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THE TOTAL SYNTHESIS OF PHYLLOCLADENE

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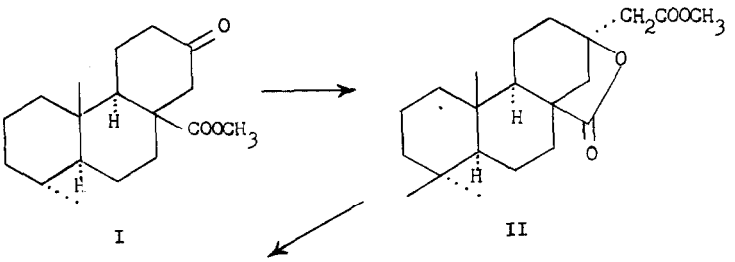
THE total synthesis of the optically active keto ester (I), a known degradation product of phyllocladene, was recently reported from this laboratory.[1] We wish at this time to record the total synthesis of phyllocladene itself.

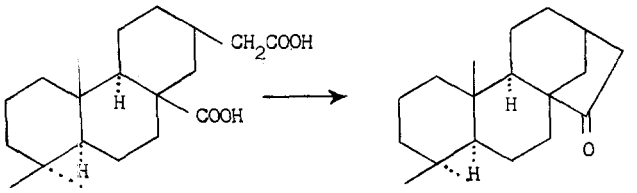
Treatment of I with zinc and methyl bromoacetate according to the Reformatsky procedure affords the lactonic ester (II), m.p. 133-134°, $[\alpha]_D^{22}$ + 17° (c, 1.00 chloroform), $\lambda_{max}^{CS_2}$ 5.63, 5.74 , (Found: C, 72.25; H, 9.08. $C_{21}H_{32}O_4$ requires: C, 72.37; H, 9.26), convertible by successive reaction with sodium methoxide, platinum-hydrogen and sodium hydroxide into the diacid (III), m.p. 204.5-205°, $[\alpha]_D^{26}$ + 7.2° (c, 0.70 chloroform), (Found: C, 71.20; H, 9.96. $C_{20}H_{32}O_4$ requires: C, 71.39; H, 9.59). Pyrolysis of III as the barium salt yields IV, m.p. 133.5-134°, $[\alpha]_D^{26}$ - 36° (c, 0.75 chloroform), $\lambda_{max}^{CS_2}$ 5.76 , which was shown by direct comparison to be identical with the corresponding ketone recently obtained from phyllocladene by Henderson and Hodges[2].

[1] R.B. Turner and P.E. Shaw, Tetrahedron Letters No.18, 24 (1960). See also R.F. Church, R.E. Ireland and J.A. Marshall, Ibid. No. 17, 1 (1960).

[2] R. Henderson and R. Hodges, Tetrahedron 11, 226 (1960).

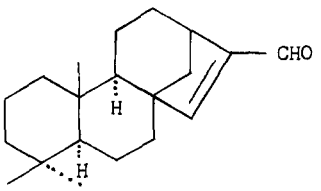


I II



III IV

Condensation of IV with ethyl formate in the presence of sodium hydride gave the expected hydroxymethylene ketone, which was converted, without purification, into the α, β-unsaturated aldehyde (V), m.p. 127-128°, $[\alpha]_D^{27}$ - 63.3° (c, 0.60 chloroform), $\lambda_{max}^{CS_2}$ 3.70, 5.96 , by reaction with butanone ethylene ketal - p-toluene-sulfonic acid, followed by treatment with lithium aluminum hydride and aqueous acid.[3] The identity of V with the product of this constitution derived by Briggs and his collaborators[4] from



V

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[3] cf. L. Ruzicka, C.F. Seidel, H. Schinz and M. Pfeiffer, Helv. Chim. Acta 31, 422 (1948).

[4] L.H. Briggs, B.F. Cain and B.R. Davis, Tetrahedron Letters No.17, 9 (1960).

isophyllocladene was established by direct comparison. The present synthesis, coupled with the conversion (Wolff-Kishner reduction) of V into phyllocladene,[4] constitutes a total synthesis of the latter compound.

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