Structure of Heliangine, a Novel Ten-membered Sesquiterpene Lactone

Sir:

In 1961 Shibaoka\(^1\) reported the isolation of a substance, which shows anti-auxin activity, from leaves of *Helianthus tuberosus* L. and named it heliangine. We now wish to present the evidence which assigns the structure I to this substance.

Heliangine I, C\(_{20}\)H\(_{26}\)O\(_6\), m.p. 213\textasciitilde215\degreeC, \([\alpha]_D^{20}=119° \ (c, 11.9, \text{chloroform}),\) shows the following spectral properties: \(\lambda_{\text{max}} 204 \text{ m}\mu \ (\varepsilon 23,200), \nu_{\text{max}} 3450, 3050, 1750, 1700, 1650 \text{ cm}^{-1} \) (nujol mull). On treatment with dilute methanolic sodium hydroxide I consumed two moles of alkali to give tiglic acid (II) together with a neutral C\(_{15}\)-compound (III), C\(_{15}\)H\(_{20}\)O\(_5\), m.p. 177\textasciitilde180\degreeC, \(\lambda 210 \text{ m}\mu \ (\varepsilon 11,800), \nu_{\text{max}} 3520, 1745, 1655 \text{ cm}^{-1},\) which further consumed one mole of alkali. This suggests that the band at 1750 cm\(^{-1}\) in I should be assigned to \(\gamma\)-lactone and 1700 cm\(^{-1}\) to \(\alpha,\beta\)-unsaturated ester carbonyl on tiglate side chain.* Moreover conjugation of this \(\gamma\)-lactone with an exocyclic methylene group is shown by UV spectrum of I, which is considered to be a composite of two isolated chromophores. An UV absorption spectral curve (\(\lambda 210 \text{ m}\mu, \varepsilon 10,000\)) obtained by subtracting the curve (\(\lambda 210 \text{ m}\mu, \varepsilon 13,200; \text{due to tigloyl moiety}\)) of dihydroheliangine (IV), m.p. 188\textasciitilde192\degreeC, afforded by hydrogenation of I with palladium-charcoal, from the curve of I, is identical with those of III and alantolactone\(^2\) containing an unsaturated lactone chromophore. This was confirmed chemically by ozonolysis of I to give formaldehyde and acetaldehyde as well as by formation of dipyrrozoline\(^3\) on treatment with diazomethane. NMR spectrum\(^4\) of I reveals a pair of doublets at low field (\(\tau 3.65\) and 4.20, \(J=2\) c.p.s.) which is typical of exocyclic methylene protons conjugated with lactone carbonyl. These signals disappear in IV and a new methyl doublet at \(\tau 8.90\) (3H; \(J=7.5\) c.p.s.) is observed.

In the presence of platinum oxide in acetic acid, I absorbed about 3 moles of hydrogen to give a mixture of dehydroxyhexahydroheliangine (V), C\(_{19}\)H\(_{18}\)O\(_5\), m.p. 162\textasciitilde163\degreeC (10\%), oily tetrahydroheliangine (VI) (10\%) and hexahydroheliangine (VII) (60\%\~), m.p. 140\textasciitilde142\degreeC, which are separable with silica gel chromatography. VI gave crystalline tetrahydrohelianginone (VIII), m.p. 150\~160\degreeC, \(\nu_{\text{max}} 1770, 1740, 1700, 1670 \text{ cm}^{-1}\) on chromic acid oxidation.

The signal at \(\tau 5.50\) (multiplet, 1H) in NMR spectrum of I shifts to low field on acetylation and disappears on chromic acid oxidation to helianginone (IX), m.p. 133\~135\degreeC, in which the presence of an isolated ketone was confirmed by IR and UV spectra, indicating the presence of \(\alpha\)-hydroxyl group in I. Bromination of hexahydrohelianginone (X), m.p. 175\textasciitilde180\degreeC, obtained by chromic acid oxidation of VII, gave monobromoderivative (XI), C\(_{20}\)H\(_{20}\)O\(_5\)Br, m.p. 164\~167\degreeC, which clearly shows quartet due to an isolated AB system at \(\tau 6.06, 6.63\) (\(J=9\) c.p.s.) in its NMR spectrum.

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4) NMR spectra were taken in deuteriochloroform with a Varian A-60 NMR spectrometer unless noted otherwise.
spectrum indicating the presence of the structure >C—CH(O)—CHBr—CO—. This was further confirmed by the NMR spectrum of isotetrahydrohelianginone (XII), m.p. 163–165°C (λ_max 248 μ, ε 9,000; ν_max 3520, 1780, 1740, 1655, 1005 cm⁻¹) obtained by warming VIII in glacial acetic acid. In XII, an isolated AB quartet newly appeared at δ 3.12, 3.70 (J = 17.5 c.p.s.), suggesting the formation of the structure >C—CH=CH—CO—. This acid isomerisation is well explained by opening of β,γ-epoxyketone system as follows:

Kuhn-Roth determination showed that I and III possess at least four and two C-methyl groups, respectively. A sharp methyl singlet at δ 8.53 in the NMR spectrum of I can be attributed to a methyl on the system CH₂—C. Thus the presence of partial structure (a) in I has been confirmed.

The 100 Mc NMR spectrum of IX clearly showed that the last C=C double bond must be included in partial structure (b) as follows. An olefinic proton and a proton attached to carbon carrying lactone alkyl oxygen appeared at δ 4.64, 4.91 as AB part of ABXY₃ system (JₐB = 12 c.p.s.). Decoupling experiments revealed that proton A is coupled with allyl methyl doublet at δ 8.02 (J = 1 c.p.s.) and proton B with a methine proton X at low δ value 6.98 (1H, multiplet with three small coupling constants J = 1~2 c.p.s., see below), which flanks on ketone carbonyl. Proton X also couples in long range with the exocyclic methylene protons, because the latters appear as two sharp singlets by irradiating the former.

Partial structures (a), (b) and tigloyl group account for eighteen carbons out of twenty in I. The remaining two carbons must constitute ten-membered carbocyclic ring. The position of tigloyl group on this ring was established as shown in structure I by the formation of methylsuccinic acid on drastic chromic acid oxidation of VII. On the basis of I, NMR spectrum of IX is successfully explained as follows. One proton quartet at δ 7.18, one proton quartet at δ 8.61 hidden in methyl region and one proton multiplet at δ 4.81, were respectively assigned to A, B and X protons in ABX system (c) >C—CH₃—CH—OTig (JₐB = 15, JₐX = 5, JₓB = 1.5 c.p.s., confirmed by decoupling study). The remaining three protons at δ 6.5~6.9 (2H) and 7.5~7.8 (1H) were reasonably assigned to ABC system of partial structure (a).

Thus heliangine was finally confirmed to have structure I.

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