Short Talk

Inter-Disciplinary Explorations in Chemistry (I-DEC 2018)

"A General Catalytic Route to Enantioenriched Isoindolinones and Phthalides: Application in the Syntheses of (*S*)-PD172938 and Related Analogues"

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Abstract: Optically active isoindolinones are prevalent in many natural products of immense synthetic importance with a myriad of biological activities. Many of these natural products display important pharmacological effects (Figure **1**, **1a-d**). For instance, (*S*)-PD172983 **1a** is a noted dopamine D_4 ligand and pazinaclone (DN2327) **1b** is a sedative and anxiolytic drug. Similarly, phthalides or isobenzofuranones are five-membered benzo-fused γ-butyrolactones frequently distributed in a wide range of bioactive compounds (Figure **1, 2a-d**). Despite the presence of some efficient approaches in the literature, there is no precedence for the syntheses of these two significant classes of compounds using a common catalytic approach in one-pot.

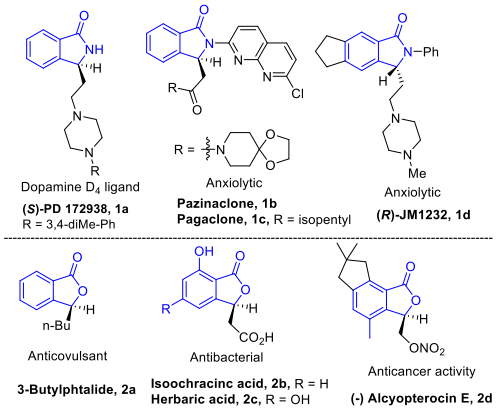
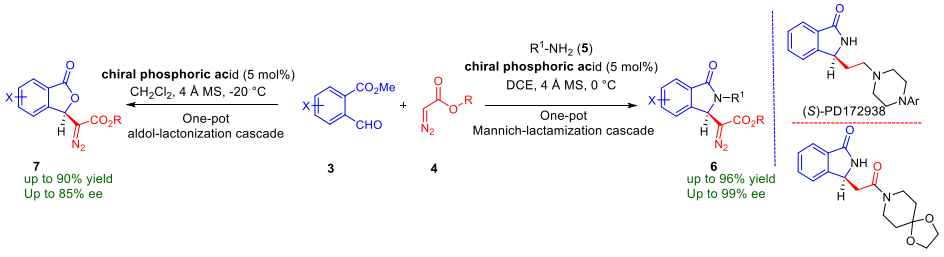


Figure 1. Selected biologically active isoindolinones and phthalides.

α-Diazoesters have been extensively used as nucleophiles in enantioselective aldol reactions, Mannich-type reactions of aldimines as well as ketimines and allylic alkylation reaction. However, *α*-diazoesters have not been investigated in asymmetric Mannich-lactamization cascade and aldol-lactonization reaction for the synthesis of 3-substituted isoindolinones and phthalides. To address this, we envisioned exploring the possibility of a common catalytic route by exploiting intrinsic nucleophilic character of α-diazoesters in multicomponent one-pot reactions leading to isoindolinones and phthalides. In this conext, we have demonstrated Brønsted acid catalyzed enantioselective one-pot synthesis of enantioenriched isoindolinones and phthalides *via* Mannich-lactamization cascade and aldol-lactonization reaction respectively from readily available precursors.



Scheme 1: Enantioselective synthesis of isoindolinones and phthalides.

References and Notes:

1. (a) Bisai, V.; Suneja, A.; Singh, V. K. *Angew. Chem. Int. Ed.* **2014**, *53*, 10737-10741. (b) Unhale, R. A.; Sadhu, M. M.; Ray, S. K.; Biswas, R. G.; Singh, V. K. *Chem. Commun.***2018**, *54*, 3516-3519.

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Bio-Sketch of Speaker

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Dr. Sumit Kumar Ray obtained his BSc in Chemistry from Midnapur College (2006) and a Masters in Chemistry from IIT Guwahati (2008), followed by a PhD (Chemistry) from IIT Kanpur in 2013. His doctoral dissertation involved enantioselective Michael addition reactions of 1,3- Dicarbonyl compounds to 2-enoylpyridine *N*-Oxides catalyzed by chiral bisoxazoline-Zn(II) Complexes. During post-doctoral research at University of Geneva, Switzerland he synthesized a series of symmetrical and unsymmetrical cryptands in three or four steps from 1,4-dioxane and successfully used them as ditopic receptors. Currently, he is working as DST inspire faculty in IISER Bhopal.