Tetrahedron Letters No.42, pp. 4097-4100, 1967. Pergamon Press Ltd. Printed in Great Britain.

SYNTHESIS OF ILLUDINS. I. SYNTHESIS OF THE SKELETON

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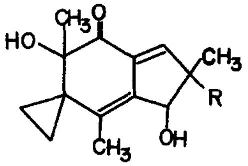
(Received in Japan 15 June 1967)

The structures of illudin S[1,2] (lampterol) and illudin M[2], antibiotic substances from fungi, have been shown to be I and II, respectively. We should like to report the synthesis of the compound (III), which has some structural features and the unique non-isoprenoid skeleton of illudins.



I : R = CH_2OH

II : R = CH_3

The β-ketosulfoxide (IV), m.p. 41-43° (ν_{max}^{nujol} 3050, 1680, 1045cm^{-1}; τ^{CDCl_3} 8.87(4H)m.*), 8.53(3H)s., 7.32(3H)s., 6.07(4H)s., 5.73, 5.99(2H)AB(J_{AB}=15c/s); Anal. Found: C, 51.70; H, 6.85, $C_{10}H_{16}O_4S$ requires C, 51.70; H, 6.94) was prepared from methylsulfinyl carbanion and ethyl 1-acetylcyclopropane-1-carboxy-

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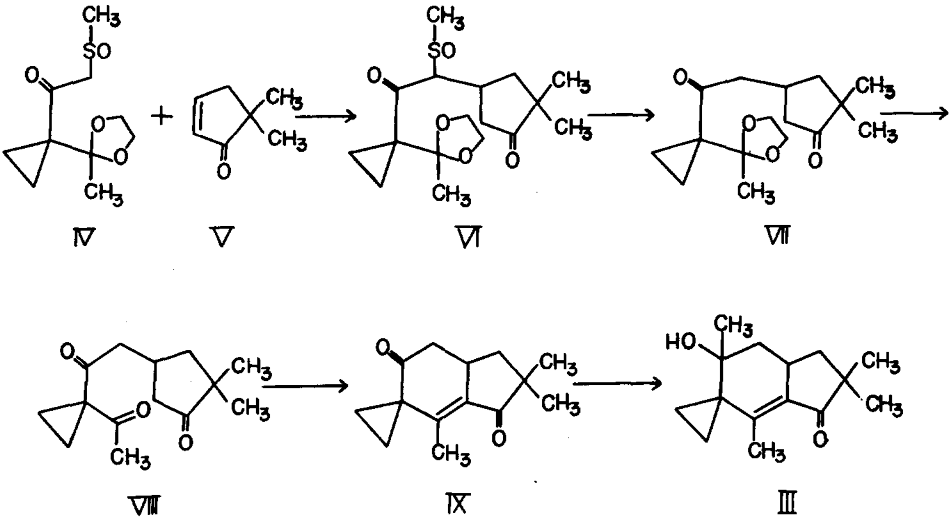
*) Multiplicities are indicated by the usual symbols s singlet, d doublet, t triplet, m multiplet, AB AB type quartet and b broad.

late ethylene ketal by the method of Corey and Chaykovsky[3]. The Michael addition of IV to 5,5-dimethylcyclopent-2-en-1-one(V)[4], b.p. 150-154° ν_{max}^{film} 3040, 1710, 1590, 1380, 1360, 810cm^{-1}; τ^{CCl_4} 8.97(6H)s., 7.53(2H)t. (J=2c/s), 4.02(1H)t.(J=2c/s) of d.(J=6c/s), 2.53(1H)t.(J=3c/s) of d.(J=6c/s); DNPzone m.p. 172-173°, Anal. data for DNPzone, Found: C, 53.77; H, 5.10;

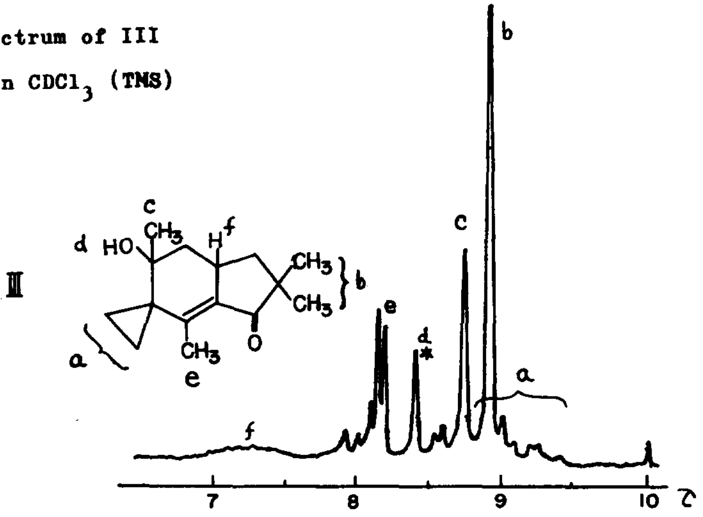


N, 19.49, $C_{13}H_{14}N_4O_4$ requires C, 53.78; H, 4.86; N, 19.30) proceeded smoothly in ethanol in the presence of sodium ethoxide to give a crystalline adduct (VI), m.p. 174-175° ν_{max}^{nujol} 1740, 1665, 1045cm^{-1}; τ^{CDCl_3} 8.6-9(4H)m., 8.43(3H)s., 7.35(3H)s., 6.02(4H)b.s., 5.37(1H)d.(J=10c/s); Anal. Found: C, 59.77; H, 7.56; S, 9.30, $C_{17}H_{26}O_5S$ requires C, 59.63; H, 7.65; S, 9.36). Although four isomeric racemates are possible for the adduct because three asymmetric centers are present, a single product was obtained in 60% yield based on the cyclopentenone (V).

Treatment of VI with amalgamated aluminum foil in dioxane-water at room temperature afforded VII ν_{max}^{film} 1740, 1690cm^{-1}; τ^{CCl_4} 9.06(4H)b.s., 8.95(6H)s., 8.52(3H)s., 7.0-8.8(7H)m., 6.07(4H)s.) in 95% yield. The desulfurated compound (VII) was then warmed at 50° in acetone containing a small amount of benzenesulfonic acid for 30 minutes to yield the triketone (VIII) ν_{max}^{film} 1740, 1690cm^{-1}). The product was not purified and subjected to the treatment with potassium tertiary butoxide in tertiary butanol. After aldol condensation was completed, the product was chromatographed to give a crystalline ketone (IX), m.p. 71-71.5°, ν_{max}^{nujol} 1700, 1620cm^{-1}; τ^{CCl_4} 9.0(3H)s., 8.92(3H)s., 8.07(3H)d. (J=2.5c/s), 6.7-9.0(9H); Anal. Found: C, 77.10; H, 8.44, $C_{14}H_{18}O_2$ requires C, 77.03; H, 8.31). Five grams of the Michael adduct (VI) gave 2.8grs of IX. In the Grignard reaction of IX, one equivalent of methylmagnesium iodide attacked selectively the nonconjugated carbonyl group to give the ketoalcohol (III), m.p. 133-134°, ν_{max}^{nujol} 3420, 1690, 1605cm^{-1}; τ^{CDCl_3} 8.8-9.5(4H)m., 8.93(6H)s., 8.75(3H)s., 8.4(1H)s., 8.16(3H)d.(J=2c/s), 7.8-8.7(4H)m., 7.2(1H)m., Anal. Found: C, 76.74; H, 9.52, $C_{15}H_{22}O_2$ requires C, 76.88; H, 9.46) in 60% yield.

Introduction of additional functional groups to the skeleton for the total synthesis of illudins is now in progress.

NMR Spectrum of III
60 Mc in $CDCl_3$ (TMS)



* disappears on treatment with D_2O.

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2) T. C. McMorris and M. Anchel, J. Am. Chem. Soc., **87**, 1594 (1965).

3) E. J. Corey and M. Chaykovsky, J. Am. Chem. Soc., **87**, 1345 (1965).

4) Procedures for the preparation of this substance will be described elsewhere.