

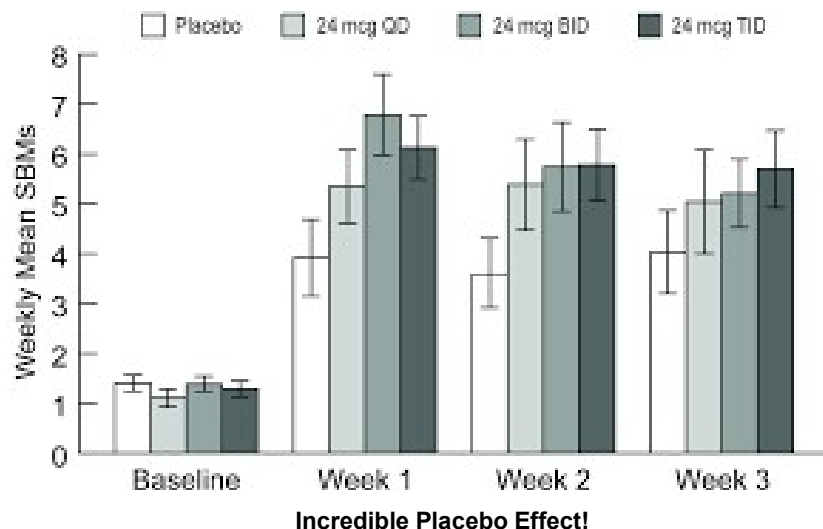
lubiprostone

Fast Facts:

- Approved in 2006, sold by Mallinckrodt (MNK)
- Used for the management of chronic constipation
 - Irritable bowel syndrome and opioid-induced constipation
 - "estimated that several billion dollars are spent each year in the US treating chronic constipation"
- \$184 million in sales by end of 2018
- Current dose at 24 µg twice daily (oral)
- Active form is drawn to the left, but compound tautomerizes readily

**Mechanism of Action**

- Activates CIC-2 channels of epithelial cells
- Efflux of chloride and sodium ions into lumen draws water into intestinal tract
- Highly specific to CIC-2, no observed effect on smooth muscle

**Pharmacokinetic Considerations****Absorption and Distribution**

- <1% bioavailability (this is optimal)
- Peak plasma concentration at 1.5h

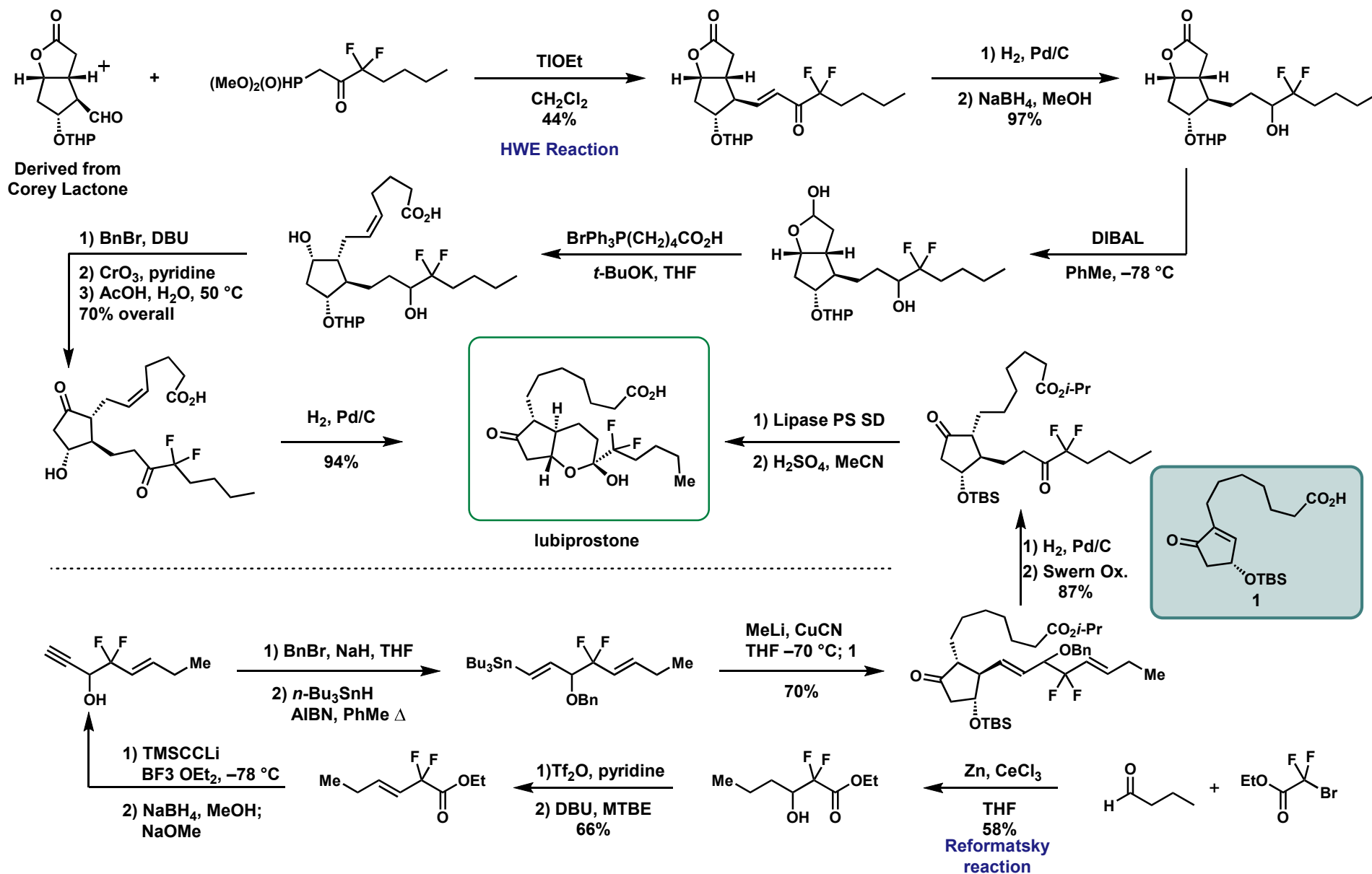
Metabolism and Elimination

- Terminal half-life of 3h
- Parent molecule undetected in stool or urine
- 60% of metabolites detected in urine after 24h
- 30% detected in stool after after one week
- CYP-P450 system not involved in metabolism. Microsomal carbonyl reductase in GI tract metabolizes most of the parent molecule

Toxicity

- No significant adverse effects noted at optimal dosage
- All side effects are normal GI symptoms

1) *Clin. Interv. Aging.* **2008**, 3, 357–364
 2) <https://www.drugbank.ca/drugs/DB01046>



Eur. Patent EP435443A2
PCT Int. Appl. WO201204847A1