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A Concise Total Synthesis of (–)-Berkelic Acid

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Total Synthesis of (–)-Berkelic Acid

Category

Synthesis of Natural Products and Potential Drugs

Key words

(–)-berkelic acid

Catellani reaction

oxa-Michael reaction

nickel catalysis

reductive coupling

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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 $(\text{Bu}_3\text{Sn})_2\text{O}$.

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