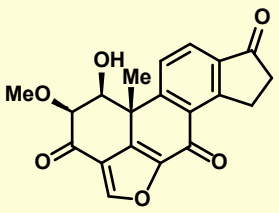
Sarlah Group

Molecule of the Week: Viridin

Guerrero, C. A. *J. Am. Chem. Soc.*, **2017**, *ASAP*. DOI: 10.1021/jacs.7b02829



(–)-viridin

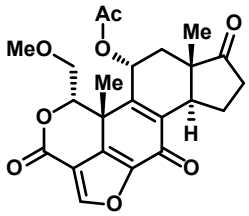
– potential PI3K inhibitor

– related compound, wortmannin, is rapidly degraded in serum, and irreversible inhibition of PI3K are therapeutic issues

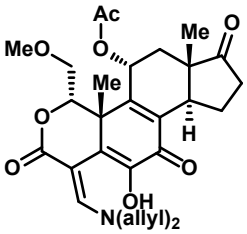
– 2,4-diketofuran moiety responsible for biological activity

– synthesized in racemic form by Sorensen in 2004

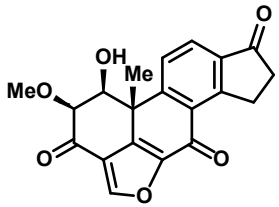
– fragment coupling strategy for potential SAR studies



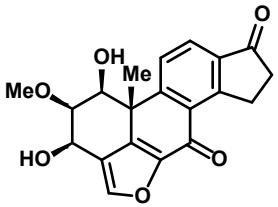
wortmannin



PX-866
wortmannin prodrug developed by Wipf



(–)-viridin



(–)-viridiol

From the SI

"We include here a retrosynthesis of our successful synthesis, in contradistinction to a retrosynthetic analysis. It is our opinion that the two are erroneously used interchangeably, but that a retrosynthetic analysis – emphasis on analysis – should include: multiple different pathways to a target; multiple different pathways to key intermediates; consideration of absolute and relative stereochemical configurations; functional group incompatibilities; consideration of available starting materials, catalysts, and reagents; topology-based strategies; mechanism-based transforms, and numerous other sub-discussions. Because such a discussion is likely to be very detail-focused and lengthy, we have opted not to include a retrosynthetic analysis. For a full delination of the elements of a complete, formal retrosynthetic analysis, please see Part One in: Corey, E. J.; Cheng, X. M. The Logic of Chemical Synthesis, Wiley, 1989."

"We define a step as a any set of chemical transformations that may be accomplished in a single reaction vessel regardless of how many additions of reagents, catalysts, solvents, and other additives are performed and regardless of hold points and temperature changes, but that the removal of any component from the reaction mixture demarcates one step from one that may follow. As an obvious example, aqueous workup demarcates the end of one step because this experimental procedure is used to remove water-soluble impurities. By this logic, solvent evaporations also demarcate a step, whether they are performed using a rotary evaporator, an atmospheric distillation, distillation under vacuum, constant volume distillation, etc. However, these and other operations, when already part of a workup or purification are ignored, because they would unnecessarily inflate the step count."

"Our measured specific optical rotation for synthetic (–)-viridin, [α]D = −145, falls short of the value reportedS10 by the isolation chemists, [α]D = −222, although the sign is identical. The differencein magnitude may be ascribed to the determination of this data using small quantities of material. We still claim a highly enantioselective synthesis on the basis of chiral HPLC data. In the section that follows, we measured (Spring 2015) and re-measured (7 March 2017) the enantiomeric excess of our enantioselective Heck product and found it to be >99%. See pages SI-57 and SI-58 for this data."

Lucas Hernandez, May 18, 2017

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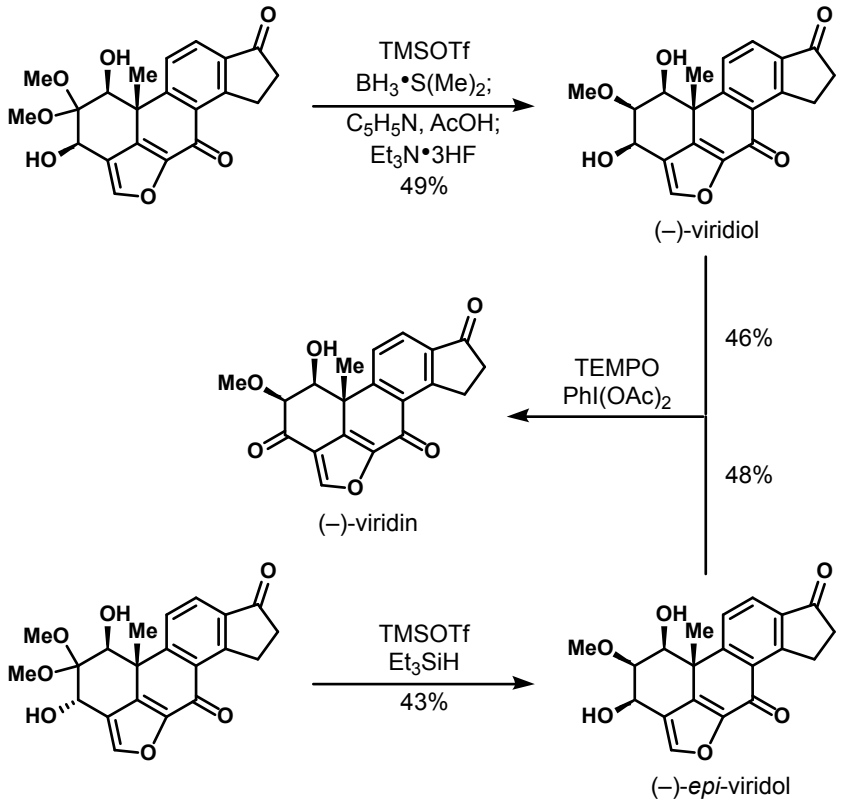

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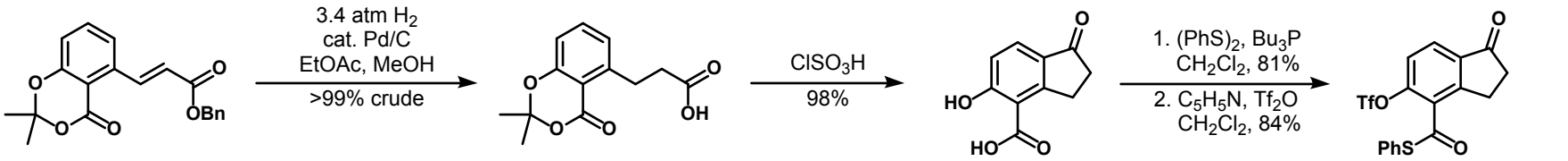

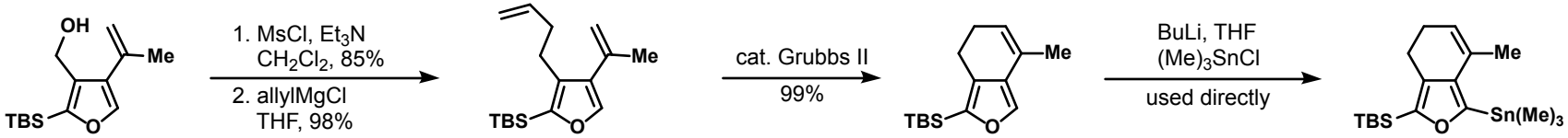

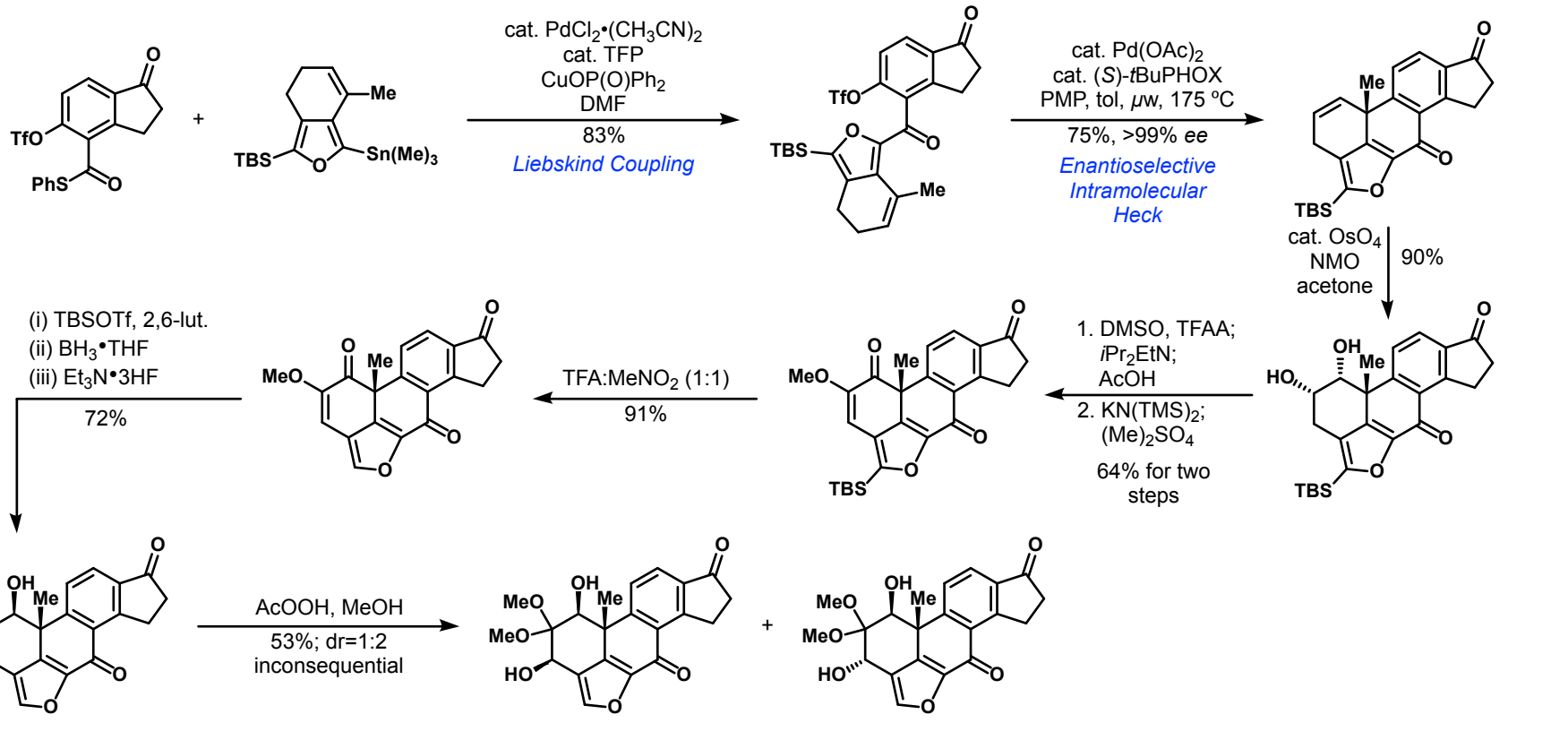

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