

SYNTHETIC STUDY ON DOLASTATIN 3 BEARING THIAZOLE RING

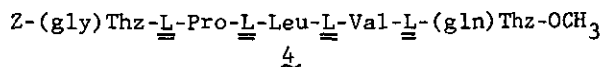
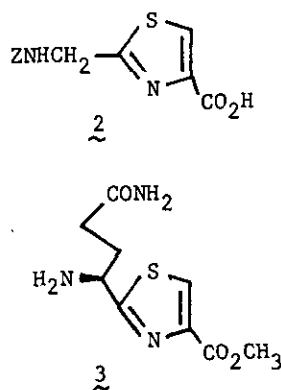
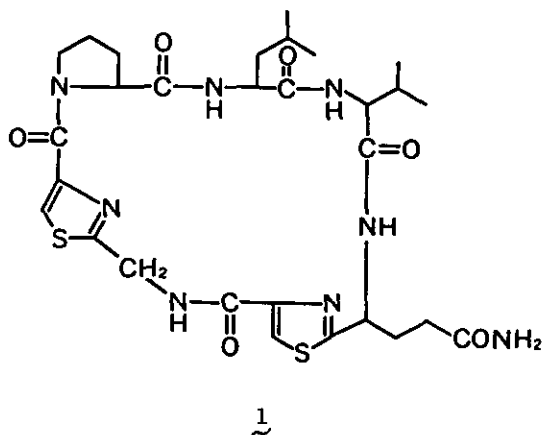
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Dolastatin 3 (1),¹⁾ a cyclic peptide containing two unusual thiazole amino acids, was isolated as one of nine antineoplastic and/or cytotoxic substances from the Indian Ocean sea hare *Dolabella auricularia*. The structure of 1 was proposed as cyclo[Pro-Leu-Val-(gln)Thz-(gly)Thz] and each amino acid unit was deduced to bear the usual L-configuration.

We attempted to synthesize the proposed structure 1 for the structural determination and biological evaluations.

Two thiazole amino acids 2 and 3 were prepared by the oxidation of the corresponding thiazolidines which were obtained by the condensation of the corresponding α -amino aldehyde derivatives²⁾ with L-cysteine methyl ester. The protected peptide 4 containing the full carbon skeleton of 1 was constructed from 3. Deprotection of 4 and cyclization in the final step is now under investigation.



1) G.R. Pettit, Y. Kamano, P. Brown, D. Gust, M. Inoue, and C.L. Herald, J. Am. Chem. Soc., 104, 905 (1982).

2) Y. Hamada and T. Shioiri, Chem. Pharm. Bull., 30, 1921 (1982).