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Title : DESIGN AND CHEMICAL SYNTHESIS OF FUSED 5-, 6OXYGEN AND/ OR NITROGENCONTAINING HETEROCYCLESg LACTAM UTILIZING 2,3-DIOXO-4CARBOXY-5-(SUBSTITUTED) PYRROLIDINE AS THE KEY PRECURSOR

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In this study, the development of synthetic strategy towards the formation of fused heterocyclic-γ-lactam rings system containing oxygen and/ or nitrogen atom were successfully established. The key intermediate γ-lactam or 2,3-pyrrolidinedione ring template was effectively constructed using a multicomponent reaction (MCR) approach utilizing primary amine, aldehyde and diethyl oxalacetate sodium salt in ethanolic medium. The γ-lactam ring compound formed exists in the more stable enol form and also appears as racemic mixture. Following this, functional group interconversion of this highly functionalized compound leads to the formation of seven new fused heterocyclic-γ-lactam rings system. The fused δ-lactam-γ-lactam was effectively constructed via Leuckart reaction, condensation, hydrogenation and Dieckmann cyclisation. The synthesis of fused γ-lactam-γ-lactam however, involves decarboxylation, insertion of ethyl acetyl group via enamine-chemistry, imine formation and hydrogenation followed by an intramolecular cyclisation. The stereoselective reduction of the ethyl acetylic product followed by ester hydrolysis and lactonization via acid activation protocol was successfully carried out to furnish the fused γ-lactone-γ-lactam compound. The syn hydrogenation product of key intermediate 2,3-pyrrolidinedione was further reacted with hydrazine to afford the hydrazide. Intramolecular cyclisation via Curtius rearrangement of the hydrazide gave the new product fused oxazolidinone-γ-lactam. In another synthetic strategy, decarboxylation followed by Friedlander condensation productively gave fused quinoline-γ-lactam (pyrroloquinoline) in moderate yields. Meanwhile the synthesis of fused quinolone-γ-lactam (pyrroloquinolone) was obtained from a nucleophilic addition and Conrad-Limpach cyclisation. The O-alkylated product of 2,3-pyrrolidinedione was further elaborated through Dieckmann cyclisation reaction to give fused furan-γ-lactam ring compound. Supplementary synthetic attempts toward the synthesis of other bicyclic compounds such as oxadiazole-γ-lactam and triazole-γ-lactam using key intermediate 2,3-pyrrolidinedione however, failed to give the targeted products.