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TITLE

Synthesis and Biological Evaluation of Benzo[j] phenanthridine-7,12-diones as Anti-tuberculosis Agents

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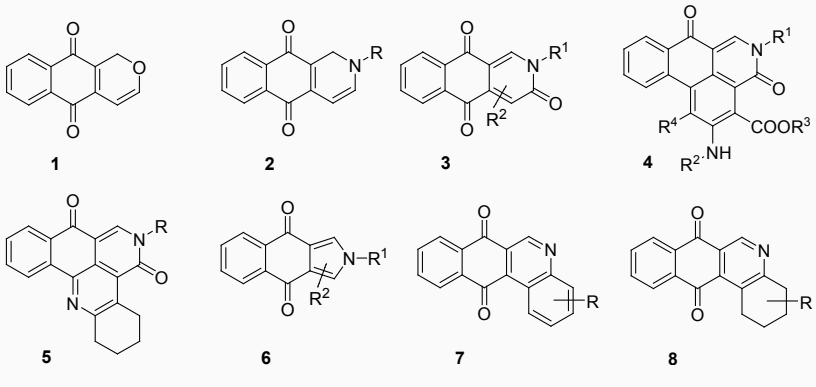
Pentalongin 1, a 3,4-dehydropyranonaphthoquinones isolated as the active principle from the roots of the Central East African medicinal plant Pentas longiflora, was synthesized by several synthetic methods including ring closing metathesis of a suitable precursor. Although pyranonaphthoquinones represent a large class of natural products, reports of their naturally occurring 2-aza analogues, all of which have been isolated as 2-azaanthraquinones, are scarce in the literature. Nevertheless, this class of compounds has been found to possess interesting anti-tumor, antifungal and antibiotic properties. Within this framework, structural modifications of the 2-azaanthraquinone skeleton were envisaged, first by synthesizing 1,2-dihydrobenz[g]isoquinoline-5,10-diones 2 as the corresponding N-analogues of pentalongin 1. These compounds 2 constitute a novel heterocyclic skeleton, which was difficult to obtain due to spontaneous oxidative aromatization to the corresponding 2-azaanthraquinones. Investigation towards structural modifications of N-substituted benz[g]isoquinoline-3,5,10(2H)-triones 3 resulted in a straightforward synthesis of new tetracyclic naphtho[3,2,1-de]isoquinoline-4,7-diones 4 and benzo[h]pyrido[3,4,5-kl]-1,2,3,4-tetrahydroacridine-5,8-diones 5. Different synthetic routes towards substituted benzo[f]isoindole-4,9-diones 6 were developed since this structural unit was found in several bioactive natural products.



Finally, benzo[j]phenanthridine-7,12-diones 7, which are compounds with promising DNA-intercalating properties, were synthesized by an intramolecular Heck reaction. The corresponding tetrahydro derivatives 8 were synthesized by coupling of appropriate naphthoquinones with enamines. In vitro testing of these compounds for their activity against Mycobacterium tuberculosis showed promising results which will be unravelled.

Biography

Norbert De Kimpe obtained the PhD degree (1975) from Ghent University. He performed postdoctoral research work at the University of Massachusetts (Boston) (1979) and at the CNRS (Paris, France) (1983). He is full professor at Ghent University and was a guestprofessor at the Universities of Perpignan, Helsinki, Siena, Barcelona, Sofia, Buenos Aires, and Pretoria. He was awarded the degree of Doctor honoris causa from the Russian Academy of Sciences in Novosibirsk (1998) and from the University of Szeged (Hungary)(2007). He is the author of 580 articles in international SCI- journals. His research interests include the synthesis of bioactive heterocycles and natural products, and flavour chemistry.