Synthesis of Chiral Tricyclic Piperazine Scaffolds from the GDB Database

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The generated databases (GDBs) are a collection of possible molecules up to a certain size which are filtered by rules of synthetic feasibility and chemical stability. Interestingly, a large number of these molecules are novel, intrinsically chiral, 3D-shaped and have never been synthesized. (1) As such the GDBs are a valuable source of new scaffolds for medicinal chemistry, which is why we are interested in exploring these databases synthetically. In the past this has already yielded interesting scaffolds such as triquinazine which has been used to discover a nanomolar and selective inhibitor of Janus Kinase 1 (see Figure 1). (2)

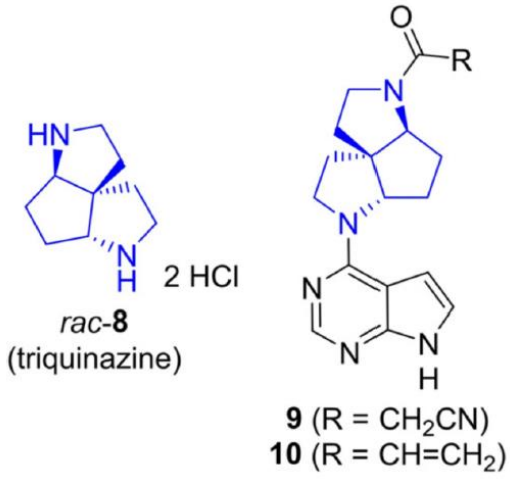

Figure 1 Structure of triquinazine and the nanomolar and selective inhibitor of Janus Kinase 1 utilizing it. Taken from (2)

Building on this success, in our ongoing research we have further explored the GDBs to identify additional interesting cases of novel chiral tricyclic scaffolds. These scaffolds are synthesized to be used in a medicinal chemistry context.

1. K. Meier, S. Bühlmann, J. Arus-Pous, J.-L. Reymond, CHIMIA 74, 241–241, issn: 2673-2424 (Apr. 2020).
2. K. Meier, J. Ar´us-Pous, J.-L. Reymond, Angewandte Chemie International Edition 60, 2074–2077, issn: 1521-3773 (2021).