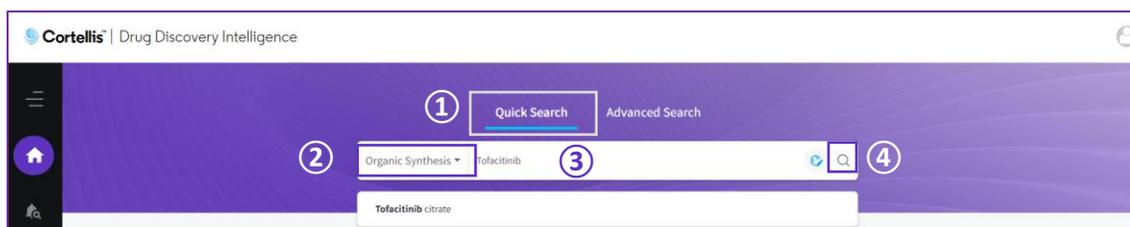


Cortellis Drug Discovery Intelligence™ 药物早期研发情报

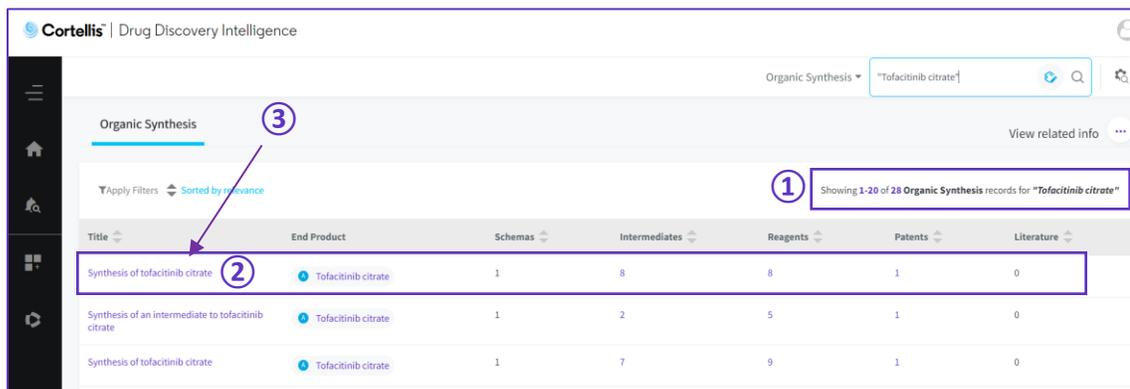
应用案例 7：如何检索药物合成路线

当我们需要查找药物的合成路线时，在数据库中可以便捷找到。具体操作方法如下：

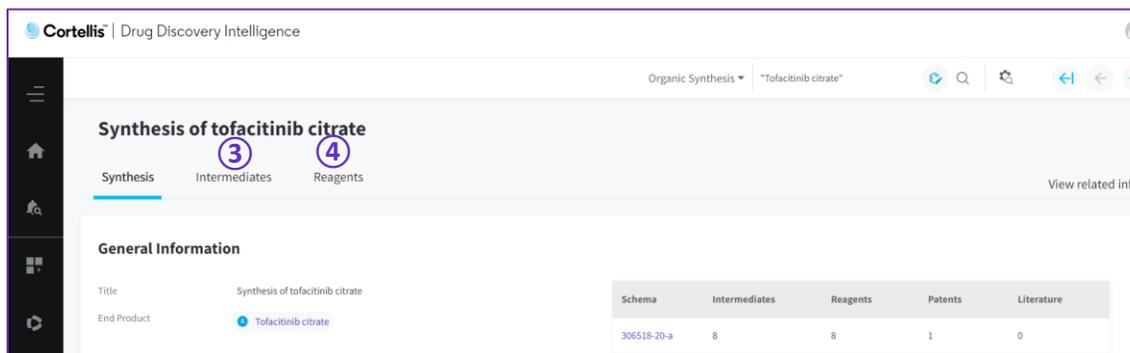
1. 在数据库主页“快速检索”^① 界面，将检索模块 设置为“Organic Synthesis”，如下图^②。在快速检索的入口^③输入检索词，如药物名称“Tofacitinib citrate”，点击^④进行检索，即可进入有机合成界面。



2. 在检索结果界面，合成路线总数量见^①，详细信息以表格形式展示。以第一条信息为例^②，分别给出了合成路线的标题、终产物名称、合成路线的数量、中间体数量、试剂数量、参考文献类型和数量。如需查看详细合成路线，可点击一条数据都有对应的参考来源如下图所示。如果需要批量查看参考来源，可点击^③查看详情。



3. 进入合成路线界面，可以查看合成路线^①、参考文献^②、合成路线中中间体^③和试剂^④，点击^⑤可跳转到参考文献界面。



Schemas

Schema 306518-20-a **1**

Summary

Synthesis of tofacitinib citrate, using 6-chloro-7-deazapurine as the starting material, is described. The process involves N-protection of the starting material, condensation with 3(R)-amino-1-benzyl-N,4(R)-dimethylpiperidine di-p-toluoyl-L-tartaric acid salt, N-debenzylation, condensation with cyanoacetic acid, N-deprotection and salification. The process is simple, cost-effective, provides high product yield with purity, is environment-friendly and suitable for industrial production. It is reported to be useful for the treatment of psoriasis, leukemia, ankylosing spondylitis and transplant rejection (1).

N-Protection of 6-chloro-7-deazapurine (I) with Boc2O in the presence of Et3N in CH2Cl2 gives N-Boc-6-chloro-7-deazapurine (II), which upon condensation with 3(R)-amino-1-benzyl-N,4(R)-dimethylpiperidine di-p-toluoyl-L-tartaric acid salt (III) by means of K2CO3 in DMF at 80 °C affords tertiary amine (IV). N-Debenzylation of 1-benzylpiperidine derivative (IV) with H2 over Pd/C in MeOH provides free amine (V), which is condensed with cyanoacetic acid (VI) in the presence of EDC, HOBT and Et3N in CH2Cl2 to yield N-protected tofacitinib (VII). N-Deprotection of intermediate (VII) using HCl in EtOAc produces tofacitinib free base (VIII), which upon treatment with citric acid in CH2Cl2 furnishes the target tofacitinib citrate (1).

Sources

2

5

1. Preparation method of tofacitinib citrate(CN 108358930)
Chen, C.; Zhang, Y.; Wang, K.
Nanjing Finetech Chemical Co., Ltd.

