Laney College, Department of Chemistry

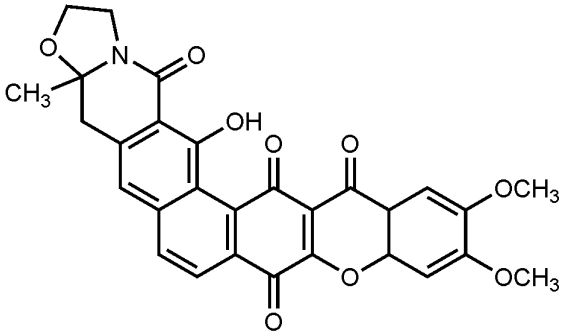
Presents

The 25th Anniversary Lecture
on
Synthetic Studies on the Total Synthesis of Cervinomycin

(Dissertation Research)

Stephen Corlett

Wednesday, May 23, 2018
1:00 - 2:00 pm
Room D-200



Cervinomycin A_2

Topic

I will present the chemistry on studies directed toward the chemical synthesis of the natural product cervinomycin. The studies were the basis of my dissertation work that led to my Ph.D., afforded 25 years ago on May 16, 1993.

The work culminated in the dissertation defense, which is presented again here, 25 years later. Where the presentation is officially a graduate-level chemistry presentation, there will be a little something for everyone. Come hear the story as it unfolded, starting 30 years ago, when the research was begun, and also the challenges of recreating a lecture from 25 years ago. The original abstract is attached.

Abstract

Synthetic studies toward cervinomycin, a heptacyclic xantheno-isoquinolone antibiotic, are described. Two convergent general strategies involving sequential annelations from similar D-ring intermediates with AB- and FG-ring fragments is presented. Diels-Alder reaction of 5-substituted-2-furfural hydrazones with maleic anhydride provided the D-ring intermediates for both methods.

In the first approach, 1,3-dihydro-5-methyl-3-oxo-1-(phenylsulfonyl)-4-isobenzofurancarboxylic acid, methyl ester, prepared in 6 steps from 5-methyl-2-furancarboxaldehyde in 36% overall yield, was condensed with 6,7-dimethoxy-4*H*-1-benzopyran-4-one to give 6,11-dihydroxy-2,3-dimethoxy-9-methyl-12-oxo-12*H*-benzo[*b*]xanthene-10-carboxylic acid, methyl ester in 72 % yield. The 9-phenylthiomethyl derivative was similarly prepared in 55% yield. Construction of the C- and remaining rings of cervinomycin from this intermediate through the derived toluate carbanion was examined.

In the second approach, 3-(1,3-dioxan-2-yl)-6-(phenylsulfinylmethyl)-1,2-benzenedicarboxylic acid, dimethyl ester, prepared in 7 steps from 5-chloromethyl-2-furancarboxaldehyde in 42% overall yield, was condensed with 4-(2-methyl-1,3-dioxolan-2-yl)but-2-enoic acid, methyl ester to afford 2-(1,3-dioxan-2-yl)-8-hydroxy-6-[(2-methyl-1,3-dioxolan-2-yl)methyl]-1,7-naphthalenedicarboxylic acid, dimethyl ester, the phenolic C-ring, in 43% yield. Subsequent hydrolysis and lactonization gave a quantitative yield of 8-formyl-10-hydroxy-3-methyl-1-oxo-1*H*-naphtho[2,3-*c*]pyran-9-carboxylic acid, methyl ester, a pivotal intermediate to a series of 3-substituted furano[8,9-*c*]naphtho[2,3-*c*]pryan-1,10-diones that were examined for construction of the benzo[*b*]xanthenone portion of cervinomycin.

The intermediate 8-formyl-2,3-dihydro-6-methoxy-12a-methyl-5(12*H*)-oxo-12a*H*-benzo[*g*]oxazolo[3,2-*b*]isoquinoline-7-carboxylic acid, methyl ester, an ABCD-fragment of cervinomycin was also synthesized.