The New Potent Anti-HIV Drug Discovery From Arylnaphthalene Lignan Derivatives

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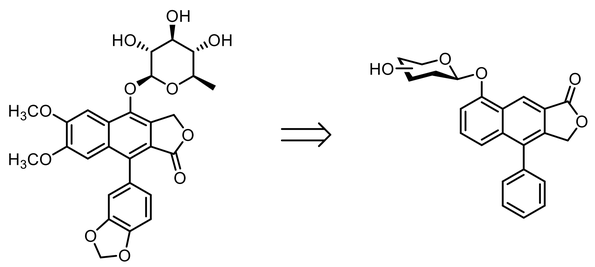
Introduction

- HIV (Human Immunodeficiency Virus) is a virus that attacks the body's immune system, specifically the CD4 cells.
- The human body is incapable of getting rid HIV completely, so once a person is infected, they have it for life.
- A combination drug treatment called HAART (Highly Active Antiretroviral Therapy) is currently available for people infected with HIV, and it has proven to significantly increase the lifespan of HIV-positive people.
- However, HAART is unable to eliminate the virus completely. It also has potential side effects and is showing decreasing effectiveness on chronic use because of the developments of mutated, drug-resistant HIV molecules.
- It is because of these reasons, that HIV drug inhibitor research is still needed, and that is the purpose of our research.
- Based on research published by Zhang and co-workers in the Journal of Natural Products[1] where, patentiflorin A was shown to have potential potent anti-HIV properties, we designed a relative arylnaphthalene lignan derivative to figure out if it would have more efficient, as well as more potent, anti-HIV characteristics.
- We attached three different sugars; galactose, glucose, and mannose to modify the arylnaphthalene lignan.[2]



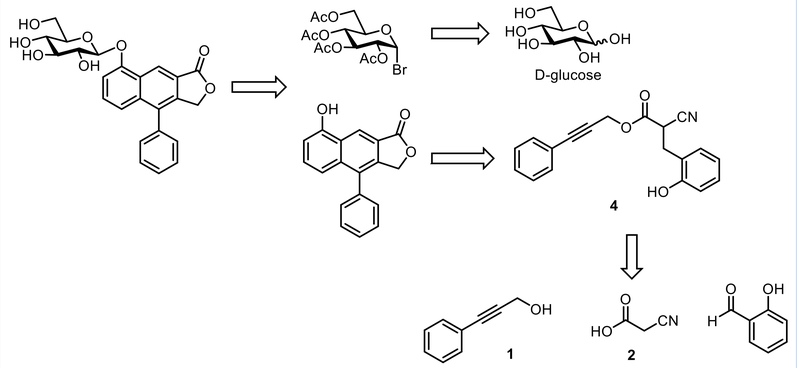
Patentiflorin A
IC_{50} = 27nM

Methods: Organic Synthesis

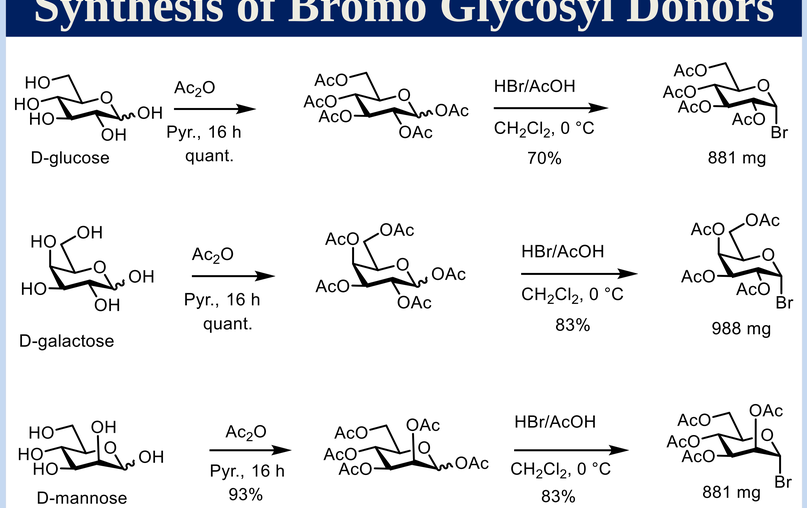
Methods include the following generalized steps:

1. **Setting up a reaction:** Combining reagents, adding catalysts and/or solvents
   - Ex.) Stirred in a flask at room temperature (RT) or on ice (0°C), heated, or heated under reflux
2. **Monitoring the Reaction**
   - Ex.) Thin Layer Chromatography (TLC), Nuclear Magnetic Resonance (NMR), and Mass Spectrometry
3. **"Work Up" :** This is purifying the compound or separating out the part of the mixture that contains the desired product.
   - Ex.) Extraction, evaporation under reduced pressure to remove solvent, filtration, column chromatography, etc.

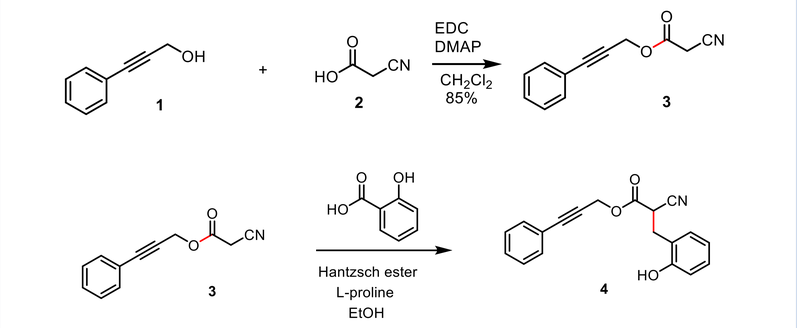
Retrosynthesis of Target Compound

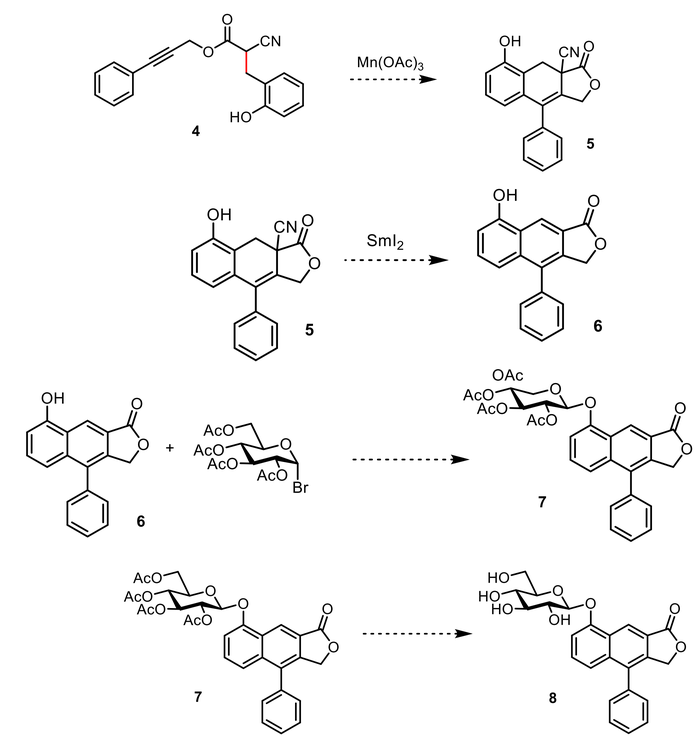


Synthesis of Bromo Glycosyl Donors



Synthesis of Arylnaphthalene Lignans





Future directions

- Synthesis of arylnaphthalene lignan derivatives containing galactose, glucose and mannose.

Future Testing: The final compounds will be tested against four HIV viral strains.
(Bal: M-Tropic, 89.6: Dual Tropic, SF162:M-Tropic, and LAV.04: T-Tropic)

Acknowledgements

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References

1. Zhang, H.-J.; Rumschlag-Booms, E.; Guan, Y.-F.; Wang, D.-Y.; Liu, K.-L.; Li, W.-F.; Nguyen, V. H.; Cuong, N. M.; Soejarto, D. D.; Fong, H. H. S.; Rong, L. *J. Nat. Prod.* **2017**, *80*, 1798-1807.
2. Kao, T.-T.; Lin, C.-C.; Shia, K.-S. *J. Org. Chem.* **2015**, *80*, 6708-6714.