TOTAL SYNTHESIS AND BIOLOGICAL EVALUATION OF PELOFEN, A NEW MICROTUBULE-STABILIZING AGENT

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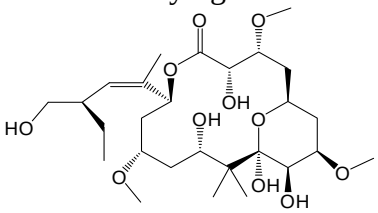
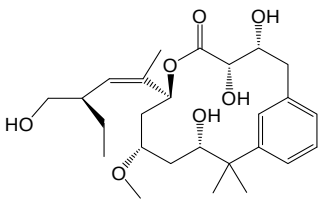
Peloruside A (**1**) is a novel macrolide with potent anti-cancer activity, discovered in 2000 from a marine sponge [1]. Like Paclitaxel (**2**) and Epothilon (**3**), Peloruside A is a microtubule-stabilizing agent, but it binds to a different binding site [2] and shows a better activity against multidrug-resistant cancer cell lines. Moreover, the presence of several hydroxyl groups causes a better solubility in the blood stream. The binding site at α-tubuline and the biologically active conformation of (+)-Peloruside were confirmed in 2006 by Miller *et al*. [3a] via NMR and in 2014 by Steinmetz *et al.* [3b] via XR-analysis. The absolute configuration was established via total synthesis by De Brabander *et al.* [4]. Since then, a number of total syntheses have been reported [5].



1 Peloruside A



2 Pelofen

In our endeavour for designing simplified analogues of Peloruside, we developed a modular synthesis for Pelofen (**2**), possessing a simple phenyl ring instead of the pyranose ring. Biological screening revealed that this compound still shows pronounced microtubule stabilizing activity, thus rendering it highly promising as a potential lead for cancer treatment [6].

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