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Total Synthesis of the Antibiotic BE-43472B
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## Total Synthesis of BE-43472B


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1. $\mathrm{BBr}_{3}$
2. $\mathrm{Boc}_{2} \mathrm{O}$

82\% (2 steps)
3. I, $\mathrm{HCO}_{2} \mathrm{H}$
4. $\mathrm{Na}_{2} \mathrm{CO}_{3}, \mathrm{MeOH}$ 83\% (2 steps)



O

$$
t \text {-BuLi }
$$





C 2. DIBA

84\% (2 steps)


1. $\mathrm{Me}_{3} \mathrm{Al}, \mathrm{H}_{2} \mathrm{O}$ TMSOTf 92\%
2. CAN-

$88 \%$ | 2. G, then $\mathrm{SiO}_{2}$ |
| :---: |
| $\mathrm{~K}_{2} \mathrm{CO}_{3}, \mathrm{MeOH}$ | $\mathrm{K}_{2} \mathrm{CO}$

$94 \%$

Diels-Alder cycloaddition


F

( $\pm$ )-BE-43472B

Significance: The aromatic polyketide BE-43472B was isolated from a marine Streptomyces species and was shown to exhibit significant activity against several drug-resistant bacterial strains. Moreover, its unprecedented structure includes two anthraquinones linked through a highly hindered carbon-carbon bond as well as five contiguous stereocenters. The strategy reported by Suzuki and co-workers relies on a highly efficient pinacol rearrangement to form the key $\mathrm{C}-\mathrm{C}$ bond between the two anthraquinone monomers.

Comment: The synthesis starts with lithiation of bromonaphthalene B, followed by addition to ketone $\mathbf{A}$. The resulting tertiary alcohol $\mathbf{C}$ was treated with triflic acid to induce a pinacol rearrangement to produce ketone $\mathbf{D}$. Construction of the tetrahydrofuran ring proceeded via acetal E followed by methylation using $\mathrm{Me}_{3} \mathrm{Al}$. Oxidation of $\mathbf{F}$ and subsequent quinone Diels-Alder reaction with diene $\mathbf{G}$ delivered anthraquinone $\mathbf{H}$. This intermediate was converted into the natural product
$( \pm)$-BE-43472B via epoxide $\mathbf{J}$.
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## Gategory

Synthesis of Natural
Products and
Potential Drugs

## Key words

antibiotics
anthraquinone natural products

## pinacol

rearrangement
Diels-Alder
cycloaddition
SYNFACheth
of the

