Long-range Coupling in the Proton Magnetic Resonance Spectrum of Methyl β-Apopodophyllate

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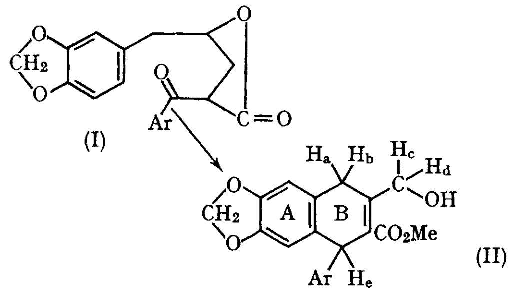
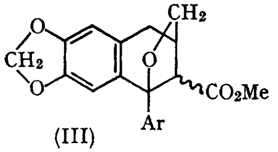
THE structure (II) (methyl β-apopodophyllate), rather than that previously suggested (III), is now allocated to the product (m.p. 172—173°) formed by cyclisation[1] of the keto-lactone (I) in methanolic hydrogen chloride solution. The presence of a carbon–carbon double bond in ring B was shown by the slow decolorisation of bromine in chloroform, a typical[2] purple colour in sulphuric acid, and a yellow fluorescence on ultraviolet irradiation. Ultraviolet absorption was used originally[3] to assign structures to the corresponding apo-lactones; α-apopicropodophyllin (IV) having $\lambda_{\max}$ 311 mμ, log ϵ 3·87, and β-apopicropodophyllin $\lambda_{\max}$ 290, log ϵ 3·64. This distinction cannot be made however when the lactone ring has been opened, for the product (II) has λ_{max} 311 mμ, log ϵ 4·084, where a redshift occurs due to enhanced end-absorption of the isolated trisubstituted acrylic ester chromophore.[4]

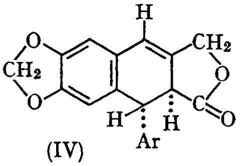


(I)

(II)



(III)



(IV)

(Ar = 3,4,5-trimethoxyphenyl)

The 60 Mc/sec. proton magnetic resonance (p.m.r.) spectrum of (II) in deuterodimethyl sulphoxide has no vinylic proton resonance (τ 3·42 for α-apopicrophodophyllin). A peak due to the diphenylmethyl proton H_e appears at τ 4·92; this is at lower field than normal for the fully reduced B ring (τ *ca.* 6·5 in $CDCl_3$[5]) owing to deshielding by the β-double bond. The spectrum also showed absorption between τ 5·3—5·8 due to the geminal pair, H_c, H_d, which were coupled with the hydroxyl proton and, in view of the multiplicity, with others in the molecule. In the 100 Mc/sec. spectrum of a solution in deuterochloroform the H_e peak, which shifted upfield to τ 5·52, was resolved as a quintet (Figure 1*a*). The resonance of the methylol pair, H_c, H_d, no longer deshielded by solvation with dimethyl sulphoxide, had shifted markedly upfield and with the resonances of H_a, H_b formed a group of sixteen peaks between τ 6·97—7·84 (Figure 1*b*). A broad temperature-dependent resonance at τ 7·94 (30°) was ascribed to the –OH group; it partly obscures the high-field portion of the double resonance spectrum (Figure 1*c*).

Long-range coupling constants of 11 c./sec. (*cis*) and 7·4 c./sec. (*trans*) have been detected in 1,4-disubstituted cyclohexadienes,[6] whilst in 1,4-dihydro-1-phenyl-napthalene $J(H_1, H_4)$ was 6 c./sec.;[7] hence eight of the lines at high field result from the AB system of H_a and H_b further split by coupling of this type. The remaining eight lines must arise from another AB system in which H_c and H_d are magnetically nonequivalent and undergo further homoallylic coupling with H_e.

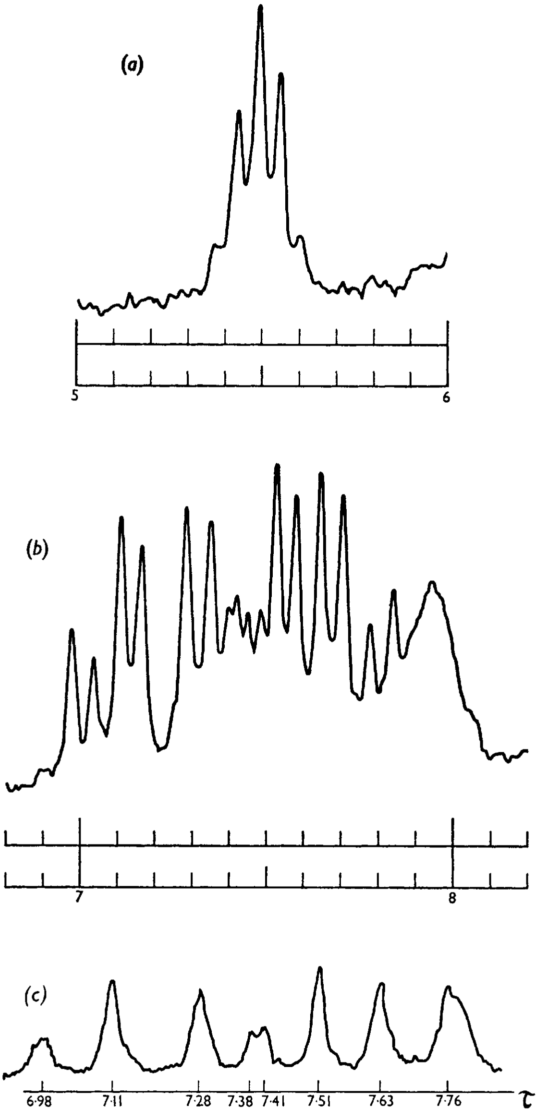


FIGURE 1

Both geminal couplings are of the same magnitude (13 c./sec.) as are the four homoallylic couplings (6 c./sec.); this latter figure is believed to be the highest so far recorded for a single path coupling

[$J(H_cH_e)$ and $J(H_dH_e)$]. The interpretation was confirmed by irradiation at τ 5·52 when the unsplit, but slightly overlapping, AB spectra were resolved (Figure 1c).

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