

THE STEREOSPECIFIC TOTAL SYNTHESIS OF  
dl-8 $\beta$ -CARBOMETHOXY-13-OXOPODOCARPANE, A DEGRADATION  
PRODUCT OF PHYLLOCLADENE

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MUCH of the work on the structure and stereochemistry of the diterpenoid hydrocarbon phyllocladene has centered around its degradation to 8 $\beta$ -carbo-methoxy-13-oxopodocarpane(XI)<sup>3,4</sup>. Hence not only would the synthesis of this keto ester be of intrinsic value itself as corroboration of the degradative work but this keto ester also offers a very attractive intermediate for further elaboration to phyllocladene itself. We should like to report here a stereospecific total synthesis of the keto ester (XI).

Base catalyzed condensation of m-methoxybenzaldehyde with isopropyl methyl ketone led to the unsaturated ketone (I) (84%) b.p. 102-103<sup>o</sup>/0.08 mm. When this ketone was treated with 1-diethylamino-3-pentanone methiodide in the presence of sodium methoxide, it was converted to the dienone(II), b.p.

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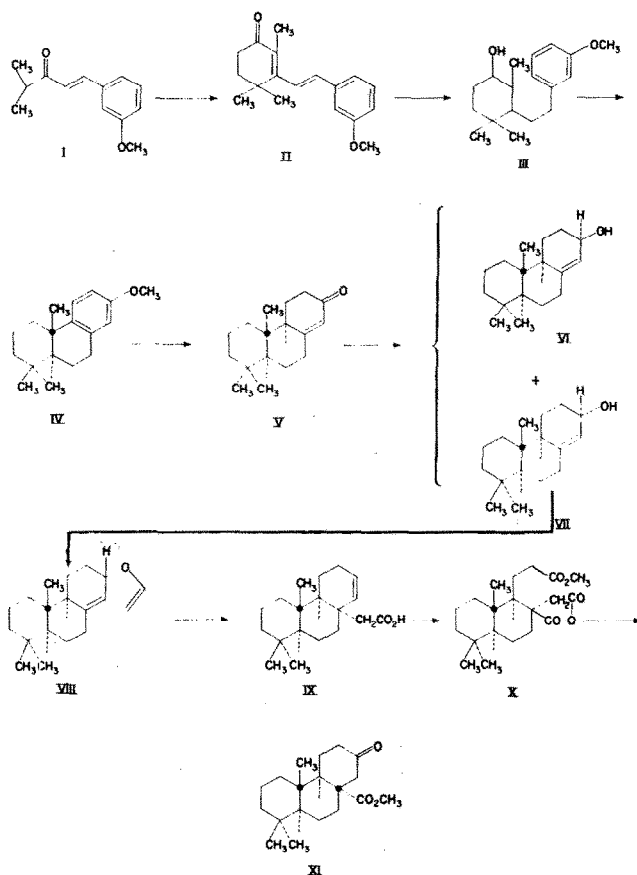
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<sup>3</sup> L. H. Briggs, B. F. Cain, B. R. Davis and J. K. Wilmhurst, Tetrahedron Letters No. 8, 8 (1959).

<sup>4</sup> P. K. Grant and R. Hodges, Tetrahedron 8, 261 (1960).

163-167°/0.1 mm  $\lambda_{\text{max}}^{\text{EtOH}}$  313m $\mu$ ( $\epsilon$ 15,800) in 40% yield. Catalytic hydrogenation



of this dienone over 10% palladium on carbon in acetic acid led to a saturated ketone b.p. 110°/0.03 mm (bath temp.) (C,78.61%; H,9.54%) which was reduced further with lithium aluminum hydride to the alcohol(III) b.p. 105°/0.03 mm (bath temp.) (82% overall) (C,78.40%; H,10.27%). On treatment of this alcohol with polyphosphoric acid at 85° for 45 min cyclization occurred affording the ether(IV), m.p. 86-88° (C,83.80%;H,10.22%). This crystalline tricyclic material was accompanied by substantial quantities of an oily isomer which may be the cis-fused ring system. That the crystalline tricyclic ether was

indeed trans-locked was shown by the fact that on reduction with lithium in ammonia and subsequent acid hydrolysis an  $\alpha,\beta$ -unsaturated ketone(V), m.p. 92-93.5 $^{\circ}$  (79%)  $\lambda_{\text{max}}^{\text{EtOH}}$  242  $\mu$ ( $\epsilon$ 15,900), was obtained which was identical with the ketone obtained by following the synthetic scheme of Barltrop and Rogers.<sup>5</sup>

Reduction of the unsaturated ketone(V) resulted in the isolation of two epimeric alcohols(VII) and (VI). The former (VII) m.p. 126.5-127.5 $^{\circ}$ , (C,82.33%; H,11.19%) was isolated in 76% yield and the latter (VI) m.p. 109.5-111 $^{\circ}$  (C,82.66%; H, 11.21%) in 20% yield. The close similarity of the behavior of this ketone to cholestenone on chemical reduction<sup>6</sup> coupled with the fact that the less proponderant, lower-melting alcohol was eluted from a Florisil column first indicated that the lower melting isomer possessed the quasi-axial hydroxyl group. Accordingly the more proponderant, higher-melting isomer(VII) was assigned the desired quasi-equatorial conformation and was converted to the vinyl ether (VIII) (80%) m.p. 45.5-46.5 $^{\circ}$  (C,83.24%; H, 10.88%) by equilibration<sup>7</sup> with ethyl vinyl ether in the presence of mercuric acetate. Pyrolysis<sup>8</sup> of this vinyl ether(VIII) at 195 $^{\circ}$  for four hours afforded an aldehyde, b.p. 105 $^{\circ}$ /0.02 mm (bath temp.) (95%) (C,82.96%; H, 10.99%) which on oxidation with silver oxide<sup>9</sup> gave the corresponding acid (IX), m.p. 150-152 $^{\circ}$  (88%) (C,78.63%; H,10.13%; N.E. = 278). Further

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<sup>5</sup> J. A. Barltrop and N. A. Rogers, J. Chem. Soc. 2566 (1958).

<sup>6</sup> Pl. A. Plattner, H. Heusser and A. B. Kulkarin, Helv. Chim. Acta 32, 265 (1949).

<sup>7</sup> W. H. Watenabe and L. E. Conlon, J. Amer. Chem. Soc. 79, 2828 (1957).

<sup>8</sup> A. W. Burgstahler and I. C. Nordin, J. Amer. Chem. Soc. 81, 3151 (1959).

<sup>9</sup> K. J. Clark, G. I. Fray, R. H. Jaeger and R. Robinson, Tetrahedron 6, 217 (1959).

oxidation of the unsaturated acid according to the conditions of Lemieux and Rudloff<sup>10</sup> followed by treatment of the resulting crude triacid with first thionyl chloride and then, methanol in the presence of one-equivalent of pyridine yielded the anhydride-ester (X) b.p. 140°/0.03 mm (bath temp.) (62% yield) (C,68.11%; H,8.58%)  $\lambda_{\text{max}}^{\text{film}}$  5.78  $\mu$ (ester CO); 5.39  $\mu$ , 5.62  $\mu$  (strained anhydride CO). The final steps were accomplished by treatment of the anhydride-ester(X) with sodium methoxide in benzene, hydrolysis and decarboxylation of the resulting crude  $\beta$ -keto ester, and esterification of the acid thus obtained with diazomethane. This led to a 35% overall yield of the keto ester(XI) m.p. 135-137° (C,74.52%; H,9.91%). Comparison of the infrared spectrum of this material with that of an authentic sample of 8 $\beta$ -carbomethoxy-13-oxopodocarpane showed them to be identical. The confirmation thus afforded the structure of the keto ester(XI) places the structure of phyllocladene on a firm footing. The conversion of the keto ester(XI) to phyllocladene itself is being actively pursued.

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<sup>10</sup> R. E. Lemieux and E. von Rudloff, Canad. J. Chem. 33, 1701 (1955).