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The polyhydroxy cyclopentene, a total synthesis of (–)-pentenomycin

Mohindra Seepersaud and Yousef Al-Abed*

The Picower Institute for Medical Research, 350 Community Drive, Manhasset, NY 11030, USA

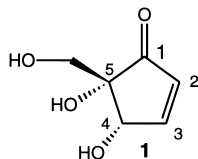
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Abstract

The functionalized cyclopentene **2** was converted in five steps to (–)-pentenomycin **1**. © 2000 Elsevier Science Ltd. All rights reserved.

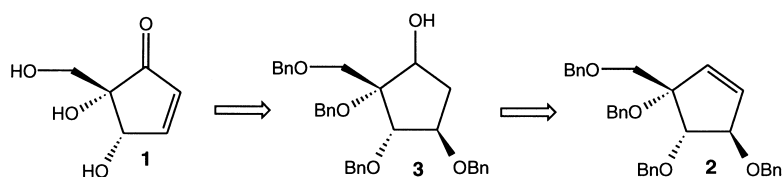
Keywords: cyclopentenes; cyclopentenones; cyclization; antibiotics.

The pentenomycin antibiotics have attracted considerable attention due to its wide range of structural and stereochemical features and biological activities.^{1a} Pentenomycin **1** was isolated by Umino and co-workers in 1973 from the culture broths of *Streptomyces eurythermus*,^{1b,c} while epipentenomycin the C-4 diastereomer, was isolated from carpophores of *Perziza* sp.² There have been several approaches³ to synthesize these antibiotics and their derivatives however, an expeditious and efficient approach is still needed.



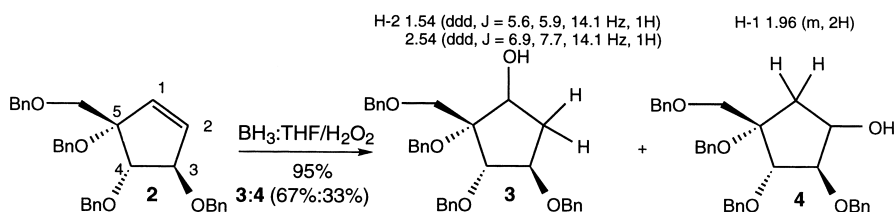
In connection, we recently reported the synthesis of a polyhydroxylated cyclopentene **2**,⁴ a useful template that can be widely utilized in synthesis of highly functionalized five-membered rings. The synthesis of **2** was done via a ring closing metathesis (RCM) in five steps with a 90% yield. A comparison of cyclopentene **2** with pentenomycin **1** indicates that the stereochemistry around the C-4 and C-5 are identical. Therefore, logical retrosynthetic analysis suggests that our key cyclopentene intermediate **2** can be converted to pentenomycin **1**, via elaboration of precursor **3** (Scheme 1).

* Corresponding author. E-mail: yal-abad@picower.edu



Scheme 1.

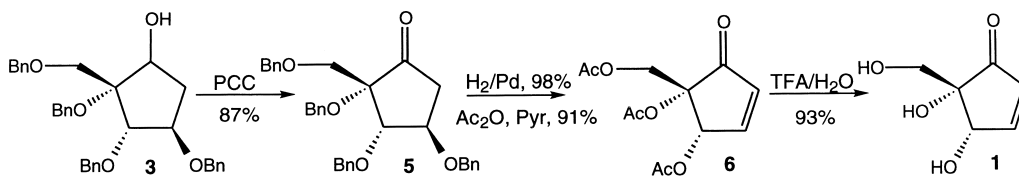
Thus, compound **2** was treated with $\text{BH}_3\text{:THF}$ to give the two regioisomeric alcohols **3** and **4** (2:1) (Scheme 2). The use of $\text{BH}_3\text{:SMe}_2$ gave no additional selectivity while catecholborane and 9-borobicyclo[3.3.1]nonane gave no reaction.⁵ The structural identification of these regioisomers **3** and **4** were based on the coupling constants of the new methylene protons at C-2 and C-1, respectively (Scheme 2).



Scheme 2.

Compound **3** was oxidized by PCC to afford the corresponding ketone **5** (Scheme 3). Additional confirmation of the regiochemistry of the carbonyl group came from the coupling constants of the C-2 methylene protons of **5**, where two signals at δ 2.30 (dd, $J = 7.7, 20.0$ Hz, 1H) and δ 2.79 (dd, $J = 7.4, 20.0$ Hz, 1H) were observed. However, the corresponding ketone of the other regioisomer **4** showed only one signal for the C-1 protons at δ 2.61 (d, $J = 3.7$ Hz, 2H).

The ketone **5** was hydrogenated, then treated with pyridine/acetic anhydride to furnish the acetylated enone **6**. Deprotection of the acetate **6** with trifluoroacetic acid/ H_2O afforded (–)-pentenomycin **1** (Scheme 3). The ^1H and ^{13}C NMR of **6** and **1** were identical with those reported in the literature.^{1,2,6}



Scheme 3.

In summary, a concise and efficient synthesis of the (–)-pentenomycin **1** was demonstrated in five steps (46% yield), using our key polyhydroxy cyclopentene intermediate **2**.

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6. For compound **1**: ^1H NMR (D_2O , 270 MHz) δ 3.61 (ABq, $\Delta\delta=0.07$ ppm, 2H, $J=11.6$ Hz), 4.72 (dd, $J=1.2, 2.7$ Hz, 1H), 6.34 (dd, $J=1.2, 6.2$ Hz, 1H), 7.74 (dd, $J=2.7, 6.2$ Hz, 1H) ^{13}C NMR (D_2O , 67.5 MHz) δ 63.3, 71.7, 76.3, 133.5, 164.6, 209.8.