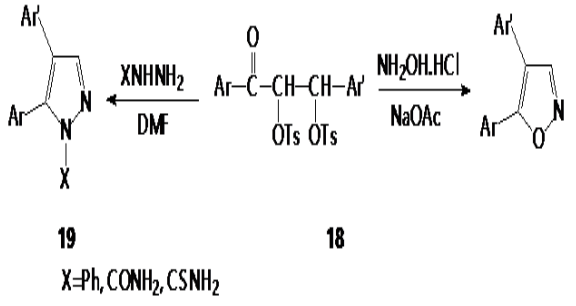
Scheme-5

The condensation of α-tosyloxyketones **15** with thioureas (substituted thioureas) and thiamides produces 2-amino (substituted amino) (**16**) and 2-alkyl/arylthiazoles (**17**) respectively.[12-15] These syntheses provide a superior alternative of the well known Hantzsch thiazole synthesis.[16,17] The one pot procedure are also employed for these syntheses starting from corresponding ketones (**Scheme-6**).



Scheme-6

Further, α,β-ditosyloxyketones **18** provide another green alternative to the conventional one for the synthesis of heterocyclics. The reaction of α,β-chalcone ditosylates **18** with various reagents such as phenylhydrazine hydrochloride, semicarbazide hydrochloride and thiosemicarbazide in suitable conditions leads to 1,2-aryl shift, thereby providing a novel route for the synthesis of 1,4,5-trisubstituted pyrazoles[18] **19** whereas the reaction with hydroxylamine hydrochloride provides a conveniont route to 4,5-disubstituted isoxazoles **20**(**Scheme-7**).[19]



Scheme-7

Conclusion

α-Tosyloxyketones and α,β-ditosyloxyketones are green alternative to their highly lachrymatory

bomo analogs. The green route involves simple experimentation and yields are fairly good.

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