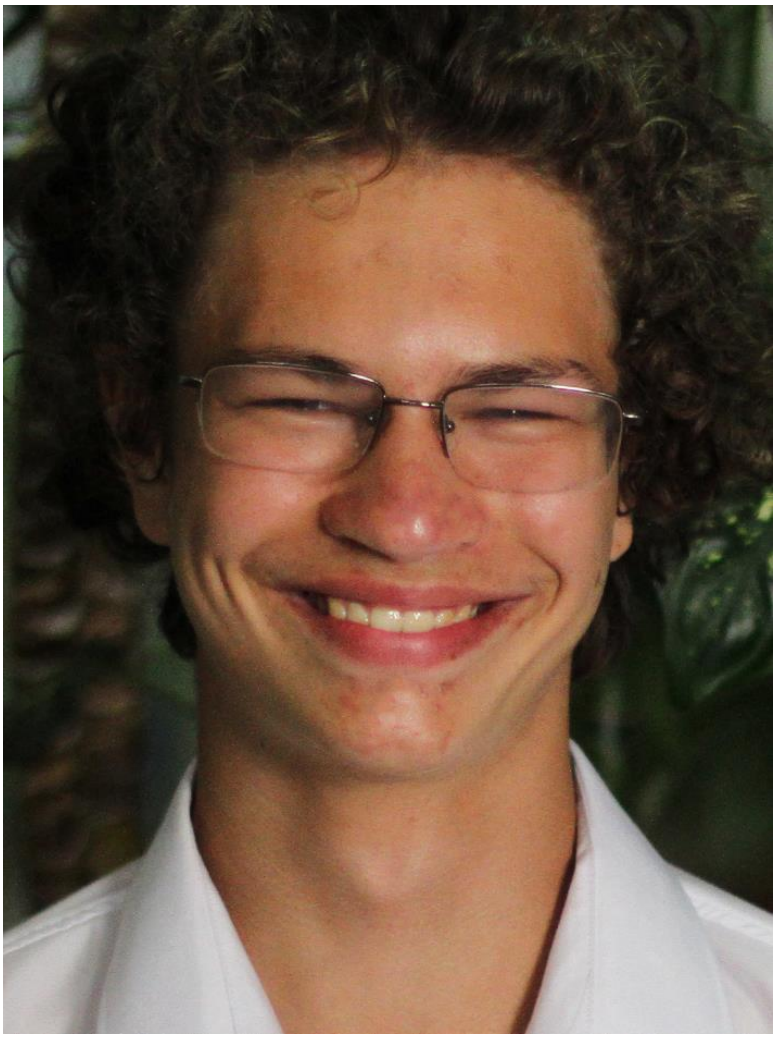
2023 年臺灣國際科學展覽會
優勝作品專輯

作品編號	030038
參展科別	化學
作品名稱	Synthesis of Substituted Pyrrolidin-2-ones and Isoindolines from Donor-Acceptor Cyclopropanes and Anilines/Benzylamines
得獎獎項	二等獎

國　　家	Russia
就讀學校	Moscow South-Eastern School named after V.I.Chuikov
指導教師	
作者姓名	Danila Lebedev

關鍵詞　chemistry、organic、bioactive

作者照片



The development of rapid and efficient synthetic approaches to the bioactive cyclic and polycyclic azaheterocycles is one of the most important challenges in organic synthesis. In this work effective and simple synthetic approaches to polysubstituted pyrrolidin-2-ones **2** and isoindolines **3** from donor-acceptor cyclopropanes **1**, bearing the ester group as the one of acceptor substituents, and amines were developed. The γ-pyrrolidone based skeletons and isoindoline ring system is a constituent of many biologically active molecules, both natural and synthetic, and a key component of clinically relevant entities (Fig.1,2) [1,2].

The synthesis of pyrrolidin-2-ones **2** includes Lewis acid-catalyzed opening of the donor-acceptor cyclopropane with primary amines (anilines, benzylamines, etc.) to γ-amino esters, followed by in situ lactamization and dealkoxycarbonylation. The reaction has a broad scope of applicability; a variety of substituted anilines, benzylamines, and other primary amines as well as a wide diversity of donor-acceptor cyclopropanes bearing (hetero)aromatic or alkenyl donor groups and various acceptor substituents, can be involved in this transformation. In this process, donor-acceptor cyclopropanes react as 1,4-C,C-dielectrophiles, and amines as 1,1-dinucleophiles. The resulting di- and trisubstituted pyrrolidin-2-ones can be also used in subsequent chemistry to obtain various nitrogen-containing polycyclic compounds of interest to medicinal chemistry and pharmacology, such as benz[*g*]indolizidine derivatives.

The synthesis of the substituted isoindolines **3** is based on the domino-reaction between donor-acceptor cyclopropanes, bearing in *ortho*-position of aromatic substituent a bromomethyl group, and different primary amines (*e.g.*, anilines, benzylamines, cycloalkylamines) was developed. The reaction involves the generation of secondary amine followed by nucleophilic ring opening of cyclopropane with amino group. Moreover, this process provided a new practical method for the rapid synthesis of benzo[*b*]pyrrolizidinone **4** from readily available starting materials.

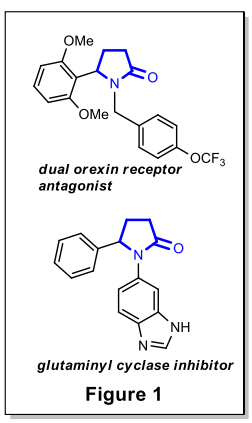
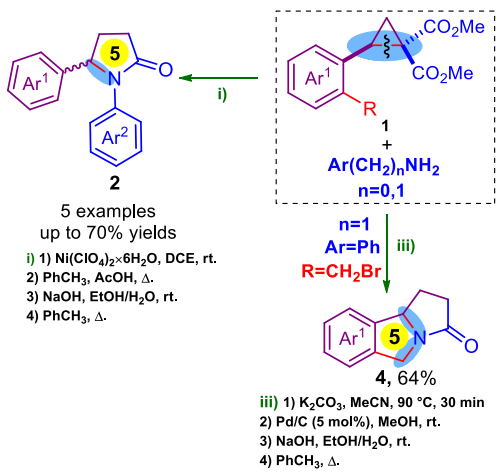
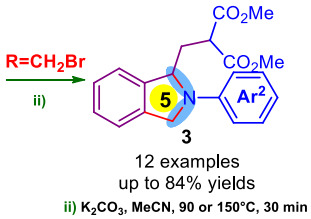


Figure 1





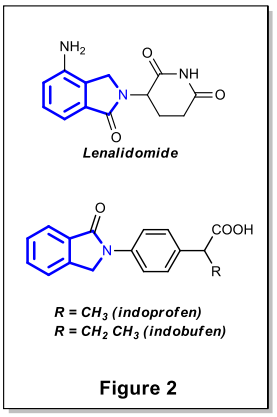


Figure 2

1. Pevarello, P.; Brasca, M. G.; Orsini, P.; Traquandi, G.; Longo, A.; Nesi, M.; Orzi, F.; Piutti, C.; Sansonna, P.; Varasi, M.; Cameron, A.; Vulpetti, A.; Roletto, F.; Alzani, R.; Ciomei, M.; Albanese, C.; Pastori, W.; Marsiglio, A.; Pesenti, E.; Fiorentini, F.; Bischoff, J.R.; Mercurio, C. *J. Med. Chem*. **2005**, *48*, 2944.
2. Muller, A.; Hner, G.; Renukappa-Gutke, T.; Parsons, C. G.; Wanner, K. T. *Bioorg. Med. Chem. Lett.* **2011**, *21*, 5795.

【評語】030038

The student developed a unique approach for many interesting heterocyclic compounds. The research is quite comprehensive and advanced considering it was done by a high school student.