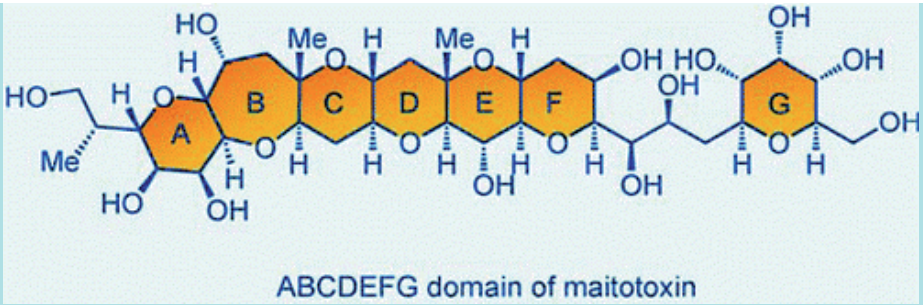
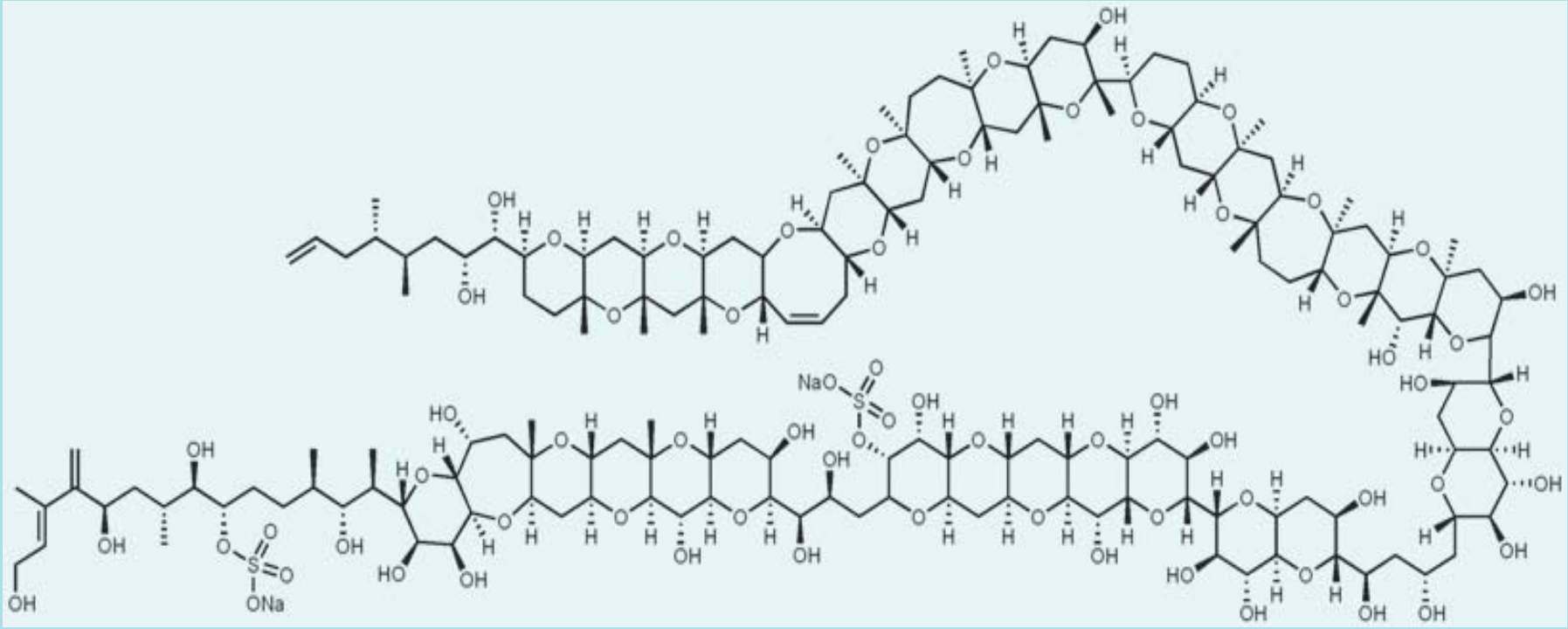
RCC/19/5/10
Kishor



ABCDEFG domain of maitotoxin



Synthesis of the ABCDEFG Ring System of Maitotoxin

K. C. Nicolaou, Robert J. Aversa, Jian Jin, and Fatima Rivas, J. Am. Chem. Soc. 2010, 6856*

Introduction….

Maitotoxin or MTX is an extremely potent toxin produced by Gambierdiscus toxicus, a dinoflagellate species. it has been demonstrated that an intraperitoneal injection of 0.13 µg/kg was lethal in mice.

Maitotoxin was named from the ciguateric fish Ctenochaetus striatus—called "maito" in Tahiti—from which maitotoxin was isolated for the first time - later it was shown that maitotoxin is actually produced by Gambierdiscus toxicus.

The toxicity of maitotoxin to mice is the highest in nonprotein toxins: the LD50 is 50 ng/kg

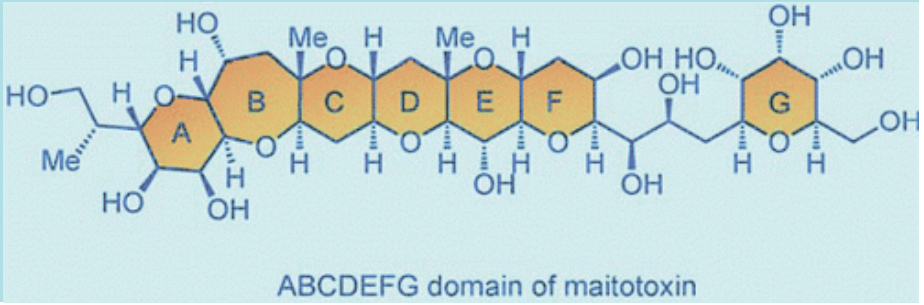
Molecular weight **3422**

Key steps..

Achmatowicz rearrangement

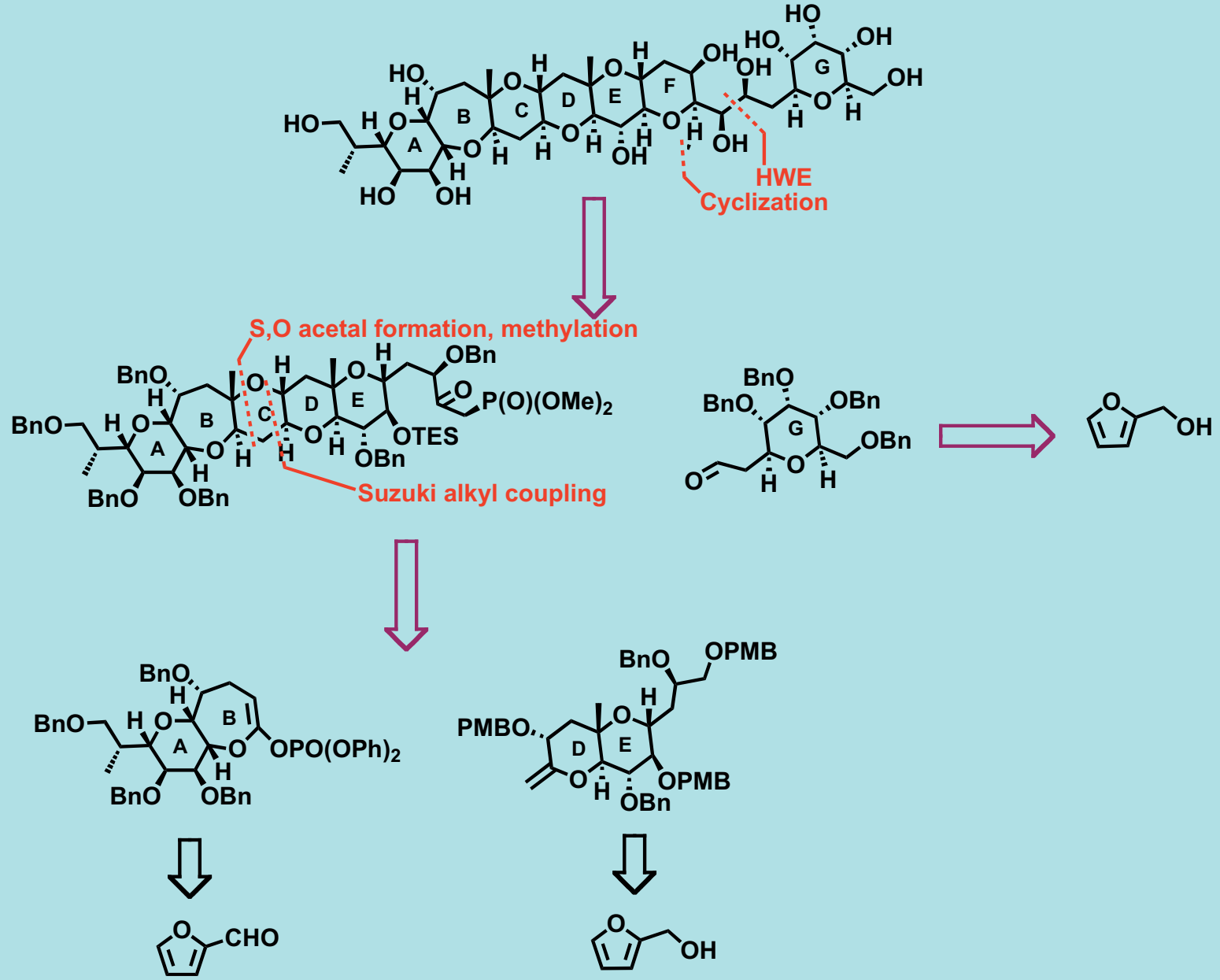
Noyori reduction

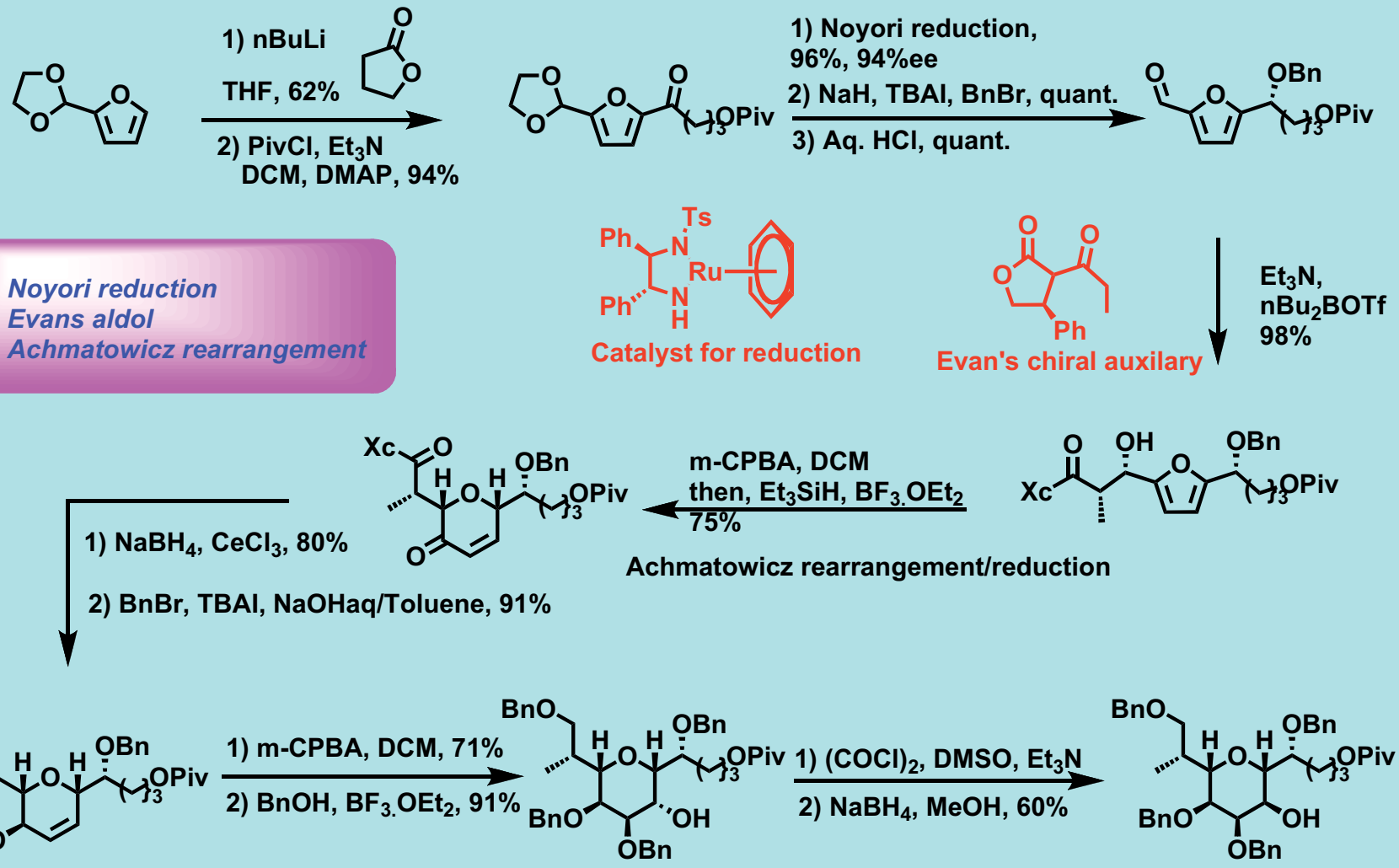
B-alkyl suzuki coupling



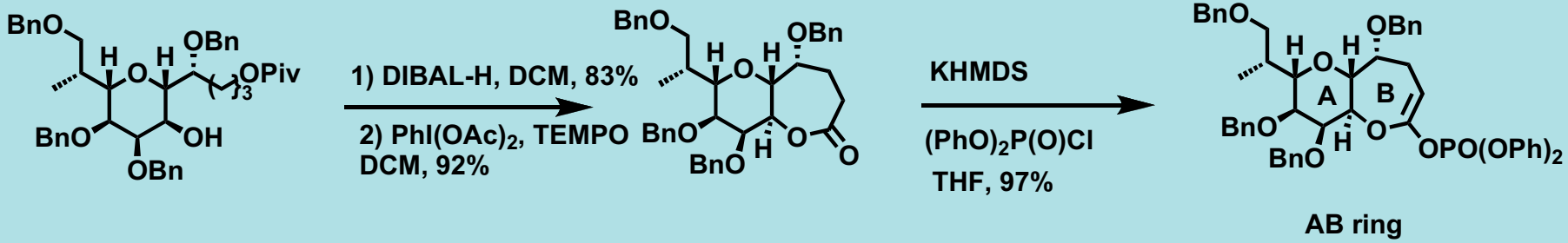
ABCDEFG domain of maitotoxin

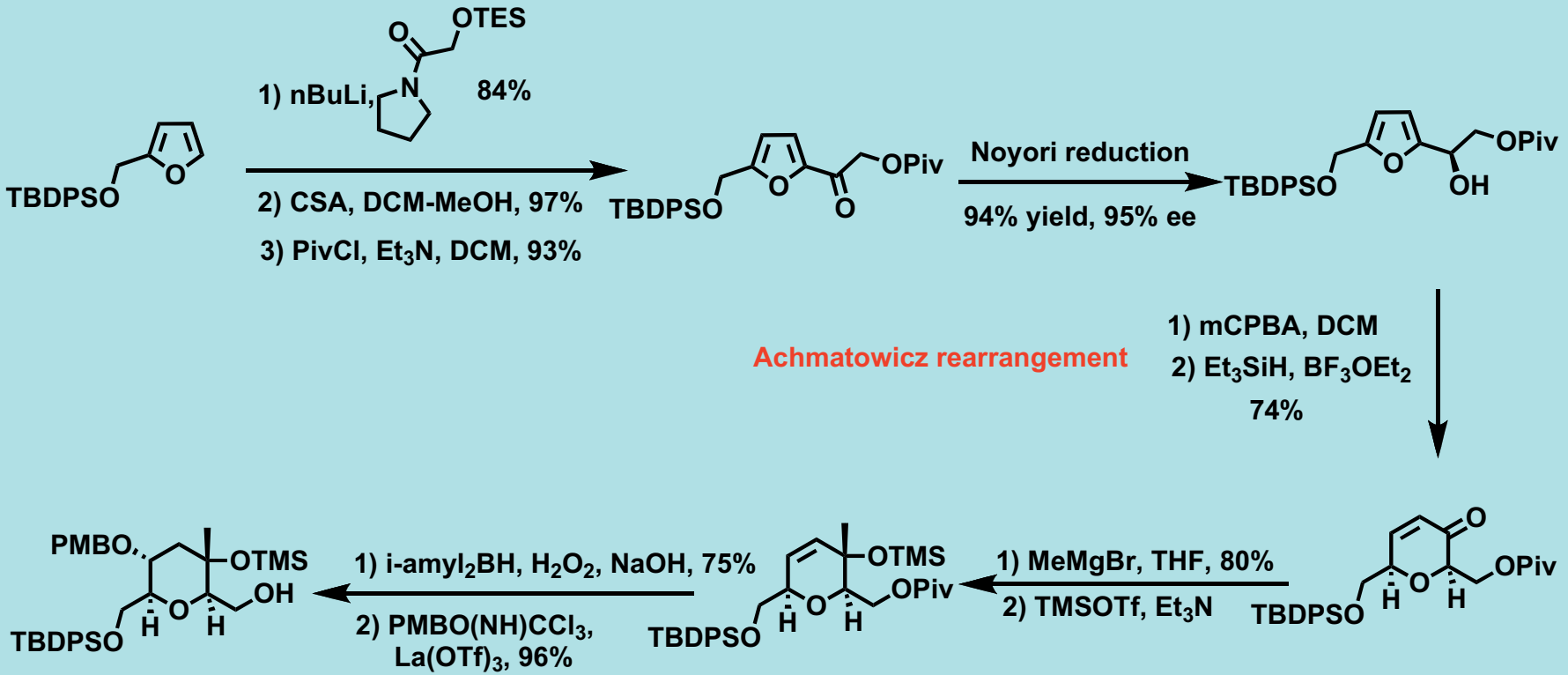
Retrosynthetic Analysis



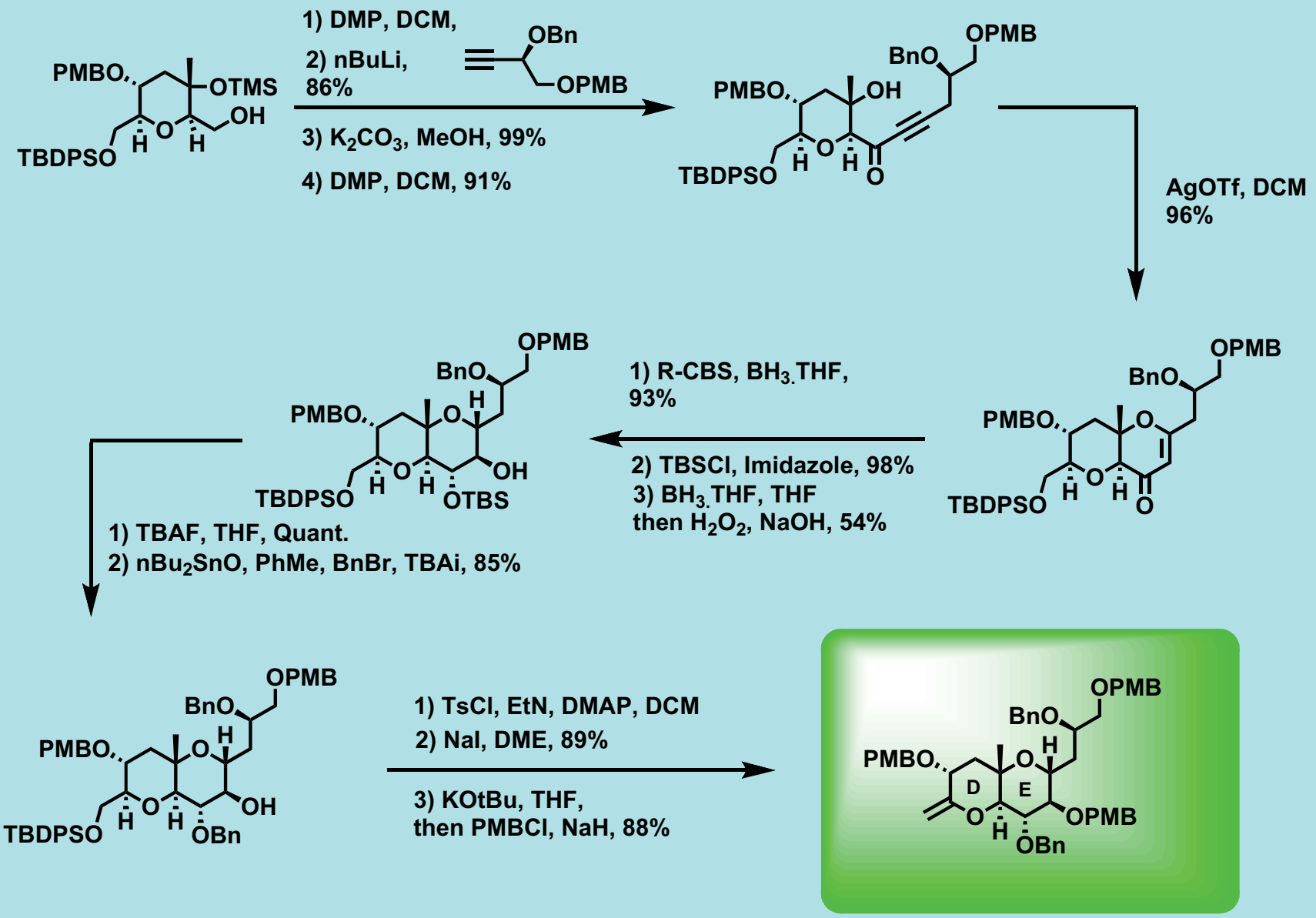

1) nBuLi
THF, 62%
2) PivCl, Et3N
DCM, DMAP, 94%
1) Noyori reduction,
96%, 94%ee
2) NaH, TBAI, BnBr, quant.
3) Aq. HCl, quant.
Noyori reduction
Evans aldol
Achmatowicz rearrangement
Catalyst for reduction
Evan's chiral auxilary
Et3N,
nBu2BOTf
98%
m-CPBA, DCM
then, Et3SiH, BF3.OEt2
75%
Achmatowicz rearrangement/reduction
1) NaBH4, CeCl3, 80%
2) BnBr, TBAI, NaOHaq/Toluene, 91%
1) m-CPBA, DCM, 71%
2) BnOH, BF3.OEt2, 91%
1) (COCl)2, DMSO, Et3N
2) NaBH4, MeOH, 60%

Synthesis of AB ring..

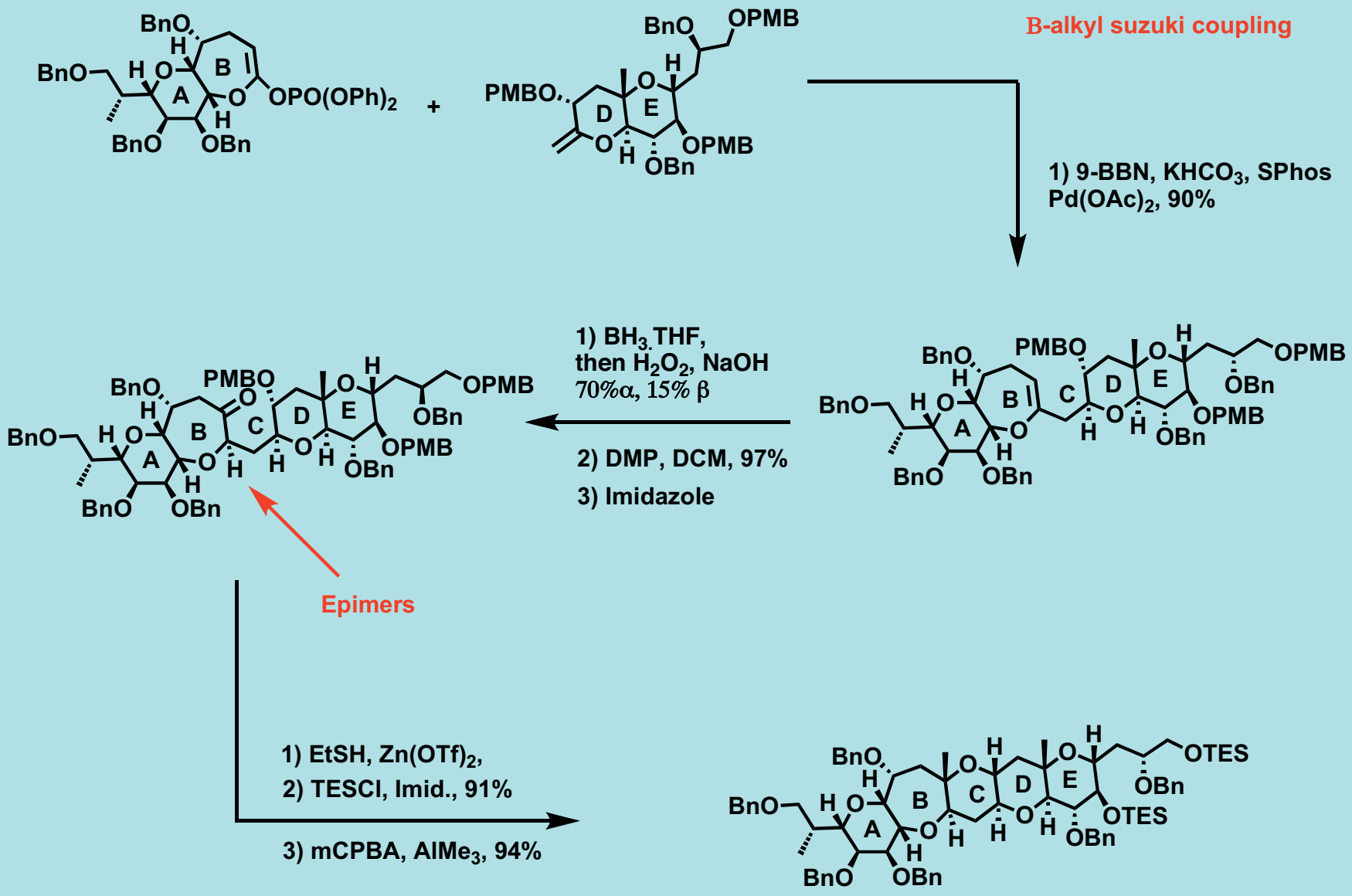




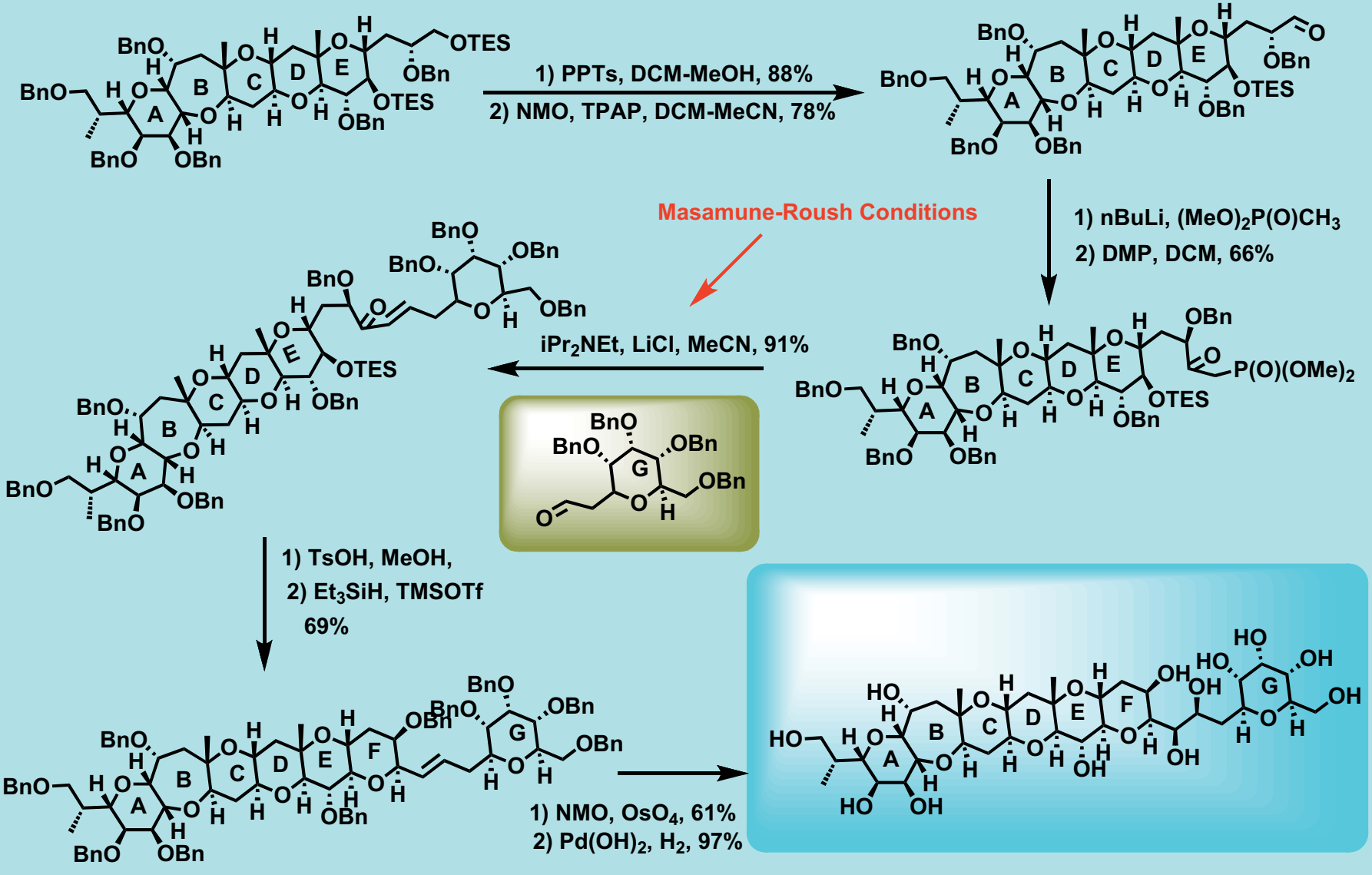
Synthesis of DE ring



Synthesis of ABCDE ring system..



Completion of the synthesis

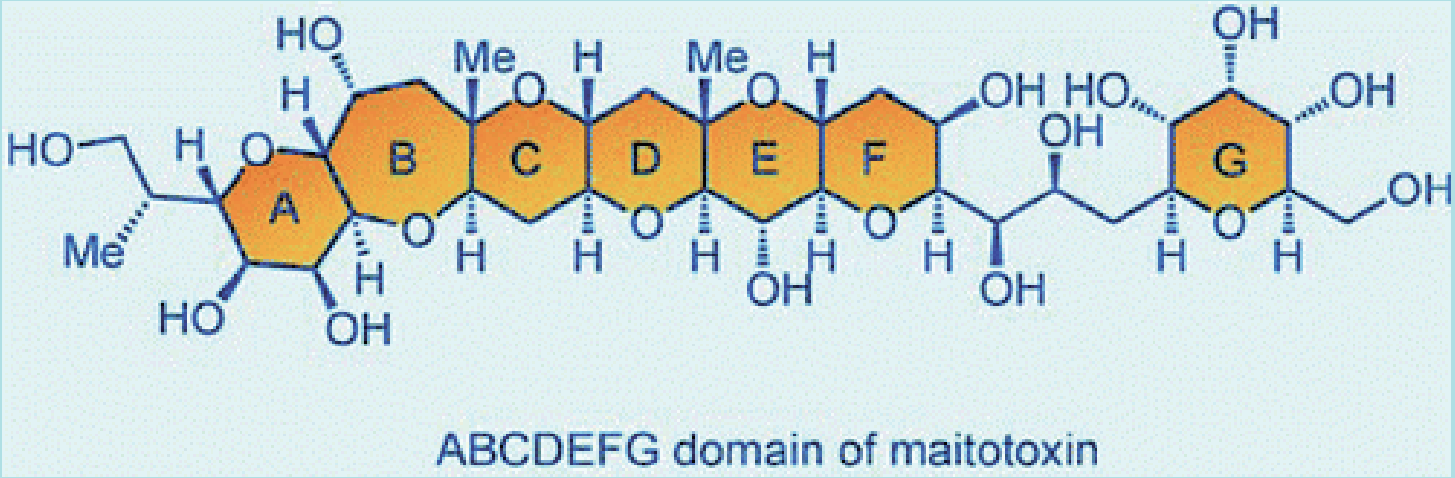


Conclusion

Thank You

The success of the developed synthetic route demonstrates the power of the furanbased, Noyori reduction/Achmatowicz rearrangement approach to tetrahydropyran building blocks suitable for incorporation into polyether assemblies of the type found in maitotoxin.

It also secures further support for the originally assigned structure to this region of maitotoxin.



ABCDEFG domain of maitotoxin