PharmaBlock

SCIENTIFIC INSIGHTS

Application of Scaffold Hopping in Drug Discovery

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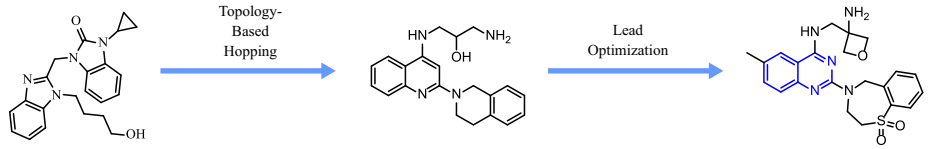
Introduction

The general goal of drug discovery is the rapid identification of novel compounds, which are active against a preselected biological target relevant to a disease with sufficient safety and drug-like properties. Scaffold hopping is a central task of modern medicinal chemistry for rational drug design, which is widely used by medicinal chemists to discover equipotent compounds with novel backbones and improved properties toward known hit molecules. Most used methods in Scaffold hopping include topology-based hopping (**Figure 1**) [1,2], heterocycle replacements (**Figure 2**) [3], ring opening (**Figure 3**) [4] or ring closure (**Figure 4**) [4], and etc.

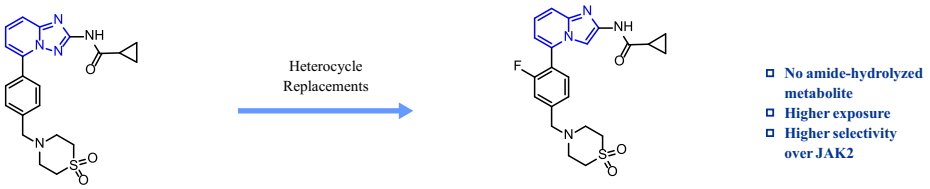


BMS-433771
RSV Inhibitor
RSV EC_{50}: 20 nM

Hit
RSV Inhibitor
RSV EC_{50}: 220 nM

AK-0529
NDA
RSV Inhibitor
RSV EC_{50}: 3 nM

Figure 1. Using Topology-based Hopping Method to Identify a Novel RSV Drug



Filgotinib
JAK1 Inhibitor
Launched_2020

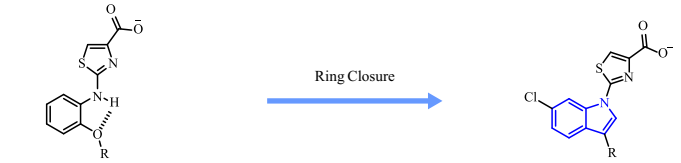
FZJ-003
JAK1 Inhibitor
Phase II

Figure 2. Using Heterocycle Replacements Method to Identify a Novel JAK1 Inhibitor

PD166285
Tyrosine Kinase
Inhibitors

Urea Derivative
Tyrosine Kinase
Inhibitors

Figure 3. Using Ring Opening Method to Identify a Novel Tyrosine Kinase Inhibitors



Biaryl Amine Series
Prostaglandin EP1
Receptor Anatagonists

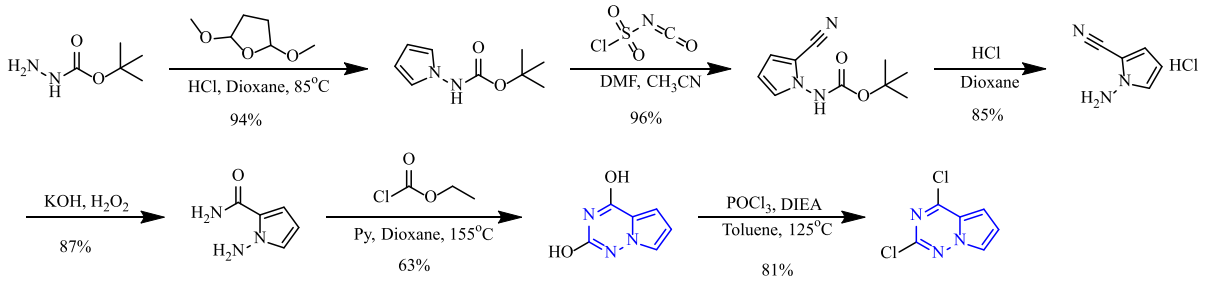
Indole Series
Prostaglandin EP1
Receptor Anatagonists

Figure 4. Using Ring Closure Method to Identify a Novel Prostaglandin EP1 Receptor Anatagonists

Heterocyclic chemistry Developed at PharmaBlock

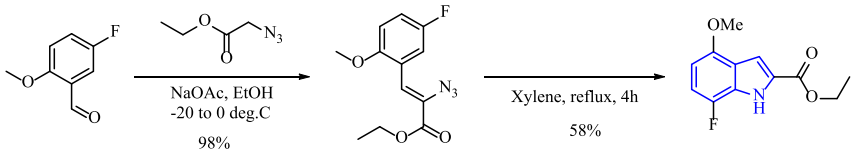
The core structures of drug molecules are generally heterocyclic compounds, and heterocycle replacement is a commonly used scaffold hopping method. PharmaBlock has rich experience in heterocyclic chemistry, and has a large number of heterocyclic products in stock. We can also provide customized synthesis services for our customers. Here are some common methods for the synthesis of heterocyclic compounds.

1) Synthesis of pyrrolo[2,1-f][1,2,4]triazine derivatives

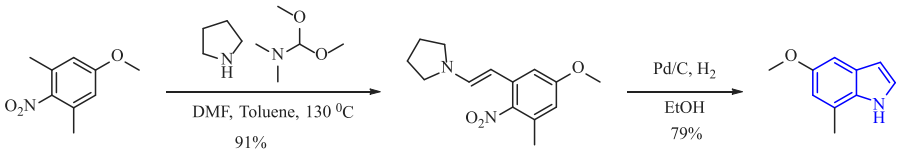


WO2008005956 A2

2) Synthesis of indole derivatives

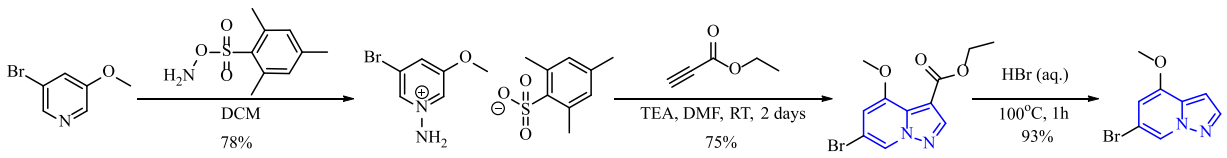


WO2009144554 A1

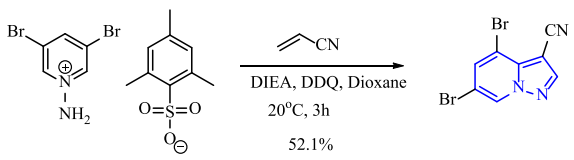


CN112457235

3) Synthesis of pyrazolo[1,5-a]pyridine derivatives

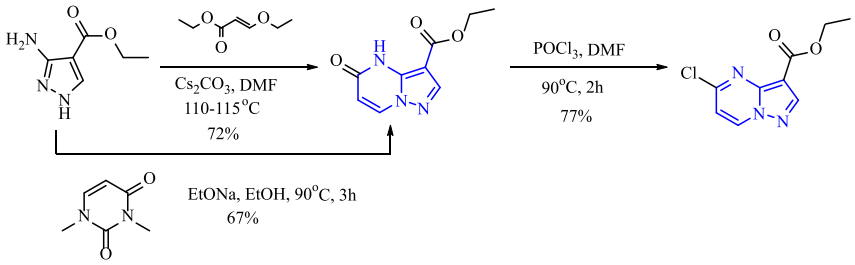


WO2022037643 A1



WO2019075114 A1

4) Synthesis of pyrazolo[1,5-a]pyrimidine derivatives

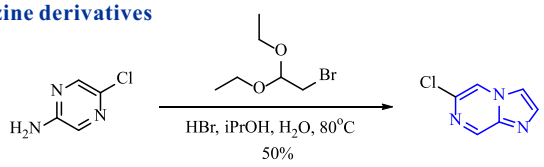


European Journal of Medicinal Chemistry. **2020**, *190*, 112092.

WO2017007759 A1

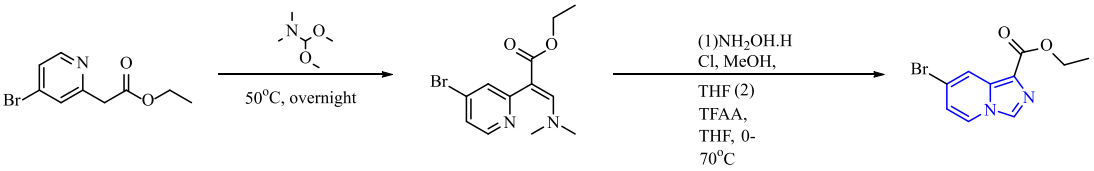
WO2015073267 A1

5) Synthesis of imidazo[1,2-a]pyrazine derivatives

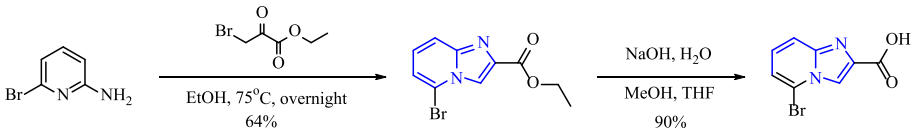


WO2016050165 A1

6) Synthesis of imidazo[1,5-a]pyridine and imidazo[1,2-a]pyridine derivatives

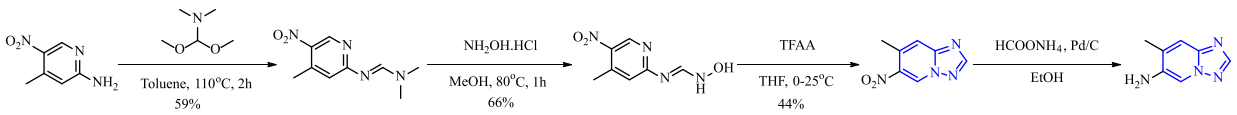


Organic Letters. **2021**, *23(12)*, 4694-4698



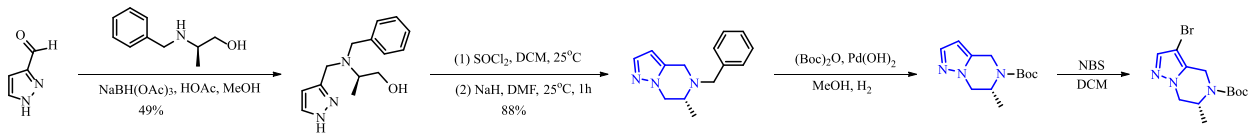
WO2017223239 A1

7) Synthesis of [1,2,4]triazolo[1,5-a]pyridine derivatives



WO2022221697 A1

8) Synthesis of 4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine derivatives



ACS Medicinal Chemistry Letters. **2015**, *6(1)*, 37-41

Building Blocks Containing Heterocycles

PharmaBlock has conducted a systematic study of clinical and preclinical drug molecules, and our chemists continue to pay attention to the latest research, design and synthesize a large number of new heterocyclic building blocks, which can be used to explore structure-activity relationship (SAR) and structure-property relationship (SPR). We offer more than 10000 unique heterocyclic building blocks, ranging from grams to kilograms, most of which are in stock (**Figure 5**).

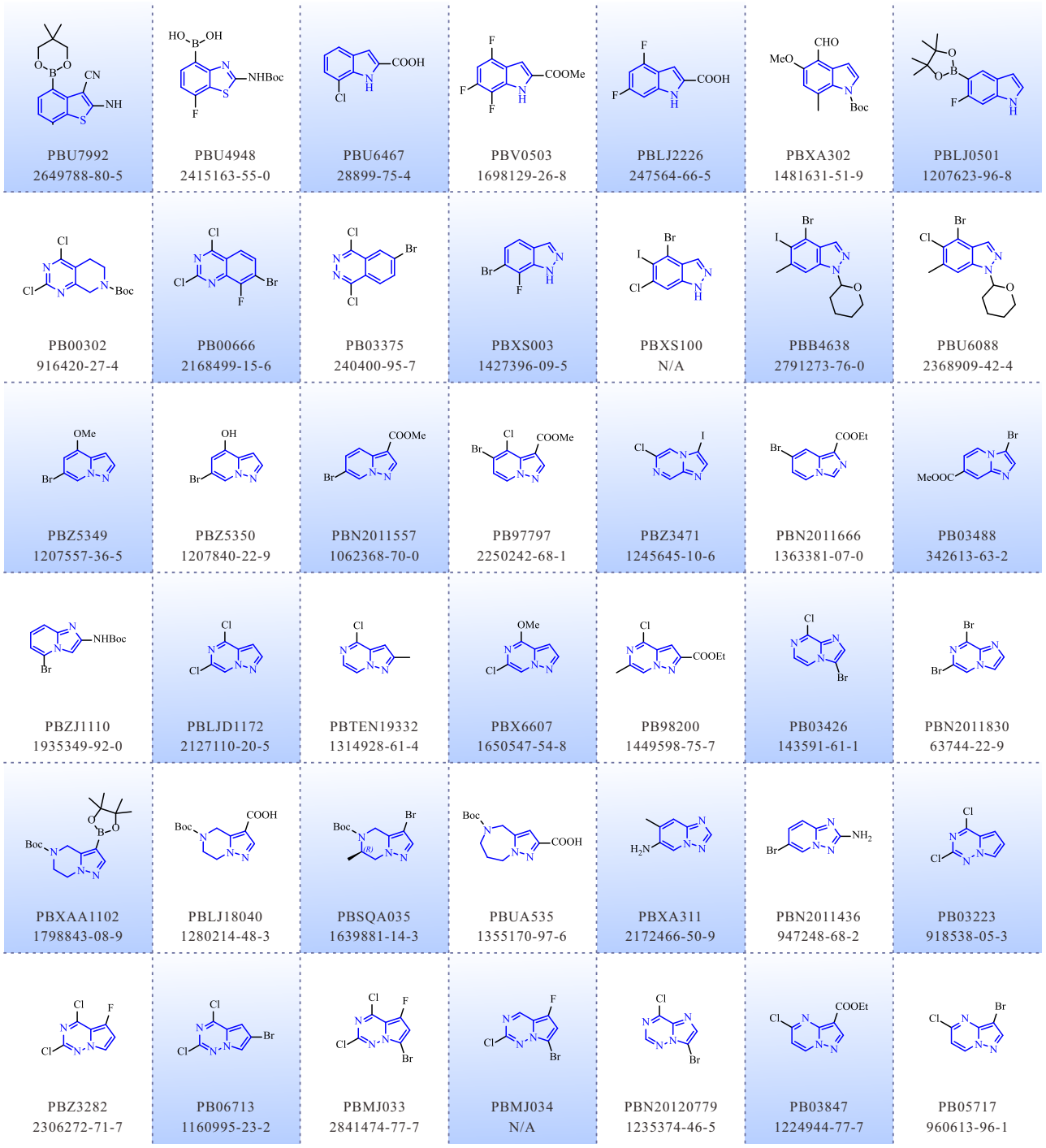


Figure 5. Representative building blocks containing heterocycles at PharmaBlock

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ナミキ商事株式会社

本社
〒160-0022　東京都新宿区新宿5-5-3　建成新宿ビル
TEL：03-3354-4026　　FAX：03-3352-2196

大阪支店
〒541-0044　大阪市中央区伏見町2-5-7　岡田伏見町ビル
TEL：06-6231-5444　　FAX：06-6233-6540

E-mail：info@namiki-s.co.jp
URL：http://www.namiki-s.co.jp