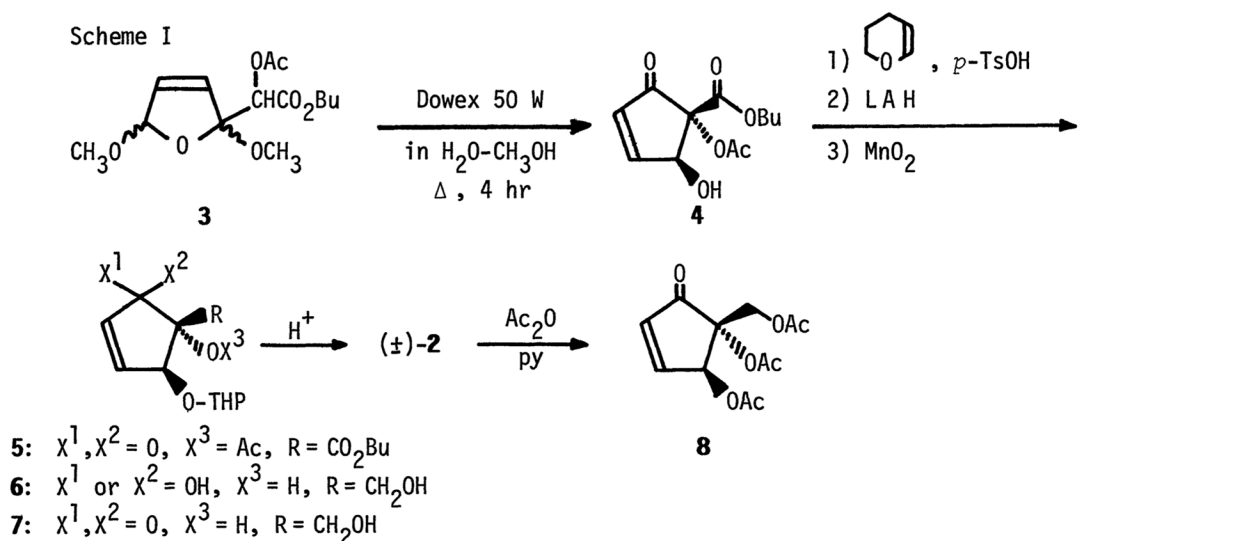


FIRST SYNTHESIS OF AN EPIMER OF (±)-PENTENOMYCIN I

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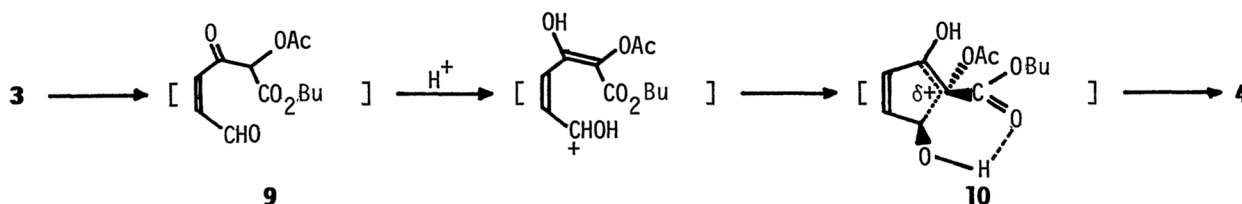
An epimer of pentenomycin I was first synthesized starting from a furan derivative. The synthetic route involves acid-catalyzed transformation of a 2,5-dihydro-2,5-dimethoxyfuran derivative to a cyclopentenone derivative, which is a key intermediate in the synthesis of the expected compound.

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 -ketovinyI 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⁾



The starting compound **3** was synthesized by the anodic oxidation of easily available α -(butoxycarbonyl)furfuryl acetate⁶⁾ 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**.



The reduction of the alkoxycarbonyl group in **4** to a hydroxymethyl group without reducing the enone carbonyl group will yield (\pm)-**2**. However, the direct formation of (\pm)-**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 dihydropyran (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 (\pm)-**2** (syrup) was obtained in a 40% yield by removal of the protection group from the resulting enone **7**. The pmr spectrum⁵⁾ of (\pm)-**2** showed a pattern different from that¹⁾ of (\pm)-**1**. Furthermore, comparison of the pmr spectrum⁵⁾ of **8** (mp 79.5-80 °C) with that²⁾ of **8'** derived from (\pm)-**1** supported the assigned structure of (\pm)-**2**.

Acknowledgment. One of the authors (Y.M.) wishes to thank the Ministry of Education, Japan, for a Grant-in-Aid (No. 475652).

References and Notes

- 1) K. Umino, T. Furumai, N. Matsuzawa, Y. Awataguchi, Y. Ito, and T. Okuda, *J. Antibiot.*, **25**, 506 (1973).
- 2) K. Umino, N. Takeda, Y. Ito, and T. Okuda, *Chem. Pharm. Bull.*, **22**, 1233 (1974); T. Date, K. Aoe, K. Kotera, and K. Umino, *ibid.*, **22**, 1963 (1974).
- 3) K. Hatano, T. Hasegawa, M. Izawa, M. Asai, and H. Iwasaki, Japan, Kokai, **75**, 70,597 (June 1975).
- 4) S. J. Branca and A. B. Smith, III, *J. Am. Chem. Soc.*, **100**, 7767 (1978).
- 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). (\pm)-**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).
- 6) A. Osman, Jr. and Z. Aleksander, *Rocz. Chem.*, **42**, 453 (1968); *Chem. Abstr.*, **69**, 77029y (1968).
- 7) B. F. Reid, A. McLean, E. M. Usherwood, and M. Yanker, *Can. J. Chem.*, **48**, 2877 (1977).

(Received October 17, 1980)