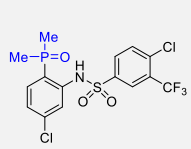
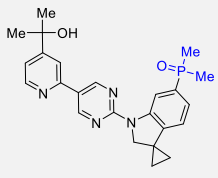
P(O)Me$_2$-containing Building Blocks for Drug Design

Introduction

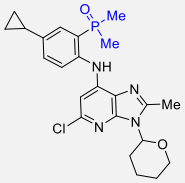
Phosphine oxides belong to a chemical class seldom employed in drug design. However, the FDA-approval of *Brigatinib* drug (ARIAD Pharm.) in 2017 may further inspire application of this unique functional group in medicinal chemistry. The highly polarized P=O bond imparts a number of important drug-like properties, including reduced lipophilicity, increased aqueous solubility, H-bond acceptor ability, and high metabolic stability.[1-4] Herein we have synthesized a library of aliphatic and heteroaromatic phosphine oxide derivatives for drug design.



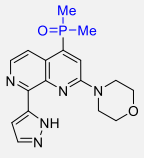
CCR2 antagonist
US2012/157413, A1
Allergan



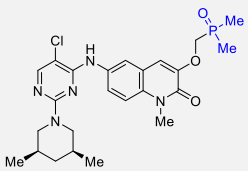
Phoshodiesterase inhibitor
WO2017/108203, A1
Grünenthal GmbH



TYK2 inhibitor
WO2018/075937, A1
Nimbus Lakshmi

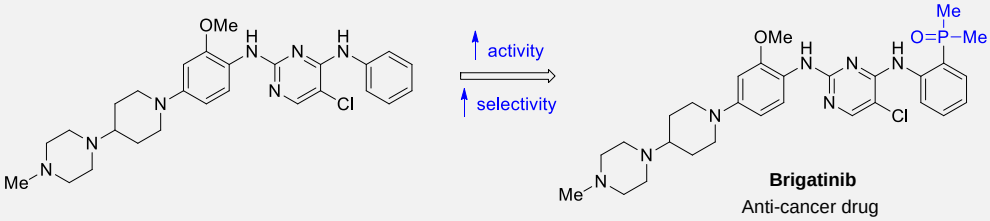


ATR kinase inhibitor
WO2018/153969, A1
Bayer Pharm.



BCL6 inhibitor
WO2018/108704, A1
Boehringer Ingelheim

Discovery of *Brigatinib*

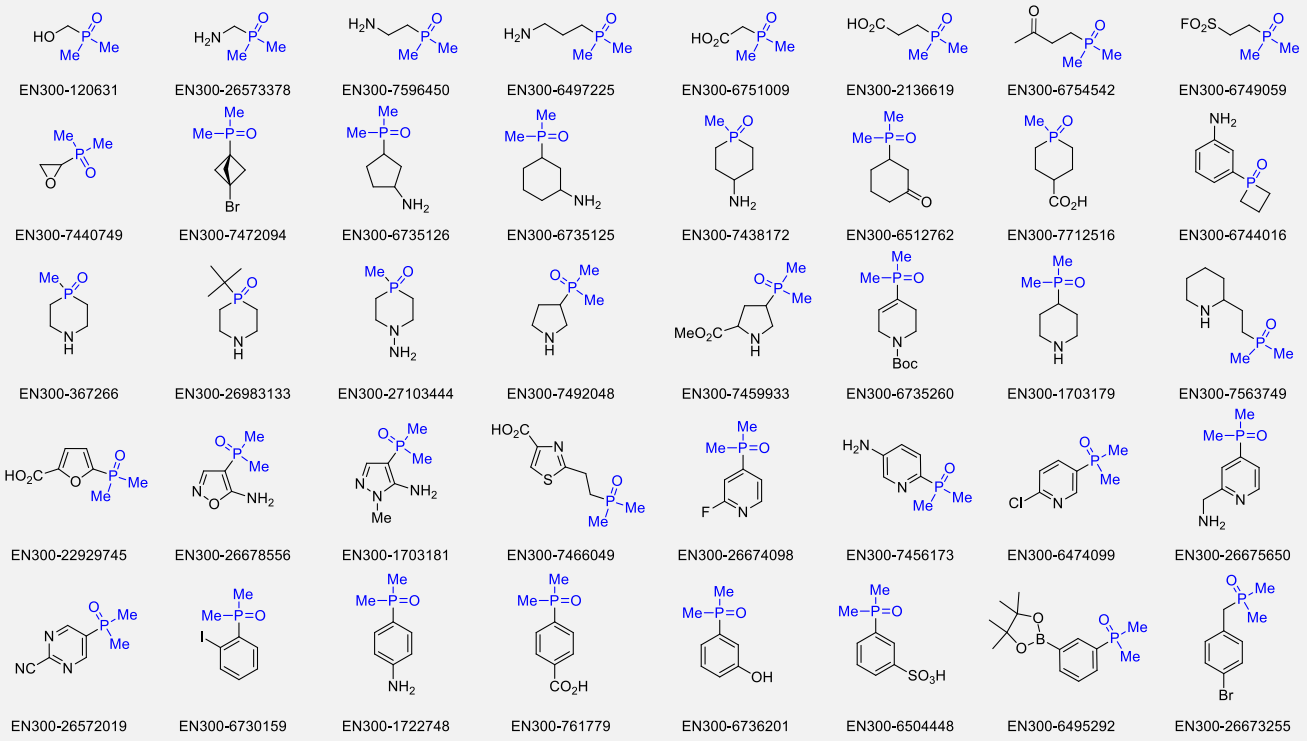


Brigatinib
Anti-cancer drug
ARIAD Pharm.

P(O)Me$_2$-group:

- chemically stable;
- metabolically stable;
- H-bond acceptor;
- increases solubility;
- decreases lipophilicity.

We offer >100 unique **P(O)Me$_2$**-containing derivatives on a 5-50 g scale from our stock.



References

1. W.-S. Huang et al. *J. Med. Chem.* **2016**, *59*, 4948.
2. P. Finkbeiner et al. *J. Med. Chem.* **2020**, *63*, 7081.
3. A. A. Kamel. *International Journal of Chemical and Biomedical Science,* **2015**,*1*, 56.
4. V. Iaroshenko. *Organophosphorus Chemistry: From Molecules to Applications*, John Wiley & Sons, **2019**, 568.