Supplement for "Divergent Oriented Synthesis For the Design of Reagents for Protein Conjugation"

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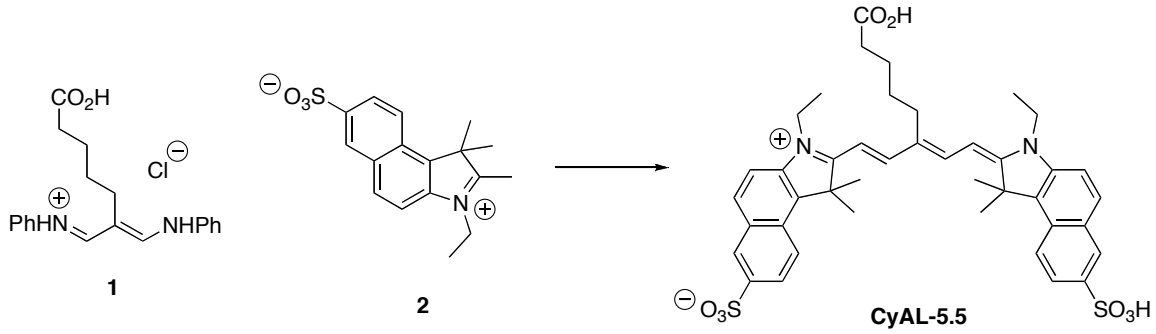
Synthesis of CYAL-5.5



Briefly, CyAL-5.5 is prepared as follows: Malonaldehyde intermediate **1** was synthesized by the Vilsmeier-Haack-Arnold aminoformylation of methyl 7,7-dimethoxyheptanoate followed by treatment with aniline during workup. Intermediate **1** was then allowed to react with two equivalents of 3-ethyl-1,1,2-trimethyl-1*H*-benzo[*e*]indolium-7-sulfonate (**2**) in a 5:5:1 mixture of acetic acid/acetic anhydride/triethylamine to generate CyAl-5.5, which was purified by reverse phase chromatography eluting with acetonitrile in water.