

BMS-986020

-Potent antagonist of LPA₁ for the treatment of idiopathic pulmonary fibrosis

-In Phase II clinical trials, hepatobiliary effects were observed, though inhibition of bile acid and phospholipid transporters

-Related compound BMS-986234 did not exhibit these side effects

DOI: 10.1183/1393003.congress-2017.PA1038

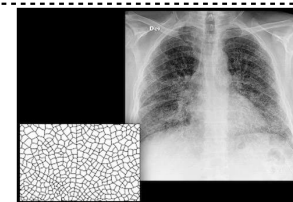
Idiopathic Pulmonary Fibrosis

-The formation of scar tissue in the lungs over time

-With the thickening lung tissue, the circulation of oxygen into the system becomes more difficult. Depriving the organs of the oxygen they need.

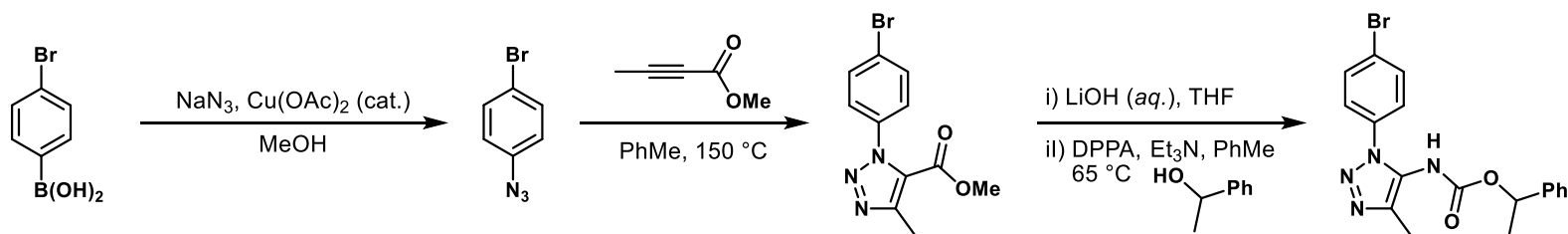
-Average lifespan post diagnosis is 3-5 years.

-Causes include: air pollutants, nitrofurantoin (antibiotic), amiodarone (heart disease treatment), methotrexate and bleomycin (chemotherapeutics), cigarette smoking and viral infections may increase the risk.

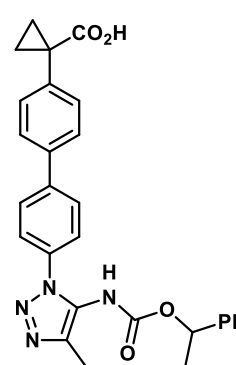
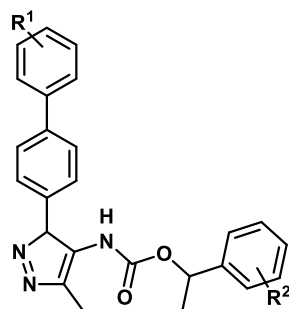


Bristol-Myers Squibb

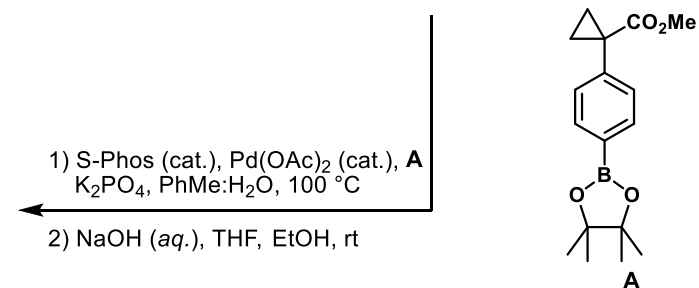
Medicinal Chemistry Route to Related AM095 (*J. Med. Chem.* **2012**, *55*, 7920.)



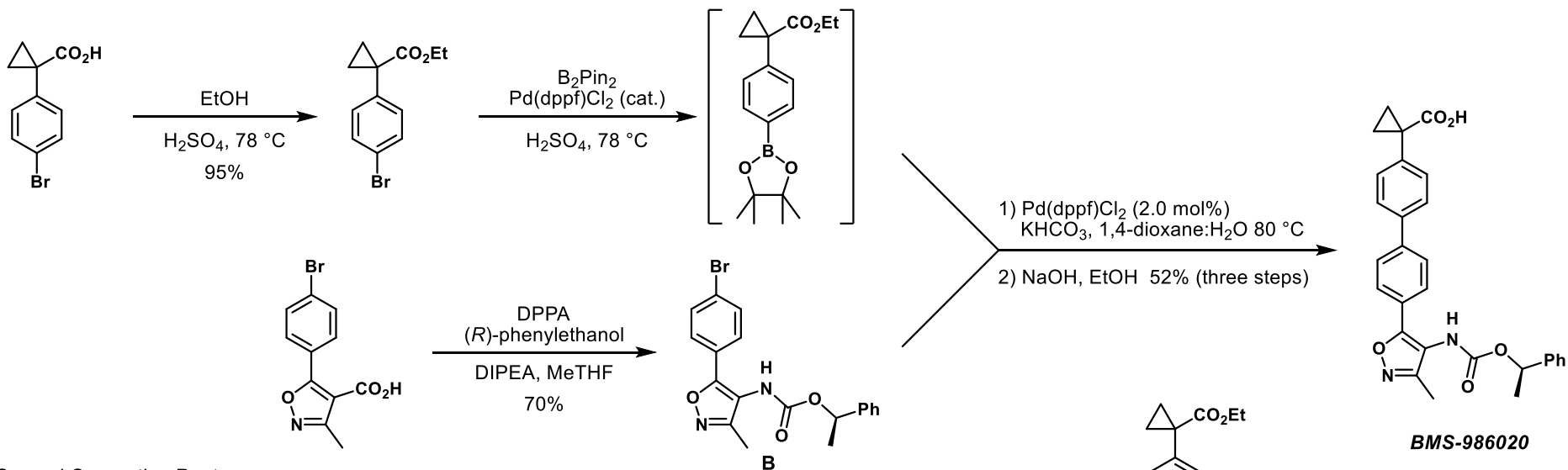
cmpd.	R ¹	R ²	(R)/(S)	LPA ₁ IC ₅₀ (μM)
1	H	H	(R)	17.5
2	4-OCH ₃	H	(R)	>30
3	4-Ph	H	(R)	>30
4	H	2-Cl	(R)/(S)	3.59
5	4-F	2-Cl	(R)/(S)	3.97
6	2-F	2-Cl	(R)	0.644
7	2-F	2-Cl	(S)	>30
8	4-CH ₂ COOH	H	(R)	>30



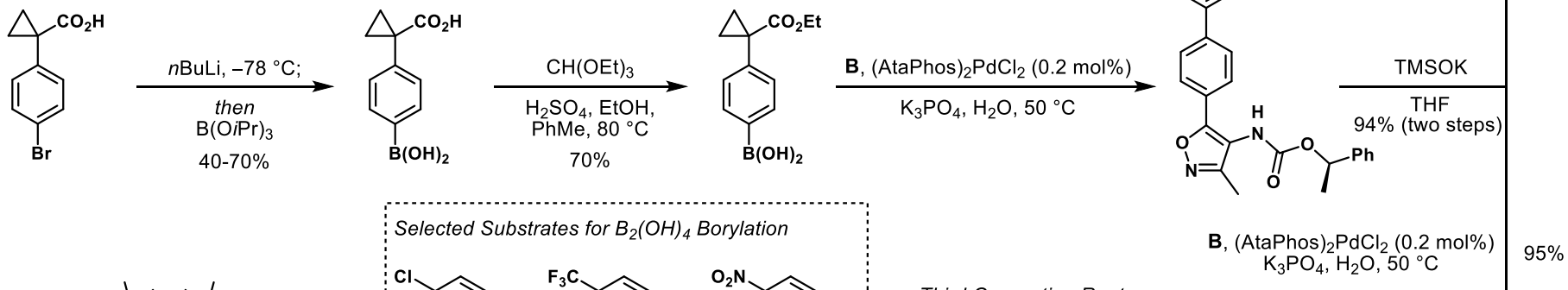
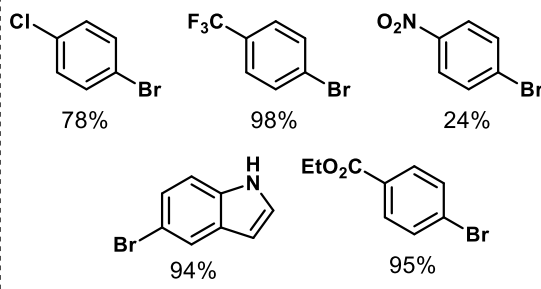
AM095



Early Route to BMS-986020



Second Generation Route

Selected Substrates for $\text{B}_2(\text{OH})_4$ Borylation

Third Generation Route

