Contribution to the discovery of the biological mechanism of Buruli Ulcer thanks to a modular total synthesis

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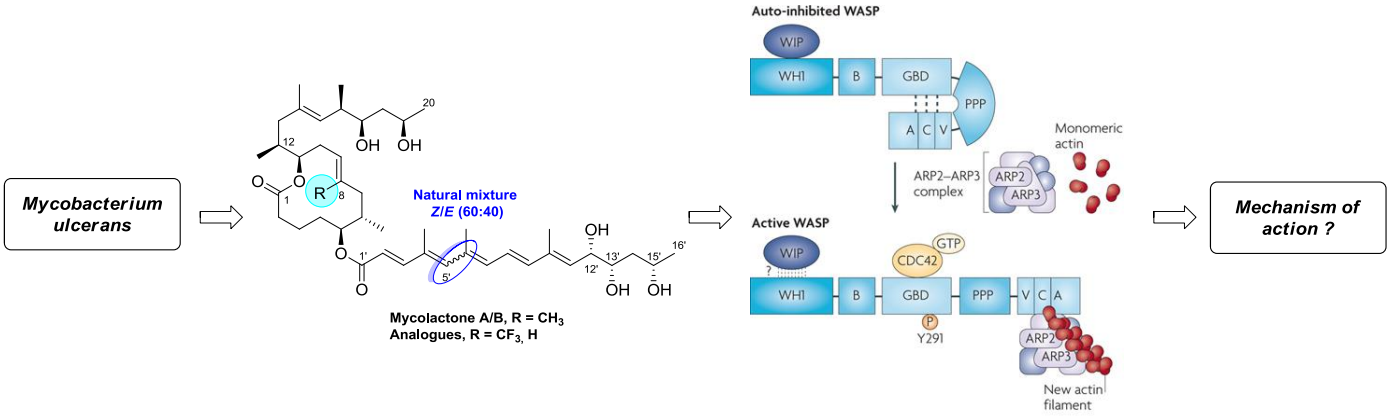
Buruli ulcer is a necrotizing skin disease present in more than thirty countries in the world, located mainly in West and Central Africa but also in Australia and in Japan.[1] This infection is caused by *Mycobacterium ulcerans* (*M. u.*) that secretes a macrolide toxin called mycolactone, which is the first polyketide isolated from a human pathogen. The disease is characterized by the formation of progressive necrotic lesions combined with a lack of acute inflammatory response, and mycolactone is known to be directly involved in the biological mechanism. Recently, two important regulators of the actin cytoskeleton, WASP and N-WASP, have been discovered as the first proteic targets of the toxin.[2-3]

To date no specific and efficient treatment of Buruli ulcer has been developed which correlates with the dramatic lack of understanding of the chemical and biological mechanisms connected to the disease. Moreover, the difficulty encountered by biologists to obtain this toxin from cultures of *M. u.*, led us to develop a diverted synthetic route for obtaining this toxin and its analogues with a high degree of purity in order to understand the onset of the disease.[4-5]



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