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FIRST SYNTHESIS OF AN EPIMER OF (±)-PENTENOMYCIN I

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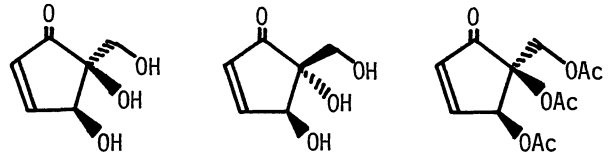
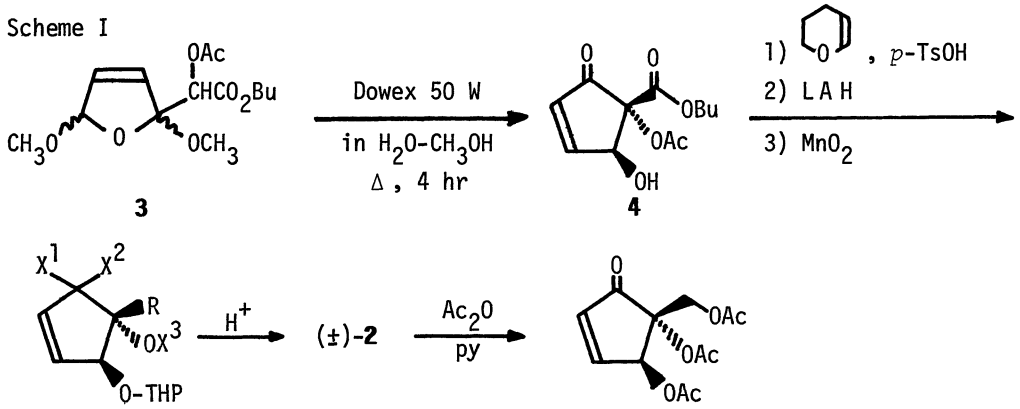
An epimer of pentenomycin I was first synthesized starting from a furan derivative. The synthetic route involves acid-catalyzed transformation of a 2,5-dihydro-2,5-dimethoxyfuran derivative to a cyclopentenone derivative, which is a key intermediate in the synthesis of the expected compound.

Pentenomycin I **1** and the epimer **2** belong to a novel class of cyclopentenoid antibiotics.[1-3] Recently, Smith and co-workers reported a total synthesis of (±)-**1** utilizing α-ketovinyl anion equivalents,[4] whereas **2** has not yet been synthesized. We wish to report herein the first synthesis of (±)-**2** in which a stereoselective transformation of 2,5-dihydro-2,5-dimethoxyfuran **3** to the hydroxycyclopentenone **4** is involved as a key step (Scheme I).[5]



1 **2** **8'**

Scheme I

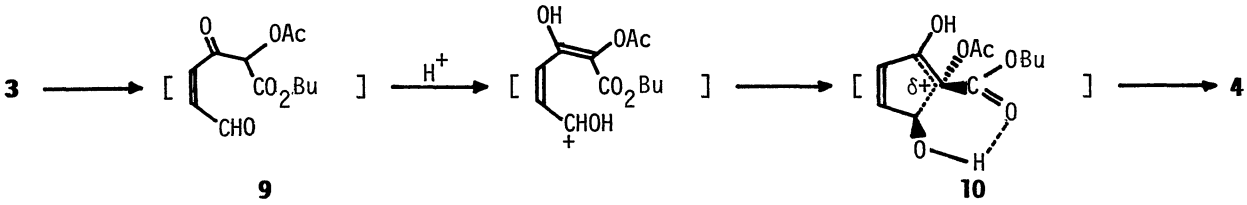


3 **4** **8**

5: X^1, X^2 = O, X^3 = Ac, R = CO_2Bu
6: X^1 or X^2 = OH, X^3 = H, R = CH_2OH
7: X^1, X^2 = O, X^3 = H, R = CH_2OH

The starting compound **3** was synthesized by the anodic oxidation of easily available α-(butoxycarbonyl)furfuryl acetate[6] in methanol, yield being 89% at the stage when 4.2 *F*/mol of electricity was passed. Subsequent acid-catalyzed hydrolysis of **3** with Dowex 50 W in methanol-water (1 : 3) resulted in the formation of a crystalline product (mp 81.8-83.0 °C, 77%). Although the stereochemistry of the product could not be determined at this stage, it was assigned the structure **4** after the spectroscopic data of the triacetate **8** derived from the final product (±)-**2** were analyzed. The process from **3** to **4** may involve generation of the intermediate **9**.

The exclusive formation of **4** from **9** may be explained in terms of a hydrogen bonding between a hydroxyl group and a carbonyl oxygen in the ester group as depicted in the intermediary state **10** which leads to the formation of **4**.



9 **10**

The reduction of the alkoxycarbonyl group in **4** to a hydroxymethyl group without reducing the enone carbonyl group will yield (±)-**2**. However, the direct formation of (±)-**2** from **4** was not successful since the protection of the carbonyl group was not achievable. Accordingly, after the hydroxyl group of **4** was protected with dihydropyrane (81%), both carbonyl and butoxycarbonyl groups were reduced with LAH to give **6** (48%). The allylic hydroxyl group in **6** was selectively oxidized by MnO_2[7] (44%), and (±)-**2** (syrup) was obtained in a 40% yield by removal of the protection group from the resulting enone **7**. The pmr spectrum[5] of (±)-**2** showed a pattern different from that[1] of (±)-**1**. Furthermore, comparison of the pmr spectrum[5] of **8** (mp 79.5-80 °C) with that[2] of **8'** derived from (±)-**1** supported the assigned structure of (±)-**2**.

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References and Notes

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5) All compounds gave reasonable spectroscopic data and elemental analyses to the assigned structures. Pmr data are as follows: **4**; δ ($CDCl_3$) 0.86 (t, 6 Hz, 3H), 1.00-1.90 (m, 4H), 2.22 (s, 3H), 3.76 (d, 5.6 Hz, 1H), 4.11 (t, 6 Hz, 2H), 5.03 (m, 1H), 6.33 (dd, 6.0 and 1.8 Hz, 1H), 7.55 (dd, 6.0 and 2.2 Hz, 1H). **5**; δ (CCl_4) 0.93 (t, 6 Hz, 3H), 1.00-1.90 (m, 10H), 2.13 (s, 3H), 3.20-3.90 (m, 2H), 4.05 (t, 6 Hz, 2H), 4.77 (m, 1H), 5.13 (t, 2 Hz, 1H), 6.30 (dd, 6.0 and 1.4 Hz, 1H), 7.25 (dd, 6.0 and 2.2 Hz, 1H). **6**; δ ($CDCl_3$) 1.20-2.00 (m, 6H), 3.20-4.00 (m, 6H), 4.38 (br s, 3H), 4.68 (m, 1H), 5.75 (s, 2H). **7**; δ ($CDCl_3$) 1.10-2.00 (m, 6H), 2.45 (m, 2H), 3.60 (m, 4H), 4.70 (m, 2H), 6.15 (dd, 6.0 and 1.3 Hz, 1H), 7.50 (dd, 6.0 and 1.8 Hz, 1H). (±)-**2**; δ (D_2O) 6.23 (dd, 6.0 and 1.8 Hz), 7.53 (dd, 6.0 and 2.2 Hz). **8**; δ ($CDCl_3$) 2.04 (s, 3H), 2.13 (s, 6H), 4.07 (d, 13 Hz, 1H), 4.56 (d, 13 Hz, 1H), 6.29 (dd, 2.1 and 1.8 Hz, 1H), 6.50 (dd, 6.2 and 1.8 Hz, 1H), 7.39 (dd, 6.2 and 2.1 Hz, 1H).

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