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속보 (Communications)

The First Synthesis of 3-*epi*-Xestoaminol C

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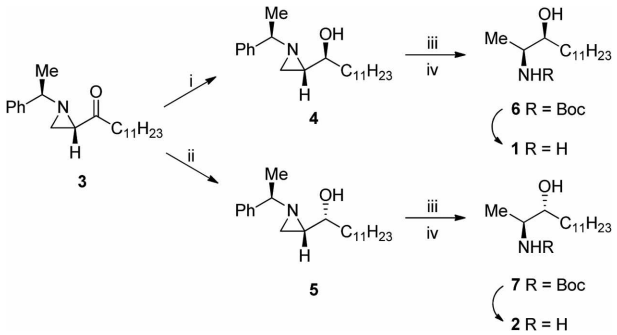
A new 1-deoxysphingoid, 3-*epi*-xestoaminol C (1), isolated from the New Zealand brown alga *Xiphophora chondrophylla* was firstly synthesized for the identification of its absolute stereochemistry *via* stereoselective reduction of 2-acylaziridine followed by hydrogenolysis.

Sphingosine as a class of lipid described almost two centuries ago[1] was characterized structurally as 2-amino-1,3-diol in long alkyl chain most of which participate in cell structure and its regulation.[2] Up to now hundreds of sphingosines were isolated and their structures were identified and some of them showed important biological activities to lead for a new drug development program.[2,3] Most of them have different number of carbon backbones, position of double bonds and the stereochemistry of olefin and other functionalities in alcohol and amine. Due to the same biosynthetic origin of sphingosine from serine and fatty acids most of them have 2-amino-1,3-diols as the common functionalities even though their carbon backbones are different. However, few isolated natural products including spisulosine,[4] clavaminol,[5] xestoaminol[5a,6] and obscuraminol[7] have only 2-amino-3-ol functionalities without one alcohol at the end of the backbone as 1-deoxysphingoid. The absolute stereochemistries of two functional groups are important for their biological actives. The epimer of the previously isolated xestoaminol C (2),[5a,6] 3-*epi*-xestoaminol C (1), was isolated for the first time from a brown alga *Xiphophora chondrophylla* by bioassay-guided isolation method last year.[8] Its structure was identified by extensive ^{1}H NMR analysis including NOE correlations of its oxazolidinone derivative. To confirm its chemical structure and absolute stereochemistry we decided to synthesize both isomers, xestoaminol C and 3-*epi*-xestoaminol C, starting from chiral aziridine.

At first we prepared 2-acylaziridine (3) from (2*S*)-aziridine-2-carboxylate[9] by the known method whose 2*S* configuration should be ended at the C2 of the final product bearing amine functional group. The hydroxy groups at C3 of the target molecules are 2*R* in xestoaminol C and 2*S* in 3-*epi*-xestoaminol C. Thereby we decided to reduce the ketone in 2-acylaziridine (3) in stereoselective manner which we already established well. Reduction with L-Selectride yielded the *threo* product (4) while $NaBH_4$ with $ZnCl_2$ gave *erythro* product (5) by different transition states.[4a] Hydrogenolysis with H_2 in the presence of catalyst $Pd(OH)_2$ yielded the product 3-*epi*-xestoaminol C and xestoaminol C with concomitant aziridine ring opening in regioselective manner and the removal of the α-methylbenzyl group at the amine. However, we were not able to get the final products in analytically pure forms by single operation. We decided to get the products as their Boc-protected forms by performing hydrogenolysis in the presence of 1.1 equiv. of $(Boc)_2O$ to afford analytically pure products **6** and **7** from **4** and **5**, respectively. Once we had Boc-protected forms of the 3-*epi*-xestoaminol C (6) and xestoaminol C (7), analytically pure and protecting group free products **1** and **2** were easily obtained by the treatment of HCl followed by the purification by Amberlite IRA-410 chloride form anion exchange chromatography. Firstly we confirmed that all physical data for our synthetic xestoaminol C (2) were completely matched with the natural product.[6] Then we compared our synthetic



Scheme 1. *Reagents and conditions*: (i) L-Selectride, THF, −78 °C, 1 h, 83%; (ii) $NaBH_4$, $ZnCl_2$, MeOH, −78 °C, 3 h, 65%; (iii) $(Boc)_2O$, $Pd(OH)_2$, H_2, MeOH, rt, 6 h, 86%; (iv) HCl, MeOH, reflux, 3 h, 82%.

3-*epi*-xestoaminol C (1). To our delight, our final synthetic product has completely matched ^{1}H NMR spectral data and optical rotation value ($[\alpha]^{20} = -6.1$ (c 0.23, $CHCl_3$)) as natural 3-*epi*-xestoaminol C.[8] Thereby we were able to conclude the natural product 3-*epi*-xestoaminol C has (2*S*)-amino-(3*R*)-hydroxy functionalities which are unusual *syn* relationship while most of the natural products have *anti* relationship.

In conclusion a new 1-deoxysphingoid, 3-*epi*-xestoaminol C (1), isolated from the New Zealand brown alga *Xiphophora chondrophylla* was firstly synthesized for the identification of its absolute stereochemistry via stereoselective reduction of the 2-acylaziridine (3) followed by hydrogenolysis.

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Supporting Information. All experimental details and analytical data with ^{1}H and ^{13}C NMR spectra are provided.

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