Tetrahedron Letters No. 19, pp 1539 - 1542, 1975. Pergamon Press. Printed in Great Britain.

THE ISOLATION AND STRUCTURE OF OBTUSILACTONE

Masatake Niwa, Masanobu Iguchi and Shosuke Yamamura*
Faculty of Pharmacy, Meijo University, Showa-ku, Nagoya, Japan

(Received in Japan 15 March 1975; received in UK for publication 1 April 1975)

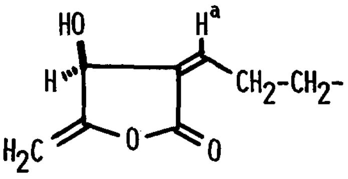
In the course of searching for the physiologically active substances in the plant Lindera obtusiloba Blume (Japanese name "Dankōbai"), we could isolate an unstable substance with a novel lactone grouping, named obtusilactone, as a main component from the leaves of the above plant. In the present paper, we wish to describe the isolation and structure of obtusilactone (I).

The fresh leaves of the plant Lindera obtusiloba Blume collected in Sanage in early November, were immediately immersed in large amounts of benzene,[1] and then allowed to stand at room temperature for 2 days. The benzene extracts were carefully concentrated under reduced pressure to give a dark brown solid, which was rapidly chromatographed on silica gel (Mallinckrodt, 100 mesh) with $CHCl_3$ as an eluent and then on florisil (Katayama Chemicals, 60 - 100 mesh) with the same eluent to afford a pale yellow oil. Further preparative TLC was carried out on 10% $AgNO_3$- silica gel (Kieselgel 60 PF_{254}) (benzene - AcOEt (3 : 1)) and then on silica gel (Kieselgel 60 PF_{254}) (benzene - AcOEt (3 : 1)) to give obtusilactone (I) as a colourless viscous liquid in 0.094% yield. This liquid so far obtained has a molecular formula $C_{17}H_{26}O_3$ (m/e 278(M^+) with the following spectral data: $[\alpha]_D^{23°}$ = -53°in MeOH (c = 0.35); λ_{max}(MeOH) 225nm (ε, 10000); ν_{max}(film) 3400, 3070, 1780, 1680, 1645 and 910cm^{-1}; δ ($CDCl_3$) 1.30(14H, br.s), 2.04(2H, q, J= 7Hz), 2.76(2H, q, J= 7.5Hz), 3.28(1H, d, J= 7.5Hz)(OH), 4.6-5.2(5H, complex), 5.80(1H, ddt, J= 17, 10 and 7Hz) and 6.64ppm(1H, td, J= 7.5 and 2Hz).

Obtusilactone (I) has a secondary OH group (3400cm^{-1} and δ3.28ppm). Furthermore, the presence of two moieties [A and B] in I can be elucidated by the exhaustive analysis of the above physical data, particularly ^1H NMR spectrum with aid of double resonance experiments together with the ^{13}C NMR spectrum of I [δ ($CDCl_3$) 28.3, 28.7, 29.4, 33.8(t), 68.8(d), 90.2(t), 114.1(t), 126.9(s), 139.1(d), 151.1(d), 157.6(s) and 165.4ppm(s)]^2.

$CH_2{=}CH{-}CH_2{-}CH_2{-}$

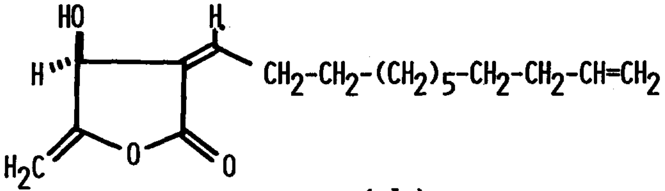
(A)



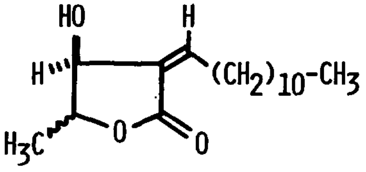
(B)

Irradiation at δ 5.80ppm caused the quartet at δ2.04ppm to collapse to triplet, whereas on irradiation at δ2.04ppm the multiplet at δ5.80ppm became double doublets (J= 17 and 10Hz). The presence of a $CH_2{=}CH{-}$ grouping in [A] is also confirmed by the ^{13}C NMR signals at δ114.1 and 139.1ppm. The presence of [B] can also be based on the IR and UV spectra coupled with the ^1H and ^{13}C NMR spectra. On irradiation at δ6.64ppm (H^a) the quartet at δ2.76ppm became triplet, whereas irradiation at δ2.76ppm caused the NMR signal at δ6.64ppm to collapse to doublet (J= 2Hz). Furthermore, irradiation at δ5.00 ppm caused the NMR signals at δ6.64 and 3.28ppm to collapse to sharp triplet and singlet, respectively. These experiments are in good agreement with the ^{13}C NMR spectral data (δ33.8, 68.8, 90.2, 126.9, 151.1, 157.6 and 165.4ppm). In particular, the presence of a $CH_2{=}\underset{\uparrow}{C}{-}O{-}\underset{\uparrow}{C}{=}O$ grouping is confirmed by observation of the signals at δ90.2 and 157.6ppm. The geometry of the remaining exocyclic double bond was determined on the basis of the δ-value of the olefinic proton (H^a) (δ6.62ppm in I; δ6.54ppm in IIa and b; δ6.52ppm in III).^{3}

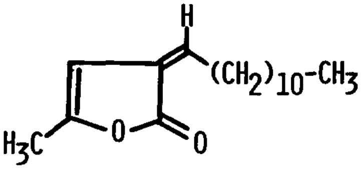
Finally, the structure of obtusilactone (I) with a molecular formula ($C_{17}H_{26}O_3$) can be deduced by connecting the two moieties [A and B] with a straight chain consisting of five methylene groups. The structure (I) so far obtained can also be confirmed by chemical evidences.



(I)



(II a and b)



(III)

On homogeneous catalytic hydrogenation using $Rh(Ph_3P)_3Cl$ in benzene (room temp., 30min) obtusilactone (I) was readily converted into a mixture of αβ-unsaturated lactones (IIa and b)[4], which was directly treated with Ac_2O - pyridine (room temp., 4hr) to give the corresponding dehydro-compound (III) as a pale yellow liquid, $C_{17}H_{28}O_2$ (m/e 264(M^+)); ν_{max}(film) 1790, 1650sh. and 1640cm^{-1}; δ($CDCl_3$) 0.90(3H, t, J≃6Hz), 1.26(18H,br.s), 2.12(3H, d, J= 2Hz), 2.30(2H, q, J= 7.5Hz), 5.76(1H, q, J= 2Hz) and 6.52ppm(1H, t, J= 7.5Hz).

From a biogenetic point of view, obtusilactone (I) with a novel lactone grouping must be derived from a C_{14}-fatty acid and pyruvyl-CoA.[3]

The authors wish to thank Professor Yasuaki Okumura and Dr. Hajime Irikawa (Shizuoka University) for measurement of the ^{13}C NMR spectrum of obtusilactone.

REFERENCES AND FOOTNOTES

1. In the case of the air-dried leaves, obtusilactone (I) is obtained only in a poor yield.
2. Letters in parentheses give off-resonance ^1H information (d, doublet;

s, singlet; t, triplet).

3. K. Takeda, K. Sakurawi and H. Ishii, Tetrahedron, **28**, 3757 (1972).
4. The mixture has the following spectral data: m/e 282 (M^+ for $C_{17}H_{30}O_3$); ν_{max}(Nujol) 3400, 1750 and 1675cm^{-1}; δ($CDCl_3$) 0.89(3H, t, J$\simeq$6Hz), 1.27(br.s) and 1.38(d, J$\simeq$6Hz)(21H), 2.48(1H, br.s)(OH), 2.75(2H, br.q, J= 7.5Hz), 4.2 - 4.7(2H, complex) and 6.54ppm(1H, br.t, J= 7.5Hz).