Synthesis of New Analogues of the Bengamides: Peptidyl Bengamides and Molecular Probes

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Isolated from sponges of the *Jaspidae* family, first members where discovered in 1986. The bengamides represent an interesting and unprecedented family of natural products that displayed striking antitumor activities [1]. The recognition of these natural products as antiangiogenic compounds, in virtue to their inhibition of methionine aminopeptidases, prompted intense research activities in the chemical and biological fields. In fact, the total synthesis of the natural products, together with an extensive variety of analogues, has been reported in the literature [2]. Particularly, we have recently developed a new synthetic methodology which allowed rapid and efficient access to the natural bengamide E (1), together with a wide library of analogues of which the cyclopentyl analogue 2 was identified as a more potent antitumor compound with respect to its natural congener [3]. As continuation of these synthetic efforts, with the objective of identifying new potent and promising analogues, we wish to report our recent synthetic studies directed to the synthesis of new bengamide analogues, featured by the replacement of the caprolactam fragment by a peptidyl residue (compounds type 3). On the other hand, in order to gain insight into the mechanism of the biological action of the bengamides, we describe the preparation of the N-alkyl derivatives 4 and 5, which represent interesting molecules that could be employed as suitable molecular probes.