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Synthetic Efforts Toward Solomonamide B: A Potential Anti-Inflammatory Agent

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Introduction and Objectives

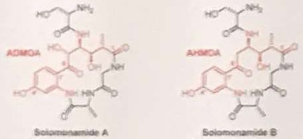
Theonella swinhoei (Figure 1), a marine sponge located in the Solomon Islands, has been recently shown to produce bioactive natural products. Two unprecedented cyclic peptides were isolated as solomonamide A and B from the sponge (207 g dry wt.). Solomonamide A (6.2 mg) exhibited the ability to reduce edema, swelling due to a suppression of fluid in body tissues, in mice by 60%.[1] Although it can be found in any part of the body, edema typically occurs in the hands, arms, feet, ankles, and legs.[2] Additionally, edema is a symptom of many conditions which include heart failure, chronic venous disease, and kidney disease.

Due to the bioactivity and therapeutic potential of the peptide solomonamide A, the structurally related compound solomonamide B is also of particular biological interest. Unfortunately, the shortage of isolated solomonamide B (3.6 mg) prohibited a proper analysis of its biological activity.[1]

Figure 1. *Theonella swinhoei*

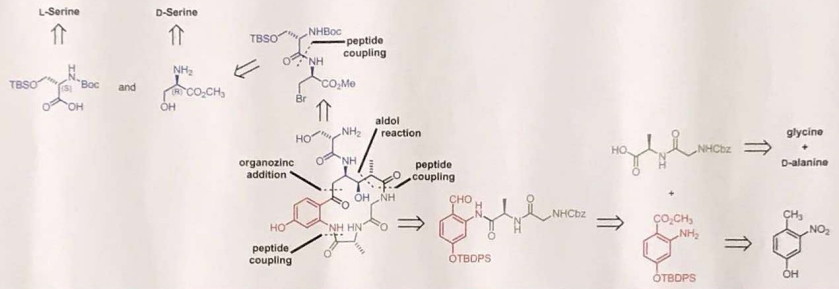
Another compound that has been studied from *T. swinhoei* is 4-methylene sterol. This particular marine metabolite has been found to be cytotoxic against many types of cancer.[3]

In this study, the synthesis of solomonamide B is the main objective so that its biological activity may be adequately studied. Solomonamides A and B are also structurally interesting due to the ADMOA and AHMOA moieties[4] (shown below in red) that are unique to these natural products. Furthermore, the synthesis in the laboratory is beneficial compared to isolation, given the ratio of dry sponge to the isolated amounts of cyclic peptides under investigation.

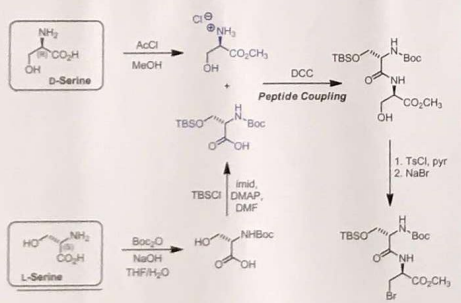


Additionally, other studies are exploring the potential treatment of major psychological disorders, including, but not limited to, MDD and schizophrenia, using anti-inflammatory drugs[5] a class in which the solomonamides are included.

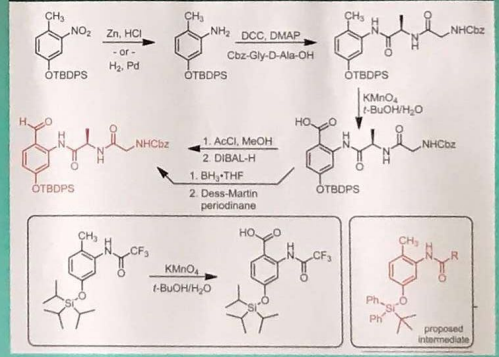
Retrosynthetic Analysis of Solomonamide B



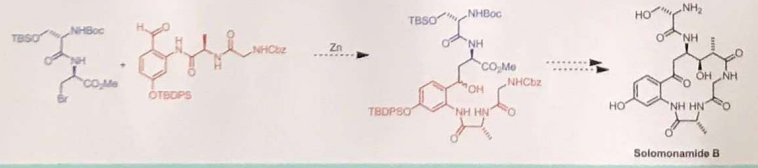
Serine Derived Subunit



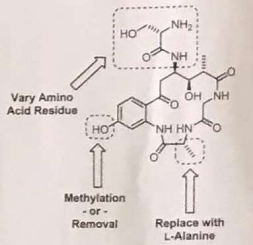
Aromatic Subunit



Proposed Fragment Coupling Through Zinc-Mediated Reaction



Future SAR Studies



The molecular activity map has yet to be constructed for the solomonamides, so further investigation may include the modification of the solomonamide skeleton. These changes encompass, among others, variation of the amino acid residues or removal of the hydroxyl group boxed above.

References

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2. Clein LJ. Edema. Palliative Medicine. Saunders Elsevier; 2009
3. Guo, J.-K.; Chiang, C.-Y.; Lu, M.-C.; Chang, W.-B.; Su, J.-H. *Marine Drugs* **2012**, *10*, 1536.
4. ADMOA = 4-amino(2'-amino-4'-hydroxyphenyl)-3,5-dihydroxy-2-methyl-6-oxohexanoic acid; AHMOA = 4-amino-6-(2'-amino-4'-hydroxyphenyl)-3-hydroxy-2-methyl-oxohexanoic acid
5. Fond, G., Hamdoni, N.; Boukouaci, W.; Drancourt, N.;Dargel, A.;Oliviera, J.; Le Guen, E.; Leboyer, M. Acta Psychiatr. Scand. **2014**, *129*, 163.

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