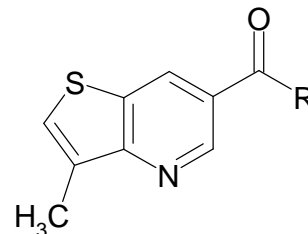
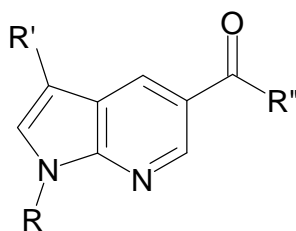
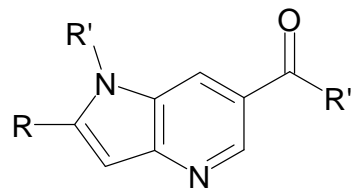
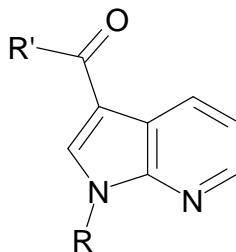


# AZAINDOLE LIBRARY KINASE & GPCR

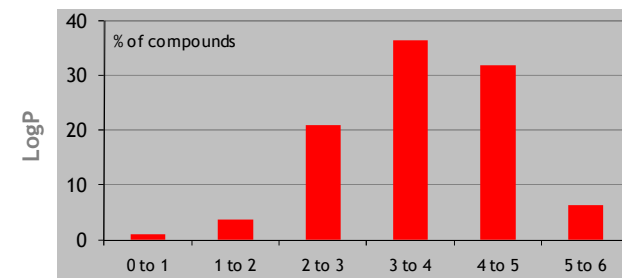
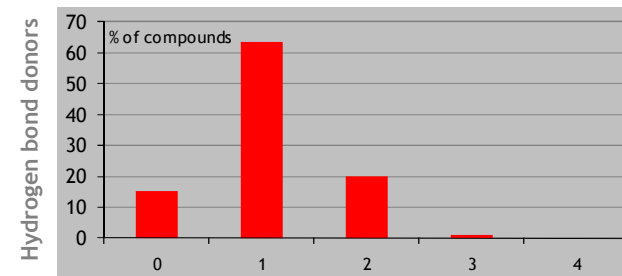
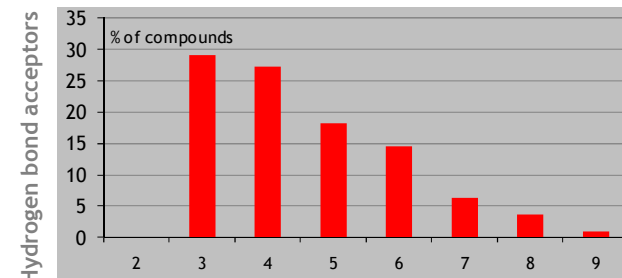
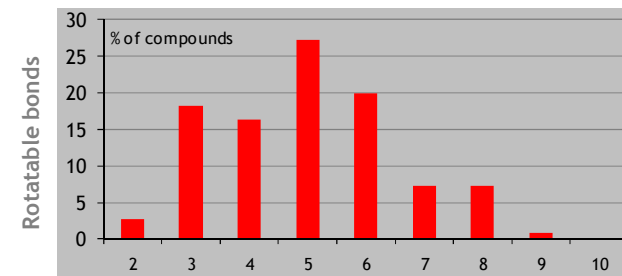
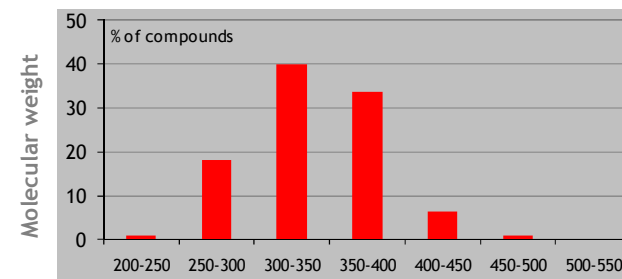
The scaffolds:



Bullet points:

- \* highly diverse exploration of original azaindoles scaffold
- \* privileged structures for kinase and enzyme inhibitors, peptide and amine GPCRs, DNA and DNA processing enzymes interactions
- \* many reports of better pharmacokinetics and oral activity for aza-isosters of indoles
- \* 700+ compounds based on 10 intermediates
- \* cherry-picking and custom format available

## CHARACTERISTIC CHARTS

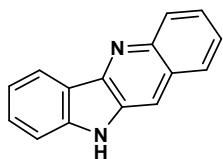


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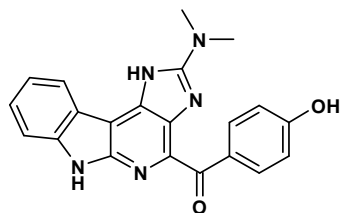
102 avenue Gaston Roussel  
93230 - ROMAINVILLE - France

+33 1 41 83 02 03  
+33 1 41 83 02 04 (fax)

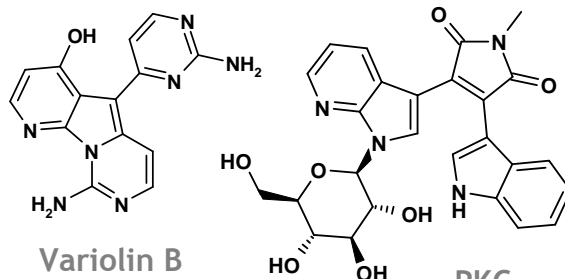
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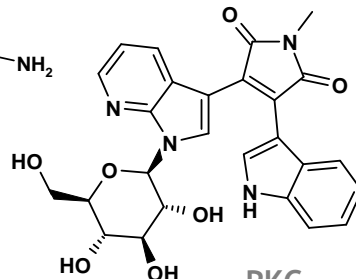
Quindoline



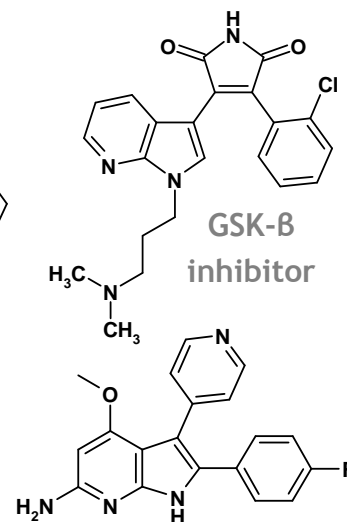
Grossularine II



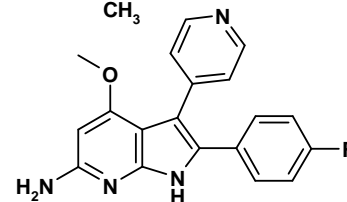
Variolin B



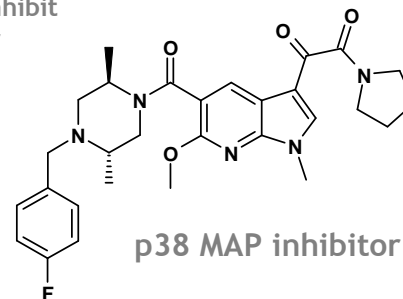
PKC inhibitor



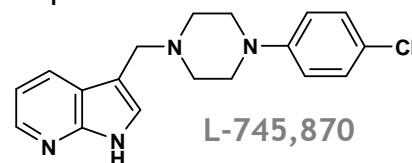
GSK-B inhibitor



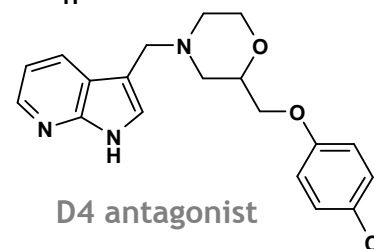
p44/42 MAP inhibitor



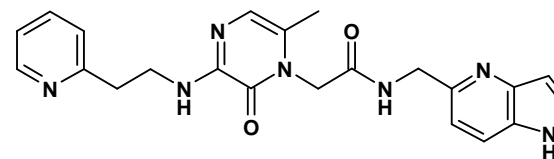
p38 MAP inhibitor



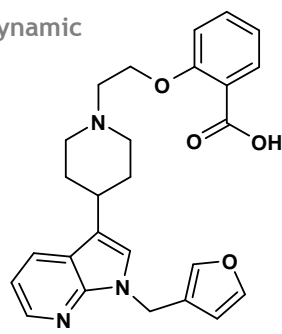
L-745,870



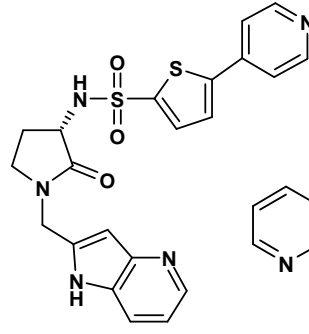
D4 antagonist



Thrombin inhibitor



H1 antagonist



Factor Xa inhibitor

4 and 7-azaindole structural fragments are rather uncommon in natural compounds. Quindoline and the related cryptolepine have been isolated from a West African medicinal plant and have been found to have anti-malarial activity. Grossularine II and variolin B are two marine anti-tumoral compounds; the activity of variolin B seems to result from cyclin-dependant kinase inhibition<sup>1</sup>.

Azaindole analogues of the anti-tumoral antibiotic rebeccamycin were found to have potent and more selective antiproliferative properties than the original compound, with significant inhibition of topoisomerase I and protein kinase C<sup>2</sup>. Unsymmetrical azaindole maleinimides have been found to inhibit selectively GSK3-B kinase<sup>3</sup>. Biaryl derivatives of 7-azaindoles were found to be potent inhibitors of p44/42 MAP kinase<sup>4</sup>. Azaindole pyruvic amide derivatives have also been recently patented as selective p38 MAP kinase inhibitors<sup>5</sup>.

Simple morpholine<sup>6</sup> and piperazinyl<sup>7</sup> derivatives of 7-azaindole such as L-745,870 have been identified as dopamine D4 receptor antagonists with excellent oral bioavailability and brain penetration. Piperidine derivatives have been disclosed as orally active H1 antagonists without sedative properties<sup>8</sup>. Other GPCR inhibitors containing the azaindole substructure include 5HT1B agonists, mixed serotonin reuptake inhibitors, 5HT1a antagonists, CRFR-1 antagonists and 5HT1-F selective antagonists.

The obtention of arginine mimetics with good oral absorption has represented a difficult and long sought challenge. Incorporation of 4-azaindole structure in peptidomimetic patterns has finally yielded orally active factor Xa inhibitors<sup>9</sup> and thrombin inhibitors<sup>10</sup> with pharmacodynamic properties better than for benzamides and their usual isosters.

We then do believe that our azaindole library will be a useful tool for the exploration of the rich pharmacological spectrum of indoles, to identify specific leads for an extended range of receptors or enzymes.



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<sup>1</sup> *Eur. J. Cancer.*, 2005, 41, 2366

<sup>2</sup> *Eur. J. Med. Chem.*, 2003, 38, 123

<sup>3</sup> *Bioorg. Med. Chem. Lett.*, 2004, 14, 3245

<sup>4</sup> *Biochem. Pharmacol.*, 2001, 62, 283

<sup>5</sup> WO4032874

<sup>6</sup> *Bioorg. Med. Chem.*, 1998, 6, 1

<sup>7</sup> *J. Med. Chem.*, 1996, 39, 1941

<sup>8</sup> *Bioorg. Med. Chem. Lett.*, 2005, 15, 1165

<sup>9</sup> *Bioorg. Med. Chem. Lett.*, 2000, 10, 1033

<sup>10</sup> *Bioorg. Med. Chem. Lett.*, 2003, 13, 795