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An efficient one-pot synthesis of functionally diverse 2-aminothiazoles from isothiocyanates, amidines/guanidines and halomethylenes†

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Abstract: An efficient one-pot method for the synthesis of 2-aminothiazoles using simple starting materials like isothiocyanates, amidines/guanidines and various halomethylenes is reported. The synthesis of 2-aminothiazoles involves reactions such as nucleophilic addition, S-alkylation and intramolecular nucleophilic substitution in which amines departs as the leaving group.

Keywords: 2-aminothiazoles, isothiocyanates, amidines, guanidines, one-pot reaction.

2-Aminothiazole is an important and classic heterocyclic scaffold used in the drug discovery programs. The broad spectrum biological activities exhibited by this structure include anticancer,[1] antiviral,[2] antibacterial,[3] antiprion,[4] and psychotropic activities[5] that assign it as an indispensible heterocyclic feature in drug design. In addition to this, recently, our group has successfully employed 2-aminothiazole scaffolds in the design of anti-inflammatory agents[6] as well as adenosine receptor antagonist.[7] Recently, 2-aminothiazole analogues have been identified as druglike candidates in the treatment of diabetes[8] and *mycobacterium tuberculosis*.[9] Apart from biological properties, films of conjugated polyaminothioazole have recently been demonstrated to have electrochemical properties with high thermal stability.[10] All the above described biological and physico-chemical properties of aminothioazole are probably due to its small ring structure with π excessive and π deficient properties, due to nitrogen atom behaving as hydrogen bond acceptor site.

In view of diverse biological and physico-chemical properties by 2-aminothiazoles scaffold, many synthetic protocols have been reported for their synthesis, which includes Hantzsch's cyclocondensation of thiourea with α-haloketones/α-tosylketone[11] and the reactions of α-thiocyanate carbonyl compounds with aromatic or aliphatic amine hydrochlorides.[12] 2-aminothiazoles are also synthesized by one-pot reaction of enolizable ketones with a mixture of N-bromosuccinimide, thiourea, and benzoyl peroxide,[13] as well as through the reaction of amidinothioureas with halomethylenes[6] in multistep synthesis.