

A STEREOSELECTIVE SYNTHESIS OF THE SPIROSESQUITERPENE (-)-ACORENONE

G. L. Lange,\* Will J. Orrom, and David J. Wallace

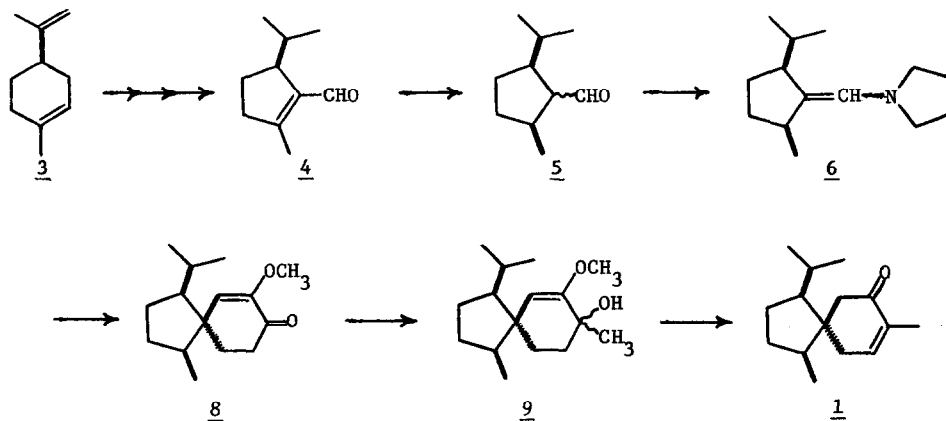
Guelph-Waterloo Centre for Graduate Work in Chemistry

Department of Chemistry, University of Guelph, Guelph, Ontario, N1G2W1, Canada

(Received in USA 9 September 1977; received in UK for publication 31 October 1977)

We wish to report the first total synthesis of natural (-)-acorenone (1), a spirosesquiterpene isolated by Sorm<sup>1</sup> from sweetflag oil (*Acorus calamus* L.). Recently ( $\pm$ )-1 was prepared from ( $\pm$ )-acorenone B (2)<sup>2</sup> while 2, which differs from 1 only in its configuration at the spiro carbon,<sup>3</sup> has been synthesized by several groups.<sup>4</sup>

Our synthesis of (-)-1 is short, experimentally simple and readily provides the pure natural product in reasonable overall yield. Conversion of (+)-limonene (3) to (-)-aldehyde 4 was previously described for the enantiomeric series.<sup>5</sup> Hydrogenation of 4 with 5% palladium on charcoal on the side opposite to the isopropyl group gave in 65% yield aldehyde 5<sup>6</sup> as a mixture of two epimers. Preparation of the pyrrolidine enamine of 5 gave 6 in 80% yield as a 4:1 mixture of double bond isomers. In the critical step of the synthesis, stereoselective spiroannellation of 6 with an excess of 1-methoxy-3-buten-2-one (7)<sup>7,8</sup> and one equivalent of acetic acid<sup>9</sup> with no solvent at room temperature for 8 hours gave in 35% yield enone 8 (short path distillation 80-100° at 0.1 Torr; 1695, 1620 cm<sup>-1</sup>; [ $\alpha$ ]<sub>D</sub><sup>25</sup> +35°;  $\lambda$ <sub>max</sub> (EtOH) 265 nm ( $\epsilon$  8000)). 8 is the product expected from initial Michael reaction of 7 with the less hindered  $\alpha$ -face of 6 followed by cycloaldolization



and tlc, glc, and nmr indicated only one isomer was present. Treatment of 8 with excess methylmagnesium iodide gave in high yield 9 (methyl singlets at  $\tau$  8.73 and 6.47 and a vinyl singlet at 5.75) which tlc showed was a 3:2 mixture of the two possible alcohols. Both dehydration and enol ether hydrolysis were effected by simply reacting 9 with p-toluenesulfonic acid in refluxing benzene<sup>10,11</sup> for 4 hours to give in 74% yield after tlc purification (-)-acorenone (1),  $[\alpha]_D^{25} -28^\circ$ . An authentic sample of 1 was isolated from European calamus oil<sup>12</sup> and was identical in all respects (e.g.  $[\alpha]_D^{25} -27^\circ$ , lit.<sup>1</sup>  $-22^\circ$ ) with synthetic 1.<sup>13</sup> The nmr spectrum of synthetic 1 was also identical to the published spectrum of ( $\pm$ )-1.<sup>2</sup> This synthesis establishes the absolute configuration of (-)-1 as depicted.<sup>14</sup>

The authors acknowledge the financial assistance of the National Research Council of Canada.

#### References

1. J. Vrkoc, V. Herout, and F. Sorm, Collect. Czech. Chem. Commun., 26, 3183 (1961).
2. W. Rascher and H. Wolf, Tetrahedron, 33, 575 (1977).
3. R. J. McClure, K. S. Schorno, J. A. Bertrand, and L. H. Zalkow, Chem. Commun., 1135 (1968).
4. (a) Synthesis of (-)-2: J. F. Ruppert, M. A. Avery, and J. D. White, Chem. Commun., 978 (1976).  
(b) Syntheses of ( $\pm$ )-2: H. Wolf and M. Kolleck, Tetrahedron Letters, 451 (1975); W. Oppolzer and K. K. Mahalanabis, *ibid.*, 3411 (1975); B. M. Trost, K. Hiroi, and N. Holy, J. Am. Chem. Soc., 97, 5873 (1975).
5. E. E. van Tamelen, G. M. Milne, M. I. Suffness, M. C. Rudler Chauvin, R. J. Anderson, and R. S. Achini, J. Am. Chem. Soc., 92, 7202 (1970). This sequence was also used by White in his synthesis of (-)-2.<sup>4a</sup>
6. Experiments to confirm the anticipated cis relationship of the isopropyl and methyl groups will be described in the full paper.
7. E. Wenkert, N. F. Golob, S. S. Sathe, and R. A. J. Smith, Syn. Commun., 3, 205 (1973).
8. Related spiroannulation reactions employing enamines and methyl vinyl ketone have been reported: V. V. Kane, Syn. Commun., 6, 237 (1976); S. F. Martin, J. Org. Chem., 41, 3337 (1976).
9. If acetic acid is omitted in the early stages of the reaction a different product is formed in low yield.
10. The water formed in the dehydration step then effects hydrolysis of the enol ether.
11. The conversion 8  $\rightarrow$  9  $\rightarrow$  1 is a new type of alkylative carbonyl transposition and a forthcoming publication will outline the general use of this sequence in organic synthesis.
12. We wish to thank Fritzsche Ltd., Toronto, for a generous sample of this oil.
13. We are grateful to Professor V. Herout, Czechoslovak Academy of Science, for an ir spectrum of 1 and to Professor White, Oregon State University, for a sample of (-)-2.
14. All new compounds reported in this paper gave spectral data consistent with their structure and satisfactory analytical data.