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インドネシア産海綿 *Spongia ceylonensis* から得られた新規ジテルペンの構造と破骨細胞形成阻害活性

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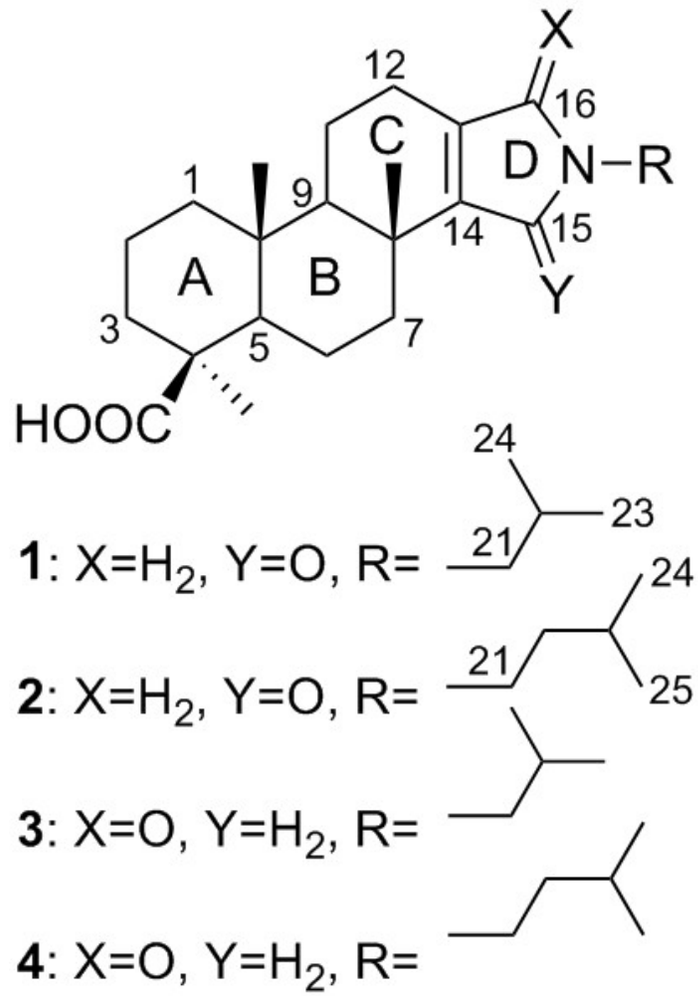
【Objective】In our continuous search for inhibitors of osteoclastogenic differentiation of murine RAW264 cells from marine organisms, the marine sponge *Spongia ceylonensis* collected in Indonesia showed significant inhibition. The bioassay-guided purification afforded four new nitrogenous spongian diterpenes **1-4**, along with 8 known spongian diterpenes and one known norscopalane diterpene. [1,2)]

【Results and discussion】The structures of **1-4** were established by 2D NMR spectra. Compounds **1-4** contain amide nitrogen replacing the oxygen of classical spongian diterpenes. The amide carbonyl groups of **1** and **2** occupy position 15 whereas those of **3** and **4** occupy position 16. The nitrogens of **2** and **4** are substituted with isopentyl residue mostly derived from the decarboxylated amino acid leucine. However the nitrogens of **1** and **3** are substituted with isobutyl residue mostly derived from the decarboxylated amino acid valine. Structure activity relationship of the isolated compounds revealed characteristic regioselective inhibition of RANK-RANKL interaction based on the position of ring D carbonyl group. A computational docking study against RANKL was exploited to predict a hypothetical mechanism for the inhibitory activity and explain regioselective inhibition.



1) Hyosu, M.; Kimura, J. *J. Nat. Prod.* **2000**, *63,* 422.
2) Pham, A. T. *et al*., *Tetrahedron Lett.* **1992**, *33,* 1147.