

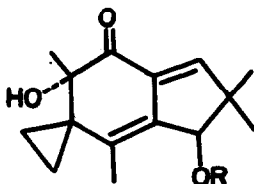
AN ALTERNATIVE SYNTHESIS OF ILLUDIN M

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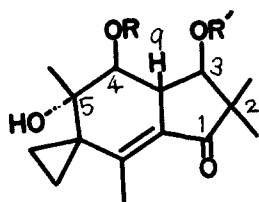
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Previously we reported a stereospecific total synthesis of dl-illudin M 1<sup>1)</sup>. This paper describes an alternative route for illudin M through the compound 2<sup>2)</sup>, which had been prepared at the exploratory stage of our study.

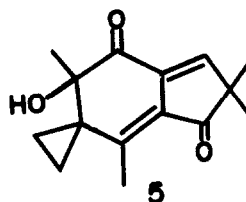


**1 R = H**  
**9 R = Ac**

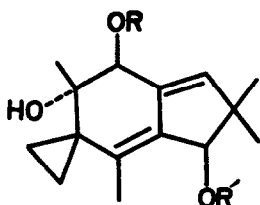
It was felt that out of the two acetoxy groups in 2, the one at C-4 could be selectively hydrolyzed by neighboring group participation of the adjacent hydroxyl group<sup>3)</sup>. In fact, a partially hydrolyzed product 3<sup>4)</sup>, m.p. 138-139°, ( $\nu_{\text{max}}^{\text{nujol}}$  3450, 1720, 1690, 1603, 1250  $\text{cm}^{-1}$ ;  $\tau_{\text{max}}^{\text{CCl}_4}$  8.89 (6H s.), 8.80 (3H s.), 8.07 (3H d., J=2.5 Hz), 7.79 (3H s.), 6.29 (1H b.d., J=11 Hz), 5.11 (1H d., J=9.5 Hz)) was obtained in 30% yield, by treatment of 2 with potassium bicarbonate (0.8 eq.) in water-methanol- benzene at 25° for 30 hours, along with a fully hydrolyzed 4, m.p. 163.5-165°, ( $\nu_{\text{max}}^{\text{nujol}}$  3300, 1703, 1605  $\text{cm}^{-1}$ ) and recovered 2. In the nmr spectra of related 3 $\beta$ , 4 $\beta$ -disubstituted 9 $\beta$ -illudane derivatives<sup>2)</sup>, the signals of the protons at C-3 and at C-4 appear as a doublet with J=11-12 Hz and a doublet J=9 Hz, respectively.



- 2 R=R'=Ac  
3 R=H, R'=Ac  
4 R=R'=H



Treatment of 3 with Jones reagent (3 eq.) at 0° for 7 minutes in acetone afforded dehydro-illudin M 5, ( $M^+$  246 ;  $\nu_{\text{max}}^{\text{CCl}_4}$  3500, 1720, 1710, 1620, 1603  $\text{cm}^{-1}$ ;  $\tau^{\text{CDCl}_3}$  8.78 (6H s.), 8.66 (3H s.), 7.97 (3H s.), 3.23 (1H s.)). The infrared spectrum in  $\text{CCl}_4$ , as well as nmr and mass spectra of 5, was perfectly identical with those of the optically active one which was derived from natural illudin M by oxidation with chromium trioxide-pyridin.



- 6 R=R'=H  
7 R=R'=Ac  
8 R=H, R'=Ac

For conversion of dehydro compound 5 to illudin M, the optically active form was used. Compound 5 was reduced by lithium aluminum hydride in ether at 0° for 1 hour to give a single triol 6<sup>5)</sup>, ( $\tau^{\text{CDCl}_3}$  8.95 (3H s.), 8.90 (6H s.), 8.40 (3H s.), 5.76 (1H d., J=2 Hz), 5.64 (1H s.), 4.36 (1H d., J=2 Hz)) in good yield. In the nmr spectrum of the compound 6 the chemical shift of the methyl group at C-5 was not shielded by cyclopropane ring<sup>7)</sup> and the allylic coupling constant between C-3 and C-4 protons was 2 Hz. Therefore the C-5 methyl group and C-4 proton are both axial and expressed as shown in the figure. The triol 6 was next converted to a diacetate 7<sup>6)</sup>.

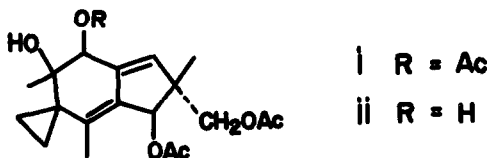
Selective partial hydrolysis of the C-4 acetoxy group in the diacetate 7 was effected by treatment with potassium carbonate in water-methanol-benzene at room temperature for 30 minutes, to afford 8, m.p. 97-98° ( $\nu_{\text{max}}^{\text{CCl}_4}$  3620, 3490, 1740, 1235  $\text{cm}^{-1}$ ;  $\tau^{\text{CCl}_4}$  9.04 (3H s.), 8.91 (3H s.), 8.80 (3H s.), 8.63 (3H s.), 7.94 (3H s.), 5.77 (1H b.s.), 4.42 (2H b.s.)), in good yield.

Oxidation of 8 with Jones reagent (ca. 3eq.) at 0° for 10 minutes in acetone gave a 30% yield of the known illudin M acetate 9<sup>6)</sup>. The acetate 9 was finally hydrolyzed by potassium carbonate in water-methanol-benzene at room temperature for 24 hours to give illudin M 1 exactly identical with the natural product in all respects.

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#### REFERENCES AND NOTES

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- 2) T. Matsumoto, H. Shirahama, A. Ichihara, H. Shin, S. Kagawa, N. Ito, T. Hisamitsu, T. Kamada, F. Sakan, K. Saito, S. Nishida and S. Matsumoto, Tetrahedron Letters, 1925 (1968).
- 3) Partial hydrolysis of triacetyldihydroilludin S (i) to dihydroilludin S (ii) has been reported; A. Ichihara, H. Shirahama, and T. Matsumoto, Tetrahedron Letters, No. 45 (1969), in press.



For neighboring group participation in hydrolysis of esters see for example; T. Yamanaka, A. Ichihara, K. Tanabe and T. Matsumoto, Tetrahedron, 21 1031 (1965); H. B. Henbest, and B. J. Lovell, J. Chem. Soc., 1965 (1957); T. C. Bruice and T. H. Fife, J. Am. Chem. Soc., 84 1973 (1962); S. M. Kupchan, W. S. Johnson and S. Rajagopalan, Tetrahedron, 7 47 (1959).

- 4) All the new compounds in this paper showed reasonable analytical and spectroscopic data.
- 5) The nmr and infrared spectra of 6 were identical with those of the compound<sup>6)</sup> derived from natural illudin M by reduction with sodium borohydride in all respects. Therefore the relative configuration at C-1 and C-5 positions is same as that of illudin M.
- 6) T. C. McMorris and M. Anchel, J. Am. Chem. Soc., 87 1594 (1965).

- 7) The line position ( $\tau$ 9.08) of the equatorial methyl group at C-5 of C-5 epimer (unpublished) of 2 was 0.3 ppm higher than that of axial methyl of compound 2 ( $\tau$ 8.77). This upfield shift of equatorial methyl group is due to shielding effect of a cyclopropane ring<sup>8</sup>).
- 8) J. L. Pierre and P. Arnaud, Bull. Soc. Chim. France, 1690 (1966); K. Tori, and K. Kitahonoki, J. Am. Chem. Soc., 87 386 (1965).