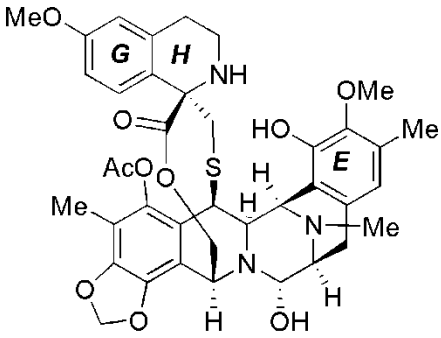
Name (Print)_____

ID#_____

Group #_____

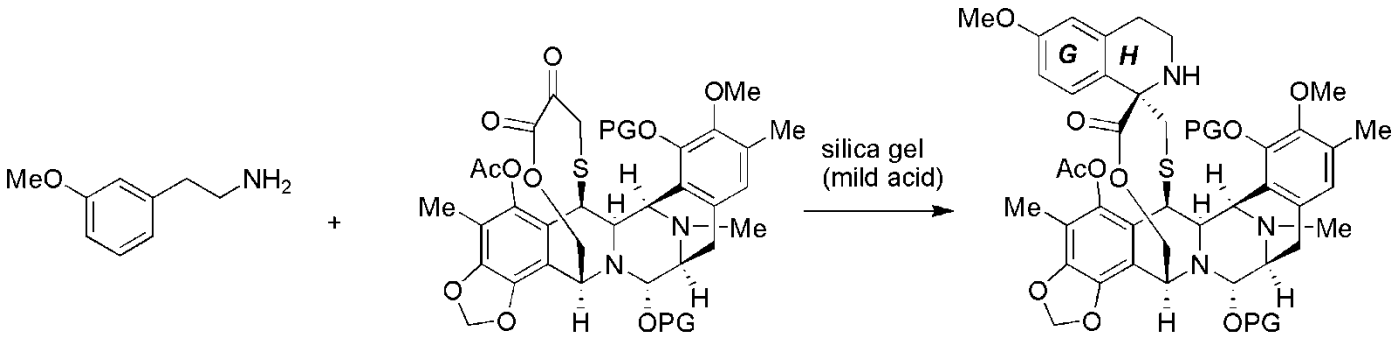
PS #6 – The Pictet-Spengler Reaction and More Synthetic Planning Practice

Ecteinascidin 743 is a natural product produced by a colorful tunicate (AKA a siphon-feeding sea squirt) that is toxic to predators. Its cancer-cell killing ability was identified by tests of a whole-organism ethanol extract (i.e. "sea squirt in a blender") in 1972, but its complex structure wasn't deconvoluted until 1990. *Ect. 743* is so potent that one analysis predicted that a human cancer patient would need only a 5 mg dose to experience curative effects. The Corey group at Harvard completed the synthesis in 1996.



Ecteinascidin 743

Part A) The **H** ring was formed in the very final stages of the synthesis by the mild and selective reaction shown below. The reaction is called a Pictet-Spengler condensation, and it is mechanistically a close relative of a Mannich reaction. Propose a detailed mechanism for this reaction, explicitly including all proton transfers and intermediates. Abbreviate the structure as needed. ("PG" = "protecting group"; "silica gel" is mildly acidic and always slightly wet, so it can be written as "H_3O^+")



Part B) The **E** ring building block at right was built up from the commercially available acid at left. Plan a synthesis, showing all intermediates and conditions. Discuss in your group the various protecting groups you might use, and justify your choice(s) in point form.