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A Concise Total Synthesis of (–)-Berkelic Acid
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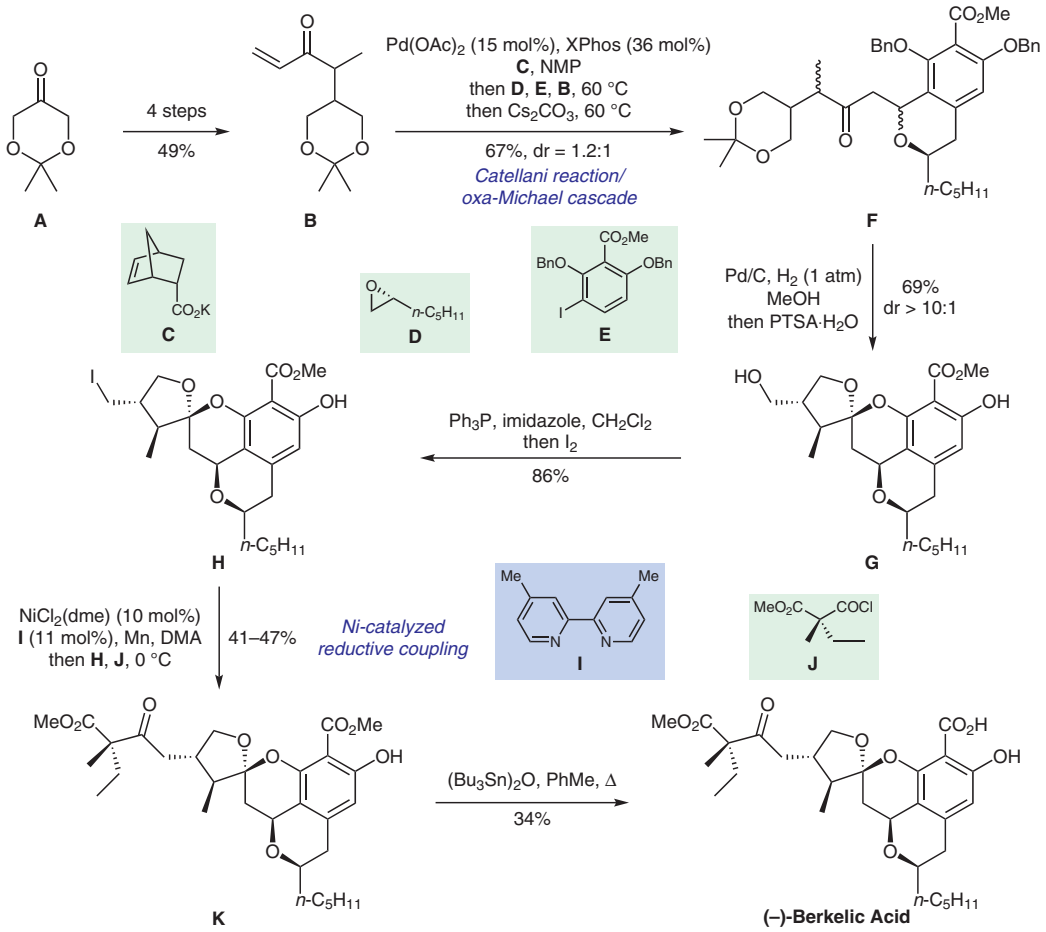
Total Synthesis of (–)-Berkelic Acid



Significance: Qu, Zhou, and co-workers report a concise total synthesis of (–)-berkelic acid, which was isolated in 2006 from an extremophilic Penicillium species. Their synthesis relies on a Catellani reaction followed by an oxa-Michael addition performed in a one-pot operation and a late-stage Ni-catalyzed reductive coupling.

Comment: The synthesis commences with the preparation of enone **B**, which is accessed from ketone **A** in four steps. A Catellani reaction/oxa-Michael cascade gives rise to **F**. Benzyl deprotection followed by spiroacetalization gives ketal **G** in good yield and excellent diastereoselectivity, setting four stereocenters from only one existing chiral center. Iodide **H** is then coupled with acid chloride **J** in a Ni-catalyzed reductive coupling to give methyl ester **K**. (–)-Berkelic acid is obtained by selective saponification in the presence of $(Bu_3Sn)_2O$.

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Category
Synthesis of Natural Products and Potential Drugs

Key words
(–)-berkelic acid
Catellani reaction
oxa-Michael reaction
nickel catalysis
reductive coupling

Synfact of the Month