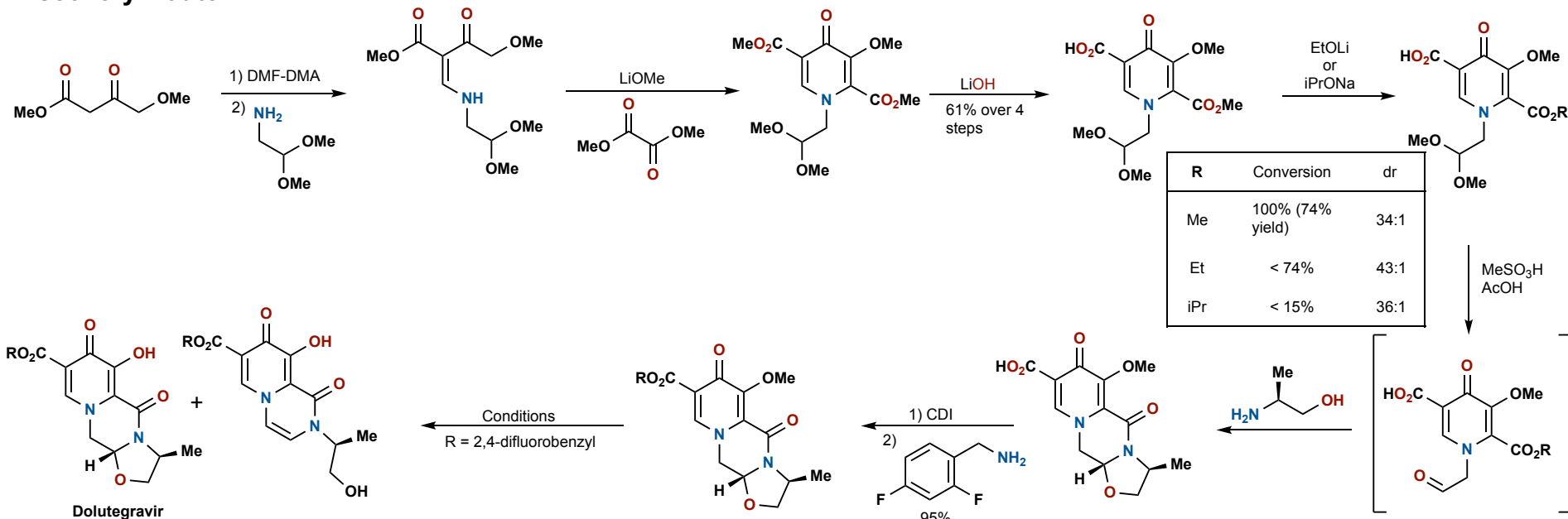
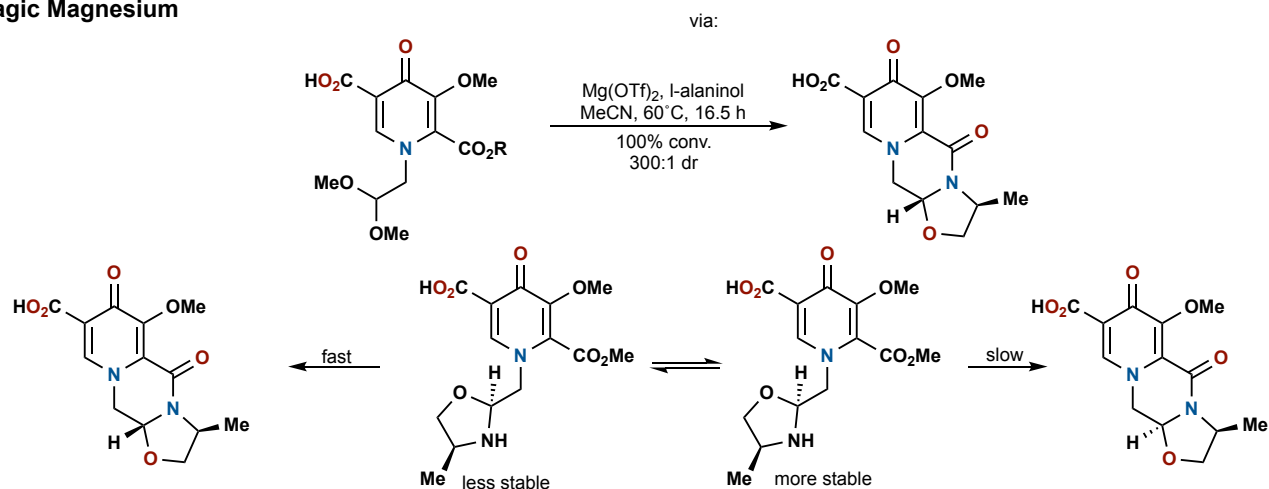


Discovery Route



	Reagent	Conditions	Result
1	BBr ₃	-78°C to rt, 2 hr	46% elim.
2	TMSCl/NaBr	50°C, overnight	71% elim
3	TMSCl/NaI	50°C, 5 h	34% product
4	MgI ₂	rt, 1 h	100% pdt
5	MgBr ₂	50°C, 1 h	100% pdt
6	MgCl ₂	70°C, 1 h	100% pdt

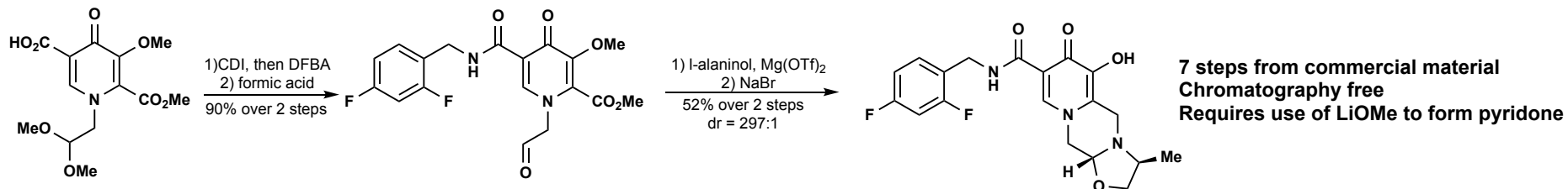
Magic Magnesium



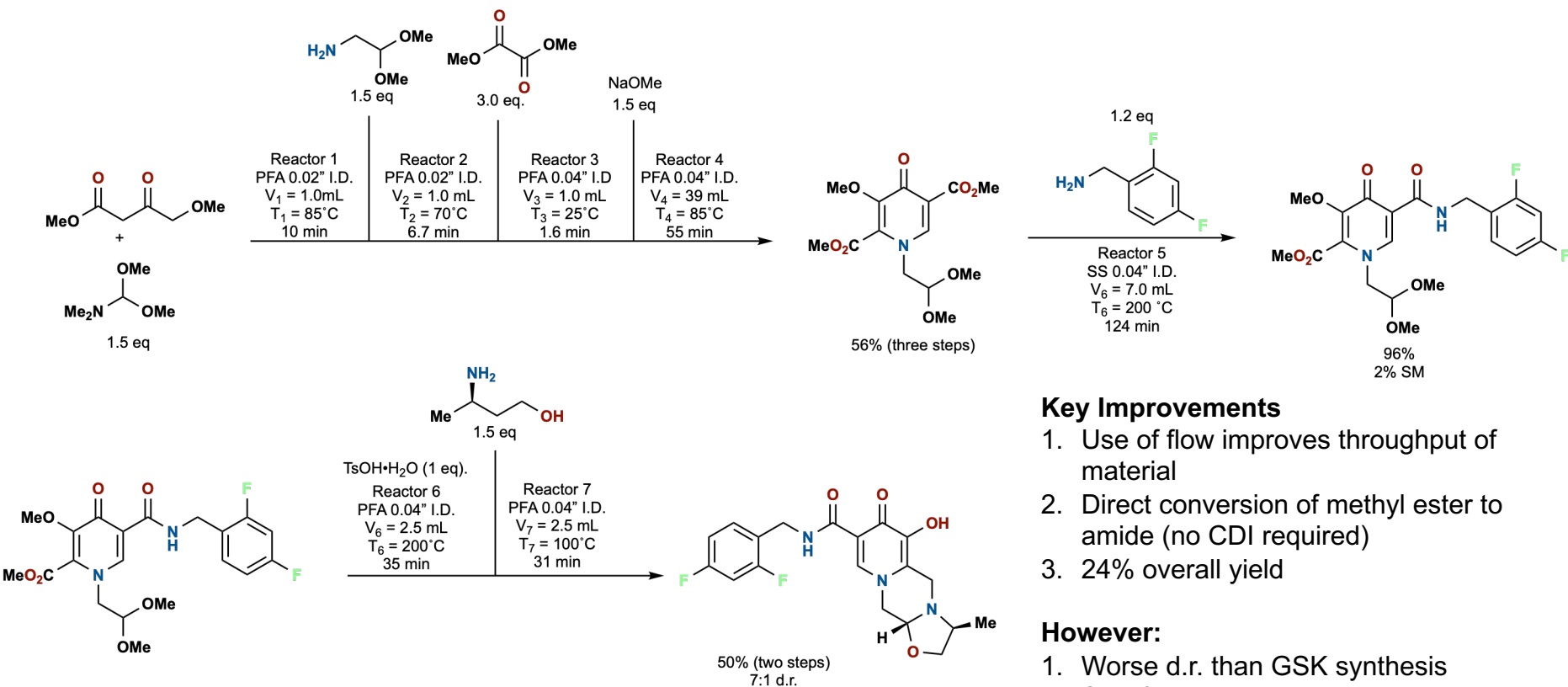
See also: Maegen POTW April 24, 2020
Bowie DOTW June 29, 2018

Org. Lett. 2015, 17, 3, 564–567 <https://doi.org/10.1021/ol503580t>

Process Route



Go with the Flow



Key Improvements

1. Use of flow improves throughput of material
2. Direct conversion of methyl ester to amide (no CDI required)
3. 24% overall yield

However:

1. Worse d.r. than GSK synthesis
2. Significantly smaller scale