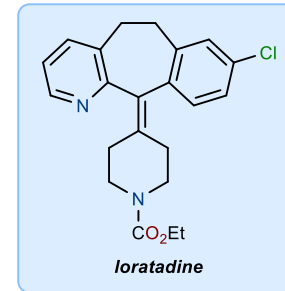
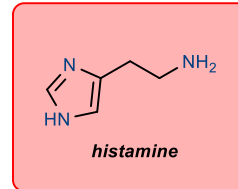


Overview

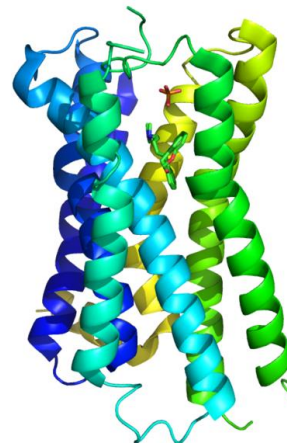
- Loratadine is a second-generation H₁-antihistamine medication commonly used to treat allergic rhinitis (seasonal allergies)
- FDA-approved in 1993 and made available over-the-counter in 2002
- Side effects can include headache, sleepiness, and dry mouth
- Marketing campaign pioneered aspects of modern pharmaceutical advertising



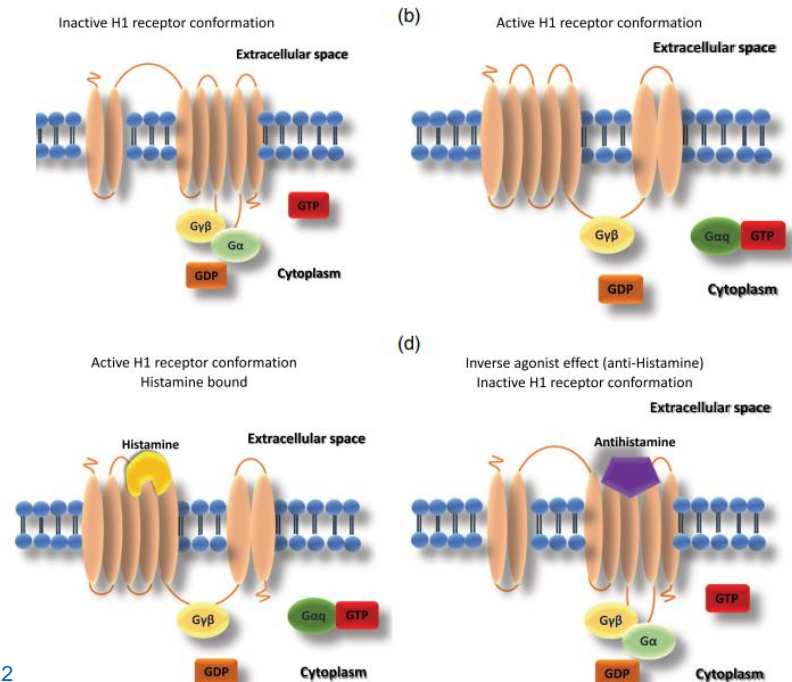
https://www.youtube.com/watch?v=tzGjmUKPXhY&ab_channel=Chi-TownTVFan
 Canonica, G. W.; Blaiss, M. *World Allergy Organ. J.* **2011**, *4*, 47. <https://doi.org/10.1097/WOX.0b013e3182093e19>

Pharmacology

- First-generation antihistamines like diphenhydramine (Benadryl) are less selective and cross the blood-brain barrier more readily, causing sedation by acting on central nervous system histamine receptors
- Second-generation antihistamines are more selective and act primarily on peripheral histamine receptors
- Loratadine is an inverse agonist, meaning it produces the opposite effect to histamine binding rather than just blocking the receptor
- Locking the H₁-receptor in its inactive conformation disrupts expression of NF-κB which lessens inflammation, itching, and sneezing symptoms

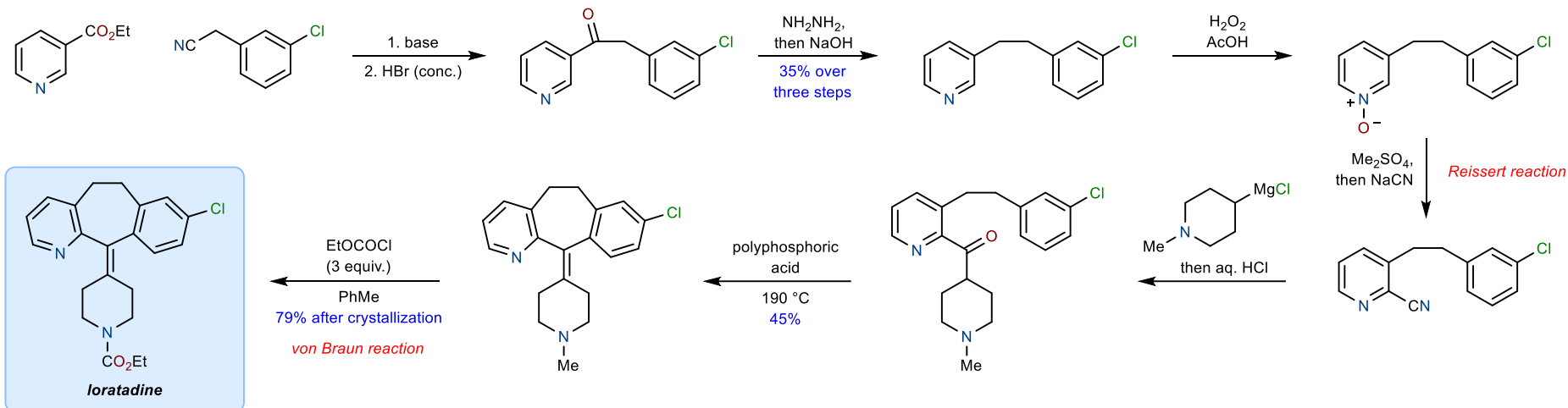


H₁-receptor



Church, D. S.; Church, M. K. *World Allergy Organ. J.* **2011**, *4*, S22. <https://doi.org/10.1186/1939-4551-4-S3-S22>
 Mandola, A.; Nozawa, A.; Eiwegger, T. *LymphoSign Journal* **2019**, *6*, 35. <https://doi.org/10.14785/lymphosign-2018-0016>

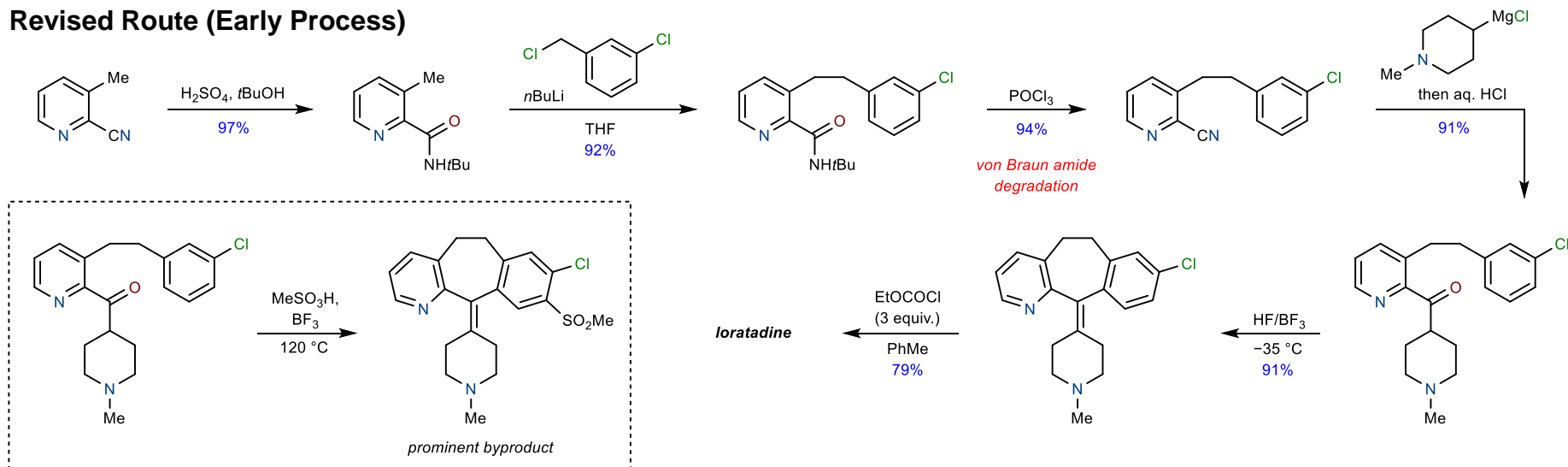
Original Schering Route (Discovery)



Villani, F. J.; Magatti, C. V.; Vashi, D. B.; Wong, J.; Popper, T. L. *Arzneim.-Forsch.* **1986**, *36*, 1311.

Villani, F. J.; Daniels, P. J. L.; Ellis, C. A.; Mann, T. A.; Wang, K.-C.; Wefer, E. A. *J. Med. Chem.* **1972**, *15*, 750. <https://doi.org/10.1021/jm00277a013>

Revised Route (Early Process)



Schumacher, D. P.; Murphy, B. L.; Clark, J. E.; Tahbaz, P.; Mann, T. A. *J. Org. Chem.* **1989**, *54*, 2242. <https://doi.org/10.1021/jo00270a041>