S32-2 Structural diversity of natural products derived by non-enzymatic processs

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In the search for biologically active compounds from marine organisms and fungi, we isolated new metabolites, which may be produced by non-enzymatic formations together with enzymatic reactions. It suggests that the non-enzymatic reaction is also an important mechanism to produce structurally diverse natural products. Recently, we found the following two examples. (1) We isolated a new compound, himeic acid A (**1**), containing a pyrone ring, from the fungus *Aspergillus japonicus* MF275 as the selective inhibitor of the ubiquitin activating enzyme E1 (*Bioorg. Med. Chem. Lett.* **2005**, *15*, 191). During the prolonged culture, **1** gradually decreased and instead a pyridone derivative, himeic acid C (**3**), increased. Recently, Fujii revealed that no gene responsible for conversion from the pyrone to pyridone was found in the *him* gene cluster. Thus, the formation from **3** to **1** was suggested to be a non-enzymatic reaction. Then, we found **1** was converted to **3** in the presence of ammonium chloride in the buffer (pH 5.5), which suggested the incorporation of a nitrogen atom in ammonium to **1** to yield **3**. (2) We isolated new compounds, ceylonins A-F, from the sponge *Spongia ceylonenesis* (*J. Nat. Prod.* **2017**, *80*, 90). From the structural point of view, they were derived from a main spongian diterpene (**4**) together with a C3 unit. We found that the reaction of **4** and acrylic acid in DMSO afforded ceylonins A-F. It suggested that acrolein that was released from ω-3 fatty acids, e.g. EPA and DHA, by oxidative cleavage or acrylic acid that was derived from acrolein may react with **4** to form ceylonins.