

## Recent advances in the synthesis of kidamycin

Guerrero-Vásquez, Guillermo A.<sup>a</sup> ; Mabit Thibaud<sup>a</sup> ; Siard Aymeric<sup>a</sup> ; Carreaux, François<sup>b</sup> ; Dujardin, Gilles<sup>c</sup> and Collet, Sylvain<sup>a</sup>

<sup>a</sup> Université de Nantes, CEISAM UMR-CNRS 6230, 2 Rue de la Houssinière, BP 92208, 44322 NANTES CEDEX 3, Tel : 0251125410, email. [Sylvain.Collet@univ-nantes.fr](mailto:Sylvain.Collet@univ-nantes.fr)

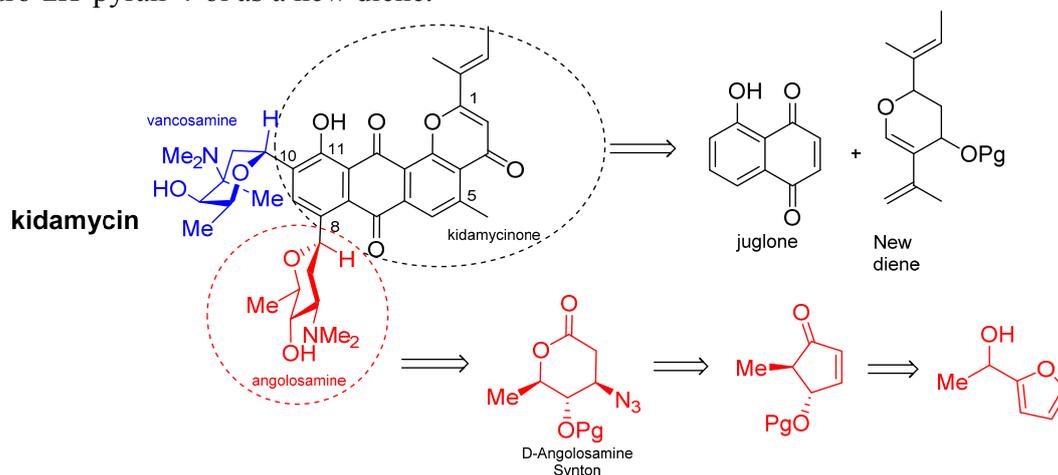
<sup>b</sup> Université de Rennes, Institut des Sciences Chimique de Rennes UMR CNRS 6226, Campus de Beaulieu, Bât 10A, avenue du Général Leclerc, 35042 RENNES

<sup>c</sup> Université du Maine, IMMM UMR CNRS 6283, Avenue O. Messiaen, 72085 Le Mans,

The pluramycins 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, one of the earliest known members of this family of antibiotics, was isolated from *Streptomyces* soil bacteria. This compound displays a wide spectrum of antimicrobial activity and also exhibits cytotoxicity against leukaemia L-1210 and Ehrlich ascites tumors.

From a structural point of view, kidamycin 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.

Our retrosynthetic analysis of kidamycin lies in the convergent binding of the both aminosugar synthon units on a naphthoquinone moiety as dienophile before using a Diels-Alder cycloaddition step to build the tetracyclic skeleton. To validate this strategy, the synthesis of kidamycin aglycone (kidamycinone) was recently achieved in a convergent manner by application of a Diels-Alder approach<sup>1</sup> to juglone as the dienophile and 5-isopropenyl-3,4-dihydro-2*H*-pyran-4-ol as a new diene.



The  $\beta$ -controlled C-arylation at C8 position will be performed by condensation of lithiated naphthalene-diol skeleton (precursor of naphthoquinone moiety) onto the D-angolosamine lactone. The first approximation to the synthesis of D-angolosamine synthon has been carried out in racemic form starting from the 2-furyl-methylcarbynol, easily synthesized from furfural.

1. a) L. Foulgoc, D. Sissouma, M. Evain, S. Collet, A. Guingant, *Synlett*, **2012**, 23, 768. b) M. Pantin ; D. Zon ; R. Vomiandry; L. Foulgoc; D; Sissouma; A. Guingant; S. Collet , *Tetrahedron Lett.* **2015**, 56, 16, 2110.