S43-5 Total synthesis and biological evaluation of natural products

◯Takayuki DOI[1]

[1]Tohoku Univ. Grad. Sch. of Pharm. Sci.

Telomestatin (**1**), isolated from *Streptomyces anulatus* 3533-SV4, is a potent specific telomerase inhibitor since it acts on a human telomere sequence to stabilize the specific DNA structure called G-quadruplex without affecting DNA polymerases or reverse trascriptases. The unique macrocyclic structure of telomestatin consists of the linkage of two methyloxazoles, five oxazoles, and one thiazoline ring. A total synthesis of telomestatin was achieved as follows: 1) Coupling of cysteine-containing trisoxazole amine and serine-containing trisoxazole carboxylic acid, followed by macrocyclization, provided a 24-membered diamide; 2) The seventh oxazole ring was constructed by a Shin's procedure via dehydroamide; 3) Cyclodehydration of a (*R*)-cysteine-(S-*t*-Bu) moiety using the Kelly's method with some modification furnished (R)-telomestatin. The absolute configuration was determined by comparison of the CD spectra of the natural product and the synthetic compound. Synthesis and biological evaluation of its enantiomer and various telomestatin derivatives will also be discussed.