

New Evaluation for Optimization Synthesis of Pyrazolo[3,4-b]pyrrolo[3,4-d]pyridine Derivatives by the Steric Modification of Pyrazolyl-2-azodienes with Maleimides

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An efficient modification synthetic methodology for pyrazolo[3,4-d]pyrimidines has developed by utilizing various steric congestion of pyrazolyl-2-azodienes as the reactants. Treatment of steric amidinyl pyrazolyl-2-azodienes, maleimides, and coupling agent POCl₃ in a sealed tube at 90 °C for 24 h puctucted the corresponding desired pyrazolo[3,4-d]pyrimidine products in good to excellent yields. Particularly, steric N,N-disisopropylformamidinylpyrazole, N,N-dibutylformamidinylpyrazole, piperidine-1-ylmethylenaminopyrazole and pyrrolidine-1-ylmethylenaminopyrazole were reacted toward maleimides in hetero Diels-Alder reaction, the yielding pyrazolo[3,4-d]pyrimidines were improved to > 85% yields. Based on reaction results and economic cost, N,N-disisopropylformamidin was alternatively determined as the best pyrazolyl-2-azodiene substrate due to N,N-disisopropylformamide is the commercially available agent.