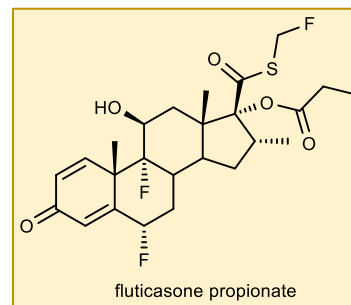


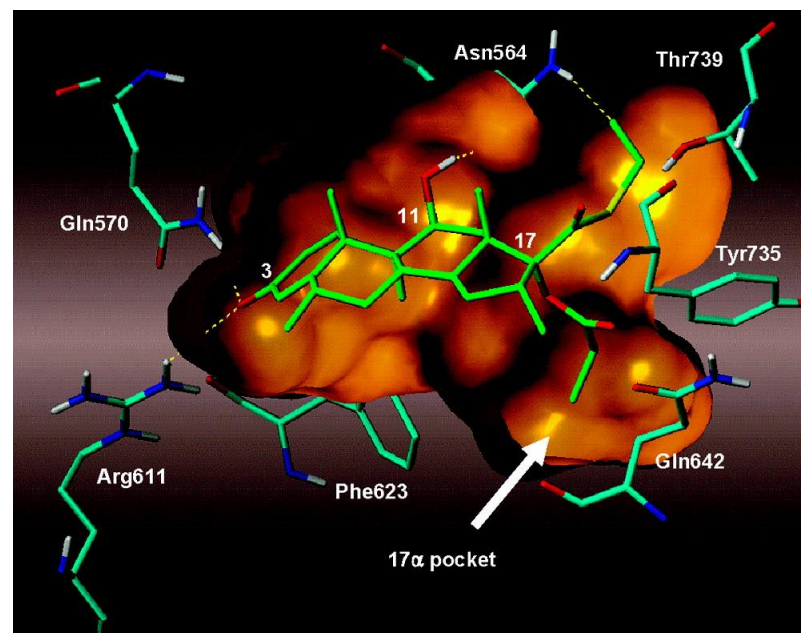
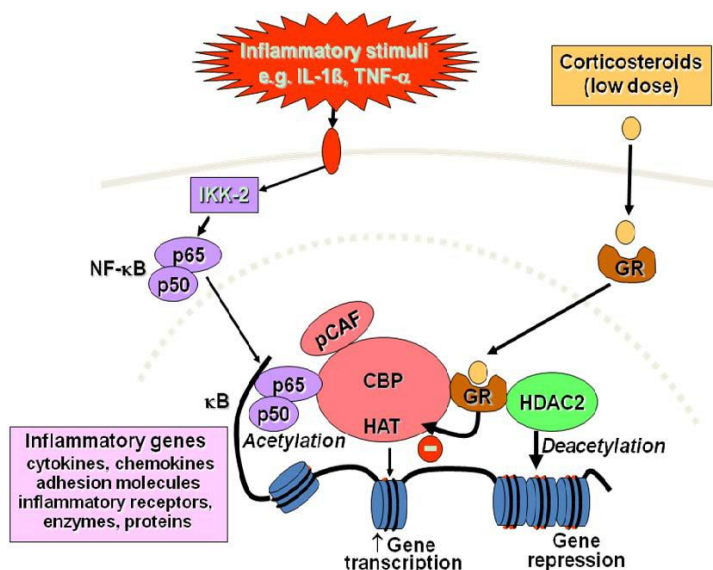
## Background and Uses

- Developed by GlaxoWellcome (GlaxoSmithKline since 2000 merger)
- Intranasal and inhale fluticasone propionate were FDA approved in 1994
- Available OTC in 2015
- Inhaled corticosteroids can reduce inflammation caused by asthma
- Intranasal corticosteroids can reduce inflammation caused by allergic rhinitis



## Mechanism of Action

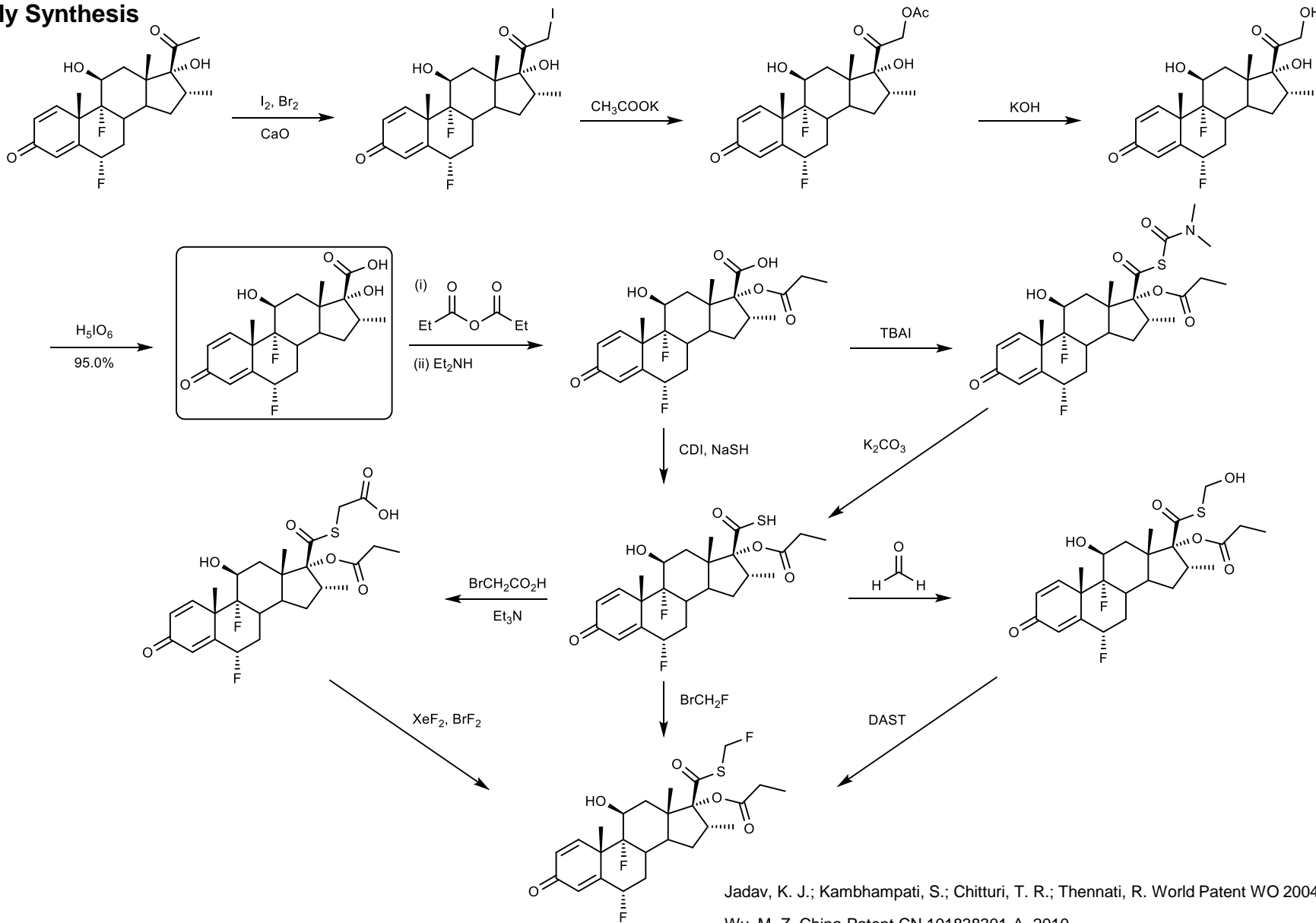
- Fluticasone propionate is a steroidal glucocorticoid agonists
- Reduces the number of inflammatory cells through suppression of the immune system
- Diffuse across the cell membrane into the cytoplasm to bind to glucocorticoid receptors specifically GR- $\alpha$
- GR- $\beta$  interacts with DNA but not with corticosteroids hence acting as a dominant negative inhibitor of glucocorticoid action
- Protein complex has half-time of 10 h



Stewart, E.L. *J. Med. Chem.* 2008, 51, 12, 3349. <https://doi.org/10.1021/jm800279t>

Barnes, P.J. *Pharmaceuticals* 2010, 3, 514; <https://doi.org/10.3390/ph3030514>

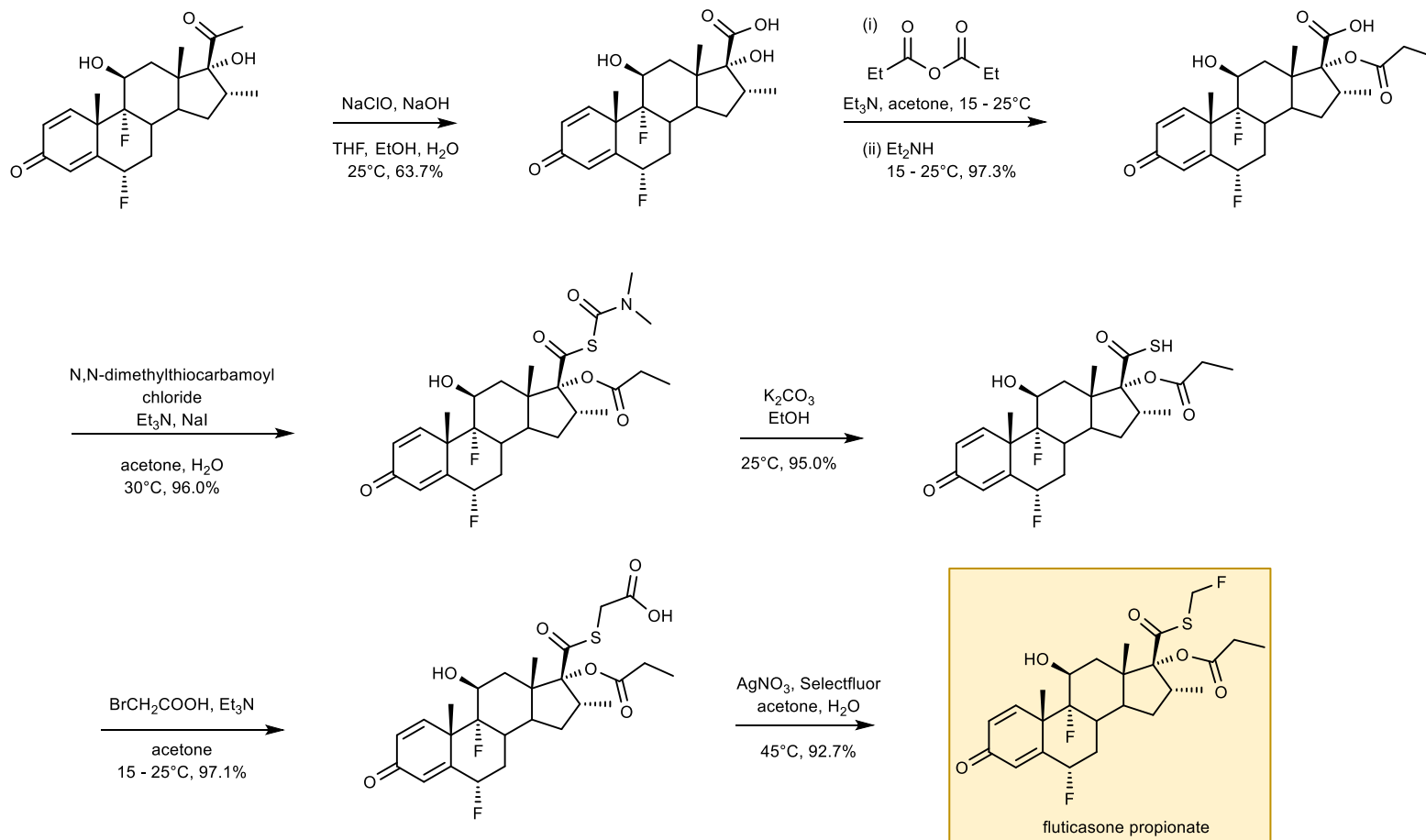
## Early Synthesis



Jadav, K. J.; Kambhampati, S.; Chitturi, T. R.; Thennati, R. World Patent WO 2004/001369

Wu, M. Z. China Patent CN 101838301 A, 2010.

## Modified Synthesis



Su, W. *Org. Process Res. Dev.* **2014**, *18*, 928. <https://doi.org/10.1021/op500126>