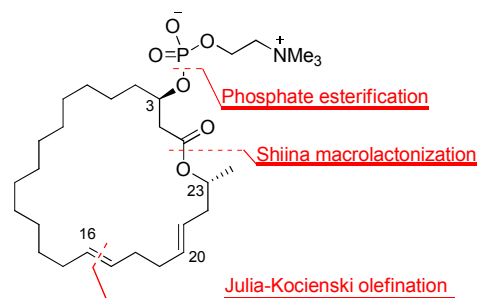


Total synthesis of (3*R*,16*E*,20*E*,23*R*)-eushearilide

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Eushearilide is antifungal activity against various fungi and yeasts including the human pathogens *Aspergillus fumigatus*, *Trichophyton* sp. and *Candida* sp. The structure of **1** comprises a novel 24-membered macrolide with two chiral carbons of unknown configuration and non-conjugated double bonds and possesses phosphate diester attached to choline at C3 hydroxyl group. To determine the absolute configuration of two chiral carbon, we synthesized two diastereomers of **1** with different chirality at C23 and compared the spectroscopic properties of natural product with those of synthetic diastereomers. Those were not completely identical to the only chemical shifts of C14–C18 in ¹³C NMR spectrum. Therefore, we speculated the geometry of double bond at 16 position of the natural product was *trans*, *E*-form. The total synthesis of the third diastereomer having both dipolar ionic choline phosphate chain and lipophilic 24-membered macrolide skeleton was achieved. The *cis* selective coupling of two long chains by Julia-Kocienski olefination set C16 geometry. Macrolactonization of seco acid using Shiina reagent was performed the heterocycle in high yield. Finally, by installing choline phosphate in the C3 hydroxyl group was converted to the target molecule (3*R*,16*E*,20*E*,23*R*)-**1**.



(3*R*,16*E*,20*E*,23*R*)-Eushearilide (**1**)