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Synthesis of Pleuromutilin

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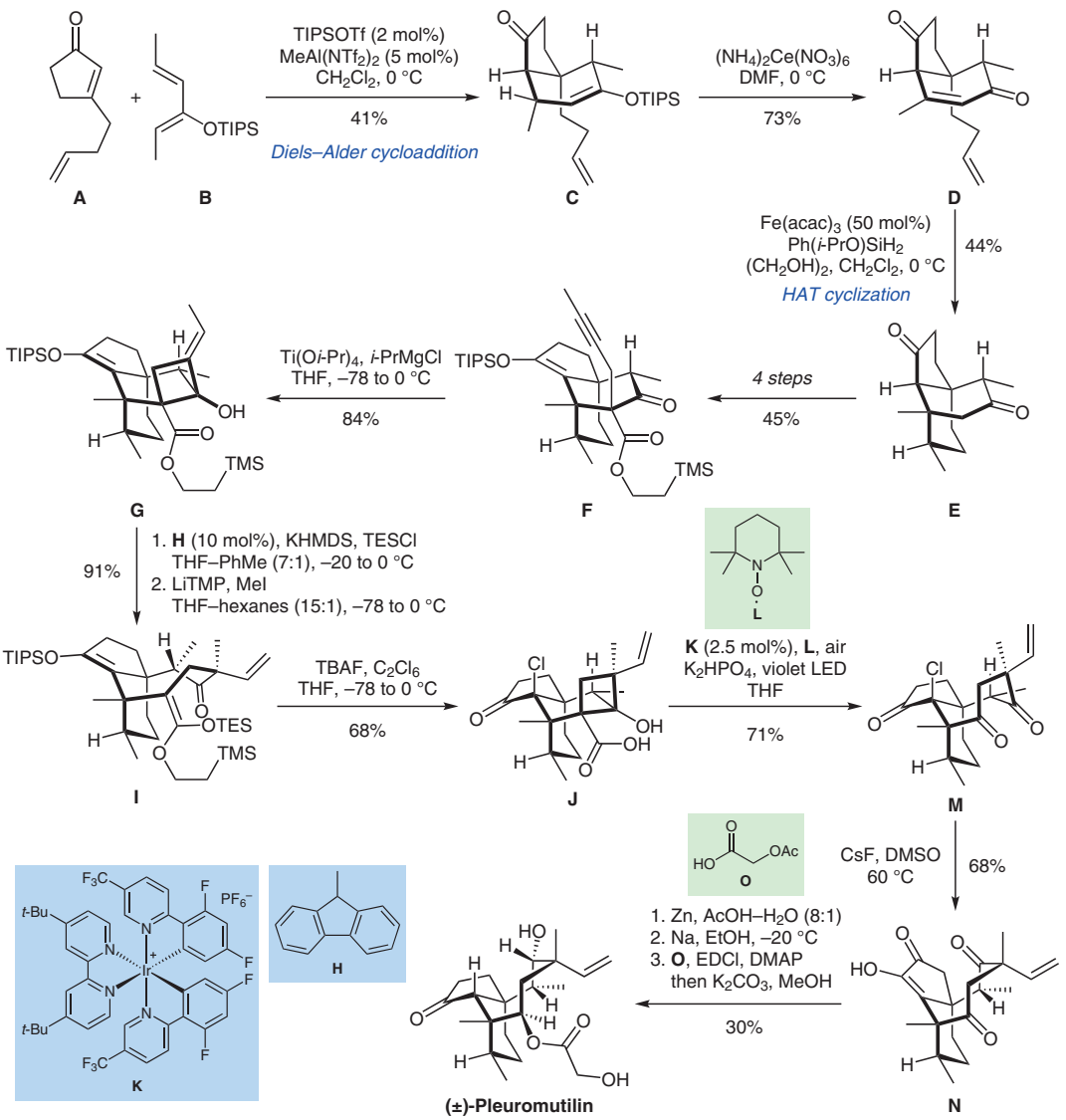
Total Synthesis of (±)-Pleuromutilin



Significance: Foy and Pronin report a short synthesis to (±)-pleuromutilin, which was found to exhibit potent activity against Gram-positive pathogens. Recently, a mutilin with the same carbon skeleton was approved for the systemic treatment of bacterial infections. This synthetic approach could facilitate the previously challenging synthesis of mutilin derivatives to further explore their intriguing biological activity.

Comment: Diels–Alder cycloaddition followed by CAN oxidation and Fe-catalyzed HAT cyclization resulted in the rapid formation of tricyclic diketone **E**. The challenging eight-membered ring was accessed from **J** through photocatalyzed oxidation and fragmentation furnishing the highly substituted 1,4-diketone **M**. The synthesis was completed in four additional steps.

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Category

Synthesis of Natural Products

Key words

(±)-pleuromutilin

Diels–Alder cycloaddition

HAT cyclization

oxidative ring expansion

Synfact of the Month