# SYNTHETIC STUDY ON DOLASTATIN 3 BEARING THIAZOLE RING

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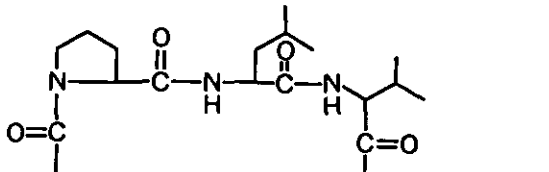
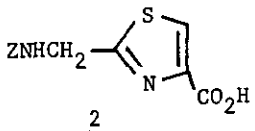
Dolastatin 3 (1),[1] a cyclic peptide containing two unusual thiazole amino acids, was isolated as one of nine antineoplastic and/or cytotoxic substances from the Indian Ocean sea hare Dolabella auricularia. The structure of 1 was proposed as cyclo[Pro-Leu-Val-(gln)Thz-(gly)Thz] and each amino acid unit 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 derivatives[2] 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



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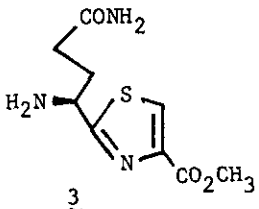

3

Z-(gly)Thz-L-Pro-L-Leu-L-Val-L-(gln)Thz-$OCH_3$

4

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).