

THE C-13 CONFIGURATION OF ANNONALIDE<sup>1</sup>

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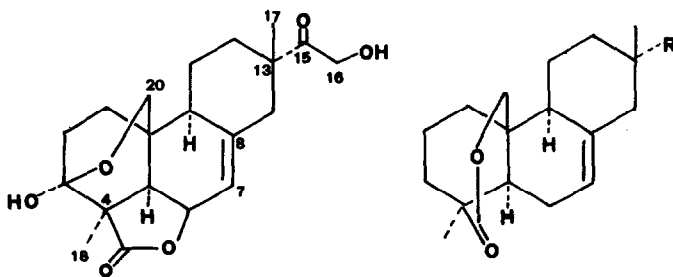
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A recent structure analysis of a diterpenic lactone constituent of Annona coriacea, herewith named annonalide, showed the natural product to possess the configuration (1) but left the C-13 stereochemistry undefined.<sup>2,3</sup> This point now has been clarified by <sup>1</sup>H and <sup>13</sup>C nmr analyses of the degradation product (5) which has been prepared in the following manner. Sodium borohydride reduction of the previously reported ester lactone (2)<sup>3</sup> yielded hydroxylactone (3); mp 166°; [α]<sub>D</sub> -204° (c 1, CHCl<sub>3</sub>); ir (CHCl<sub>3</sub>) OH 3690 (shoulder), 3640, C=O 1725 cm<sup>-1</sup>; pmr(CDCl<sub>3</sub>) δ 0.77, 1.18 (s, 3, Me each), 3.35 (s, 2, CH<sub>2</sub>OH), 3.91 (dd, 1, J = 11.5, 1 Hz, H-20), 4.36 (d, 1, J = 11.5 Hz, H-20), 5.35 (m, 1, H-7); m/e 304 (parent, 40%), 273 (55), 246 (100), 227 (55), 185 (30). Fétizon oxidation of (3) gave aldehydolactone (4) [ir (CHCl<sub>3</sub>) CH 2710, C=O 1720 cm<sup>-1</sup>; pmr (CDCl<sub>3</sub>) δ 9.40 (s, 1, CHO); m/e 302 (parent), 274 (base)], whose interaction with methylenetriphenylphosphorane produced lactone (5); mp 108-109°; [α]<sub>D</sub> -243.5° (c 1, CHCl<sub>3</sub>); pmr (CDCl<sub>3</sub>) δ 0.85 [s, 3, (H-17)<sub>3</sub>], 1.19 [s, 3, (H-18)<sub>3</sub>], 3.98 (dd, 1, J = 12, 1 Hz, H-20), 4.42 (d, 1, J = 12 Hz, H-20), 5.32 (d, 1, J = 5 Hz, H-7), lines at 4.77, 4.78, 4.80, 4.87, 4.89, 4.96, 4.97, 5.62, 5.72, 5.80, 5.90 [m, 3, H-15, (H-16)<sub>2</sub>]; m/e 300 (parent, 77%), 285

(18), 277 (38), 272 (18), 255 (62), 241 (90), 185 (100).



(1)

(2) R = CO<sub>2</sub>Me

(3) R = CH<sub>2</sub>OH

(4) R = CHO

(5) R = C<sub>2</sub>H<sub>3</sub>

Comparison of the 100 MHz <sup>1</sup>H nmr spectra of lactone (5) and isopimaric acid revealed them to have nearly identical signals in position and intensity for the methyl and olefinic hydrogens. Since differences in the chemical shifts of these hydrogens have been observed among 13-epimers of Δ<sup>8,14</sup>-pimaradienic compounds <sup>4</sup> and by analogy such differences would be expected for Δ<sup>7,8</sup>-pimaradiene 13-epimer pairs, the pmr results suggest the C-13 configuration depicted in formula (1) forannonalide.

Inspection of the natural abundance, proton-decoupled as well as single-frequency, off-resonance decoupled <sup>13</sup>C nmr spectra of lactone (5) and analysis of its carbon types showed the carbon shifts of its methyl groups to be 22.8 and 21.5 ppm and those of olefinic carbons 7, 8, 15 and 16 to be 118.5, 135.7, 149.4 and 109.5, respectively.<sup>5</sup> The 22.8 ppm methyl signal can be attributed to

the equatorial 4-methyl group on the basis of its  $\Delta\delta$  of 11 ppm in (5) vs. isopimaradiene<sup>6</sup> approximating closest the  $\Delta\delta$  9.5 ppm of the methyl groups in 2-methylcyclohexanone and methylcyclohexane.<sup>7</sup> This leaves the 21.5 ppm signal to the 13-methyl function.<sup>8</sup> Since the carbon shifts of the 13-substituents of (5) are nearly identical with those of isopimaradiene (C-15 149.6, C-16 109.5 and C-17 21.5 ppm)<sup>6</sup> and since these shifts are heavily dependent on the C-13 stereochemistry,<sup>6</sup> the cmr results support strongly theannonalide configuration portrayed in (1).

#### References

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5. The cmr spectra of deuteriochloroform solutions of (5) were run on a Varian XL-100 Fourier transform spectrometer. The  $\delta$  values are in ppm downfield from TMS;  $\delta^{\text{TMS}} = \delta^{\text{CDCl}_3} + 76.9$  ppm.
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8. The subsequent stereochemistry argument is unaffected, even if the assignment of the methyl carbon shifts is reversed.