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Multicomponent Synthesis of 4-Aryl-1,4-Dihydro-Oxochromeno[3,2-*b*] Oxoindeno[6,5-*e*]Pyridine

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ABSTRACT

One pot multi-component strategy has been developed for the synthesis of a small library of nineteen 4-aryl-1,4-dihydro-oxochromeno[3,2-*b*]oxoindeno[6,5-*e*]pyridine by the condensation of 4-aminocoumarin, aromatic aldehyde and indane-1,3-dione in acetic acid:ethylene glycol (5:1) in good yields along with the formation of di-(4-aminocoumarin-3-yl)arylmethane as by product in three cases. The use of microwave irradiation for the condensation of 4-aminocoumarin, aromatic aldehyde and indane-1,3-dione in acetic acid and ethylene glycol at 200 W and at 120 °C led to the selective formation of 4-aryl-1,4-dihydro-oxochromeno[3,2-*b*]oxoindeno[6,5-*e*] pyridine in excellent yields. Interestingly, the side product di-(4-aminocoumarin-3-yl)arylmethane could be converted exclusively to 4-(4′-nitrophenyl)-1,4-dihydro-di(oxochromeno[3,2-*b*:5,6-*e*])pyridine on microwave irradiation under identical condition.

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Introduction

Multicomponent reactions (MCRs) involve combination of more than two reactants in a single reaction flask to produce the selective product with high atom efficiency. MCRs have received considerable attention because of their wide range of applications in pharmaceutical industry for the generation of structurally diverse libraries of 'drug-like' molecules. Hantzsch 1,4-dihydropyridines (1,4-DHPs), an MCR product are well known Ca^{2+} channel blockers and have emerged as an important class of drug for the treatment of cardiovascular and other diseases. Further, coumarins and indenones are crucial scaffolds which constitute the key core of natural products and exhibit wide range of biological activities (Figure 1).

Miri et al.[1] evaluated the anti-tumor activity of coumarin-fused 1,4-DHPs and observed that their IC_{50} values were in μM range in three different human cancer cell lines (HeLa, K562 and MCF-7). These compounds are far better than nifedipine in terms of calcium channel antagonist activity. Evdokimov et al.[2] found that the indeno-1,4-dihydropyridine derivatives have significant anti-topoisomerase activity in human cancer cell lines. Thus, the promising biological importance of coumarin-dihydropyridines and indeno-dihydropyridines encouraged us to synthesize hybrid molecules comprising of all these three moieties, i.e., coumarin, indenone and dihydropyridine.

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