Evolving routes to PF-06878031. A story of selectivity; The highs and the lows

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Disclosed are three alternative routes to the technically challenging PF-06878031 intermediate used to synthesis a Glucagon-like Peptide-1 Receptor (GLP-1R) Agonist PF-06882961-82 (Danuglipron). Complexity in synthesis with respect to the oxetane functionality, chirality & chemical stability are discussed along with how the selectivity issues (chemo/regio/chiral) were overcome to end in an efficient robust route to PF-06878031 demonstrated at metric ton scale.