

Structure of GRA API 1

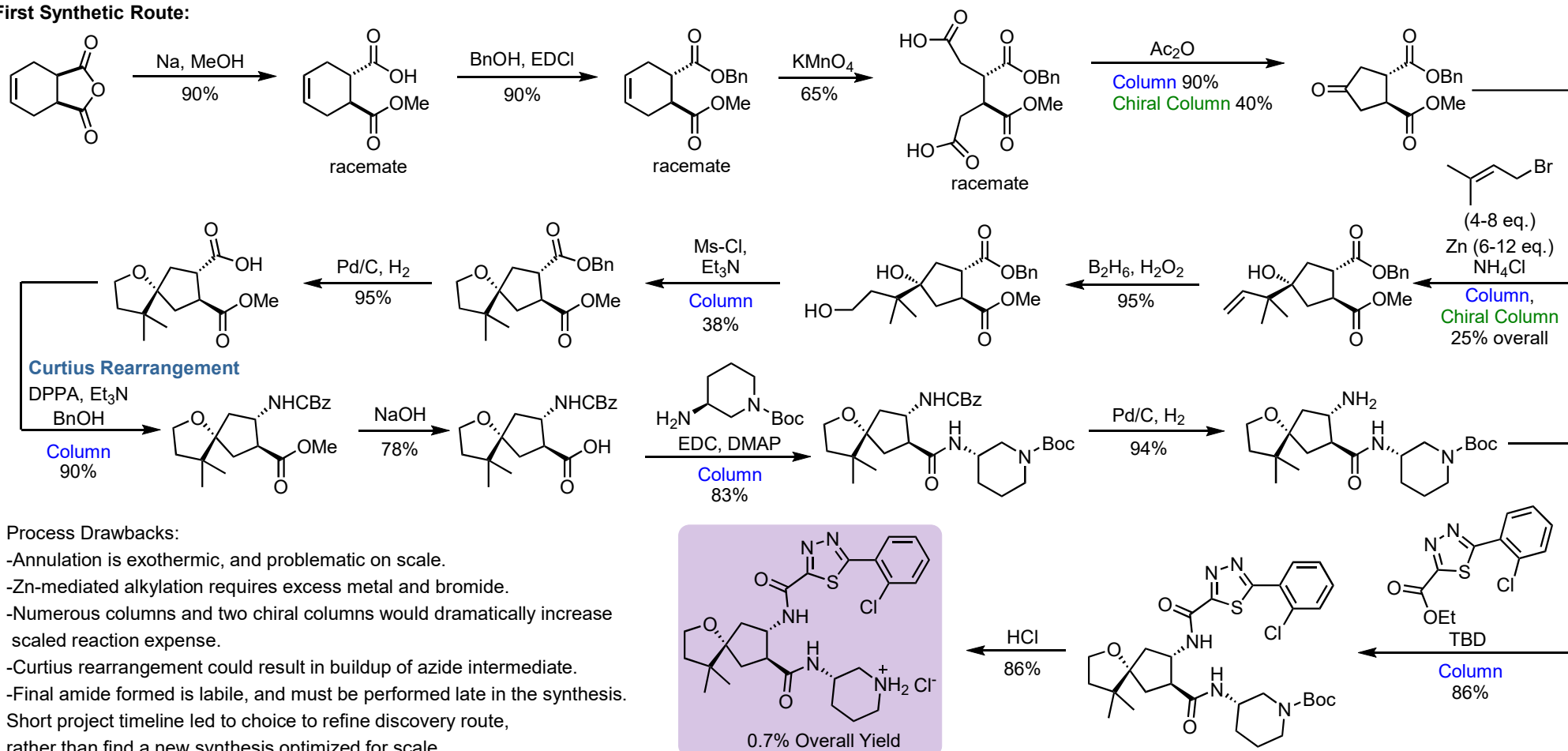
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Background:

- Ghrelin (Growth-Hormone Releasing Peptide) is a peptide hormone involved in the regulation of appetite and homeostatic processes.^{1,3}
- Commonly associated with regulation of hunger, circulating ghrelin levels are lower in obese phenotypes compared to lean phenotypes, although these levels do not recede upon food intake.³
- Cachexia (Wasting Syndrome), characterized by reduced food intake, loss of muscle and fat tissue, and increased metabolism, is a prevalent factor in the treatment-related symptoms for cancer and uremia patients⁴. This condition leads to both increased mortality and reduced quality of life.⁴
- Substantial evidence exists to suggest these symptoms may be treatable through ghrelin modulation.⁴
- GRA API 1 (CAS 2243167-93-1) has been shown to act as a potent agonist of the ghrelin receptor *in vitro*, prompting the need for a process route to produce ~0.8 kg. of material.²

1. *Nature*. **402** (6762): 6563. *Physiology & Behavior* **2014**, 136, 1212. *Org. Process Res. Dev.* **2018**, 22, 11744. *Expert Opinion on Biological Therapy* **2013**, 13 (4), 465

First Synthetic Route:

*Org. Process Res. Dev.* **2018**, 22, 1174

Multihundred Gram Scale Route

