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Significance: Dai and co-workers report the total synthesis of (±)-phaeocaulisin A. The catalytic cyclopropanol ring-opening carbonylation protocol was investigated and displayed as a general method to access various γ-keto esters. Choice of base was crucial for desired chemoselective aldol cyclization to later construct the oxaspirolactone of the tetracyclic skeleton of the natural product.

(±)-Phaeocaulisin A

Comment: Retrosynthetically devised in a concise manner, sequential Kulinkovich cyclopropanation and palladium-catalyzed cyclopropanol ring-opening carbonylation from diene \mathbf{D} gave keto ester \mathbf{G} . Subsequent ozonolysis yielded dione \mathbf{H} followed by aldol cyclization to access cycloheptanone \mathbf{I} . Ketalization, lactonization and oxidation yielded tetracycle \mathbf{K} . Installation of the α -methylene group followed by alkene migration finally gave (\pm) -phaeocaulisin \mathbf{A} .

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Synthesis of Natural Products

Key words

(±)-phaeocaulisin A

guaianolide sesquiterpene

Kulinkovich reaction

ring-opening carbonylation

aldol reaction

Tamao-Fleming oxidation



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