Synthesis of GBD Derived Bicyclic Diamine as Interesting Scaffold for Medicinal Chemistry

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The Generated Data Base (GDB), curated by the Reymond group, offers stable, feasible, 3D-shaped chiral molecules, enabling exploration a vast chemical space, providing promising scaffolds for Medicinal Chemistry. These molecules are innovative due to their complex polycyclic system, high sp^3-hybridized carbon fraction and the presence of many quaternary carbons. [1,2] This project exploits a subset of the GDB, listing 1139 mono- and bicyclic saturated diamine scaffolds containing 5, 6 or 7 membered rings, including 680 novel scaffolds. Herein I discuss initial synthetic steps for preparing a target subset of these diamines based on Diels-Alder and ring expansion reactions *(Figure 1A).* The amine functional group within the cyclic scaffolds grants straightforward functionalisation with desired moieties. Many small molecule cores in literature features this interesting structural motifs, namely, Tofacitinib *(Figure 1B),* an anti-inflammatory drug, bears one edo and one exo cyclic amine while mCMY416, an anti-infective lead, contains a bicyclic scaffold. [3]

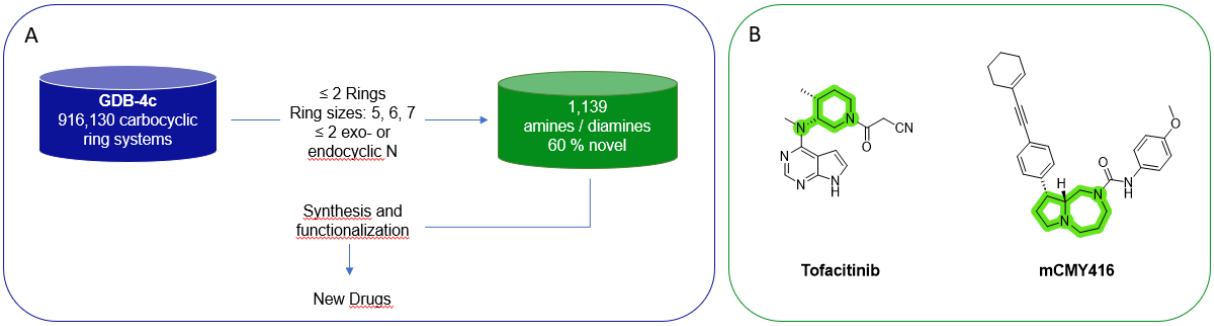

Figure 1

[1] Ruddigkeit, L.; Van Deursen, R.; Blum, L. C.; Reymond, *J. Chem. Inf. Model.* **2012**, *52* (11), 2864–2875.

[2] Lovering, F.; Bikker, J.; Humblet, C. *J. Med. Chem.* **2009**, *52* (21), 6752–6756.

[3] Ence, C. C.; Uddin, T.; Borrel, J.; Mittal, P.; Xie, H.; Zoller, J.; Sharma, A.; Comer, E.; Schreiber, S. L.; Melillo, B.; Sibley, L. D.; Chatterjee, *ACS Infect. Dis.* **2024**.