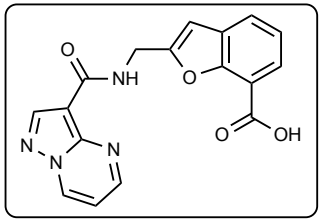
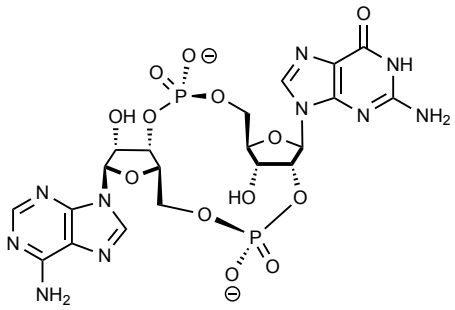
Non-Nucleotide STING Agonists (BMS)

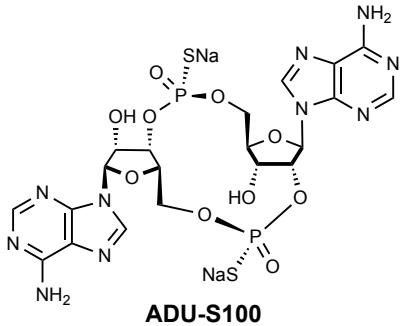
STING Agonists

- The Stimulator of Interferon Genes (STING) pathway is a new potential method for cancer treatment
  - STING Agonists elicit an immune response that can kill cancer cells
- Primary investigations in STING agonists focused on modifying 2'3'-*c*GAMP, an endogenous STING ligand
  - Normally, DNA in cellular cytoplasm activates STING which in turn activates immune response to fight infection
- Normally, intratumoral delivery of STING agonists is required for effective tumor reduction
  - Direct introduction of the STING agonist to the tumor site is necessary for activation of STING

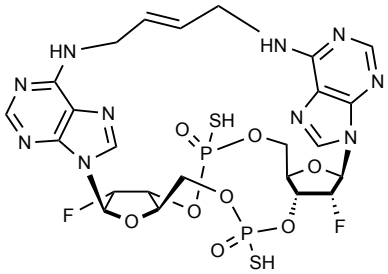




2'3'-cGAM*P*



ADU-S100



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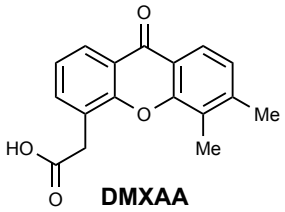
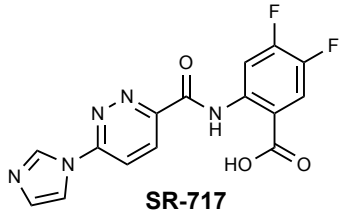
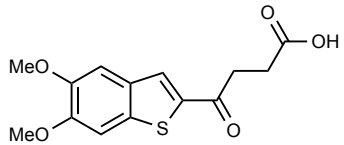


DMXAA



SR-717



MSA-2

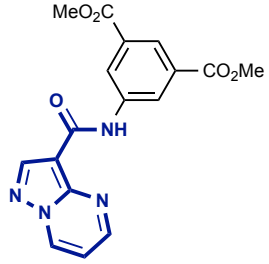
Non-CDN STING agonists

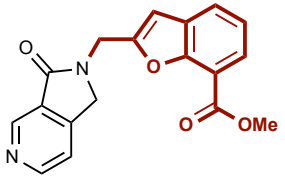
- Simplified synthesis
- Tunability
- Better PK profile
- Easier process routes
- Less-crowded patent space
- Potential oral dosing

Moderate activity

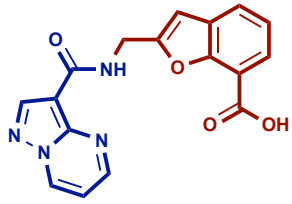
Poor PK stability

No off-target activity





Chemotype Hybridization



Excellent activity

No degradation *in vivo*

Poor membrane permeability

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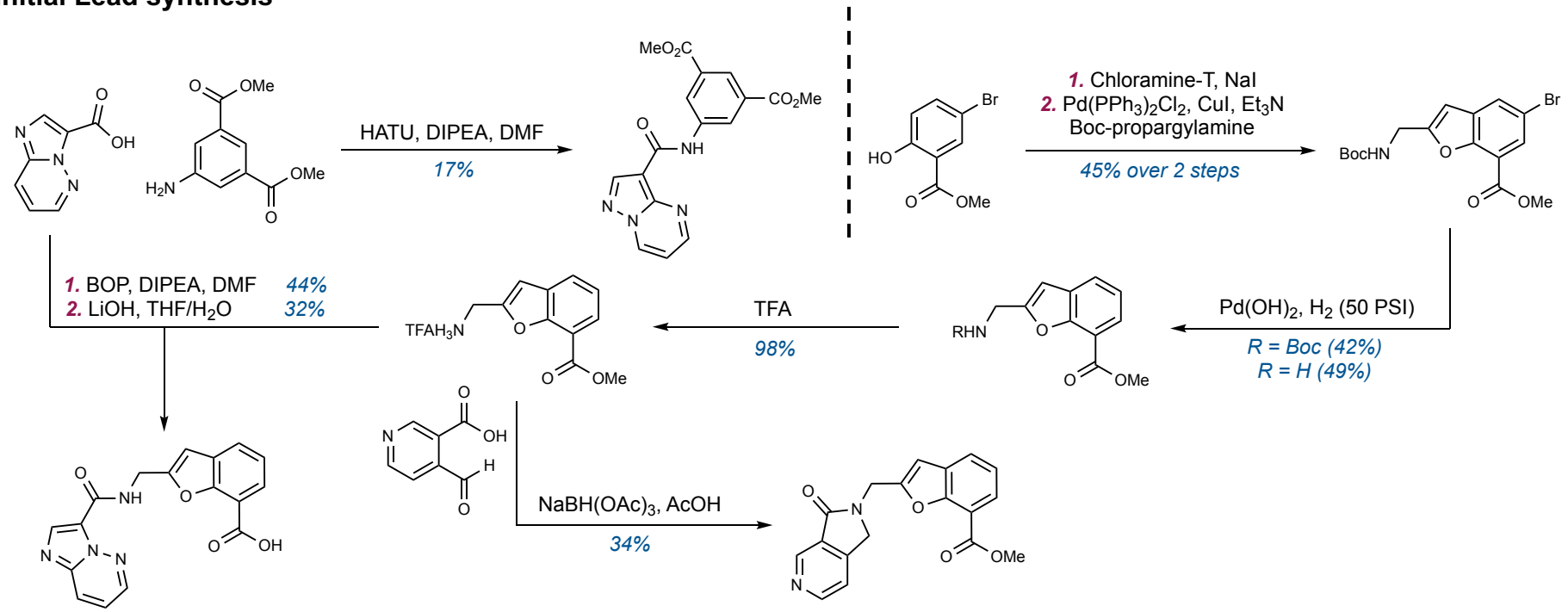
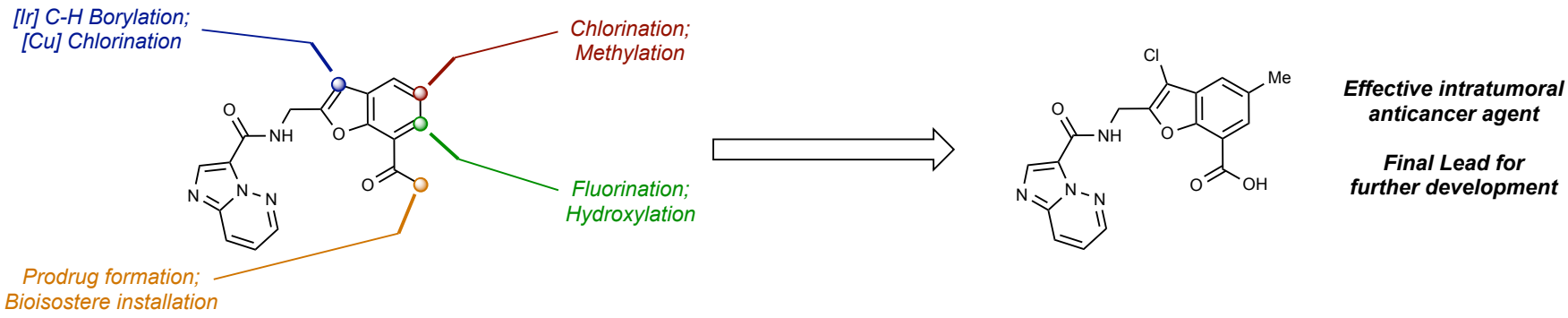
Initial Lead synthesis



Scaffold Fine-Tuning



Effective intratumoral anticancer agent

Final Lead for further development