

Total synthesis of kidamycinone

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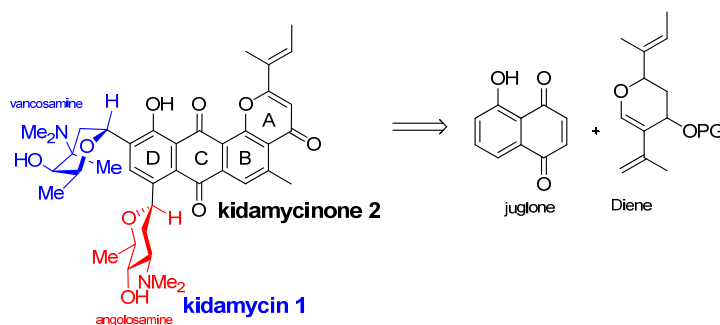
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The pluramycins¹ are a group of naturally occurring antibiotics with antitumoral activity. They display a 4*H*-anthra[1,2-*b*]pyran-4,7,12-trione structure with attached *C*-glycoside moieties at C8 and C10 as well as a lateral chain branched at carbon C1. Kidamycin **1**, one of the earliest known members of this family of antibiotics, was isolated from *Streptomyces* soil bacteria. From a structural point of view, kidamycin **1** is adorned by two *meta*-disposed aminosugars – *D*-angolosamine and *N,N*-dimethyl-*L*-vancosamine branched at C8 and C10, respectively , a 2-butenyl residue attached at C1 and two additional substituents, a methyl at C5 and a hydroxyl at C11.

Taking advantage of our experience and expertise in the total synthesis of natural compounds such as angucyclines or Brefeldin A and in the development of new methodologies in organic synthesis,² we project a novel total synthesis of kidamycin **1**. The challenge was here to propose a convergent fragment-assembly strategy with modifiable building blocks in order to open the route to the preparation of a range of pluramycins or simplified analogues to be tested as potential therapeutic agents.

In this communication we will present an efficient total synthesis of kidamycinone **2**, the aglycone part of kidamycin. The pluramycinone skeleton is formed following an original and convergent approach to construct cycle B. This one is obtained starting from original diene and juglone dienophile using a key Diels-Alder reaction. The targeted kidamycinone **2** was finally obtained in 9 steps and 22% overall yield.



References :

1. For a general review, see: Hansen, M. R.; Hurley, L. H. *Acc. Chem. Res.* **1996**, 29, 249-258.
2. a) Maingot, L. ; Vu, N-Q. ; Collet, S. ; Guingant, A. ; Martel, A. ; Dujardin, G. *Eur. J. Org. Chem.* **2009**, 3, 412-422 ; b) L. Foulgoc, D. Sissouma, M. Evain, S. Collet, A. Guingant; *Synlett* **2012**, 768. c) M. Pantin ; D. Zon ; R. Vomiandry; L. Foulgoc; D. Sissouma; A. Guingant; S. Collet , *Tetrahedron Lett.* **2015**, 56, 16, 2110.