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THREE NEW OBTUSILACTONES FROM LINDERA OBTUSILOBA BLUME

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In addition to obtusilactone (I), three new lactones (II, III and IV) have been isolated from the plant Lindera obtusiloba Blume, and their structures also been established in connection with I.

In the course of searching for the physiologically active substances in the plant Lindera obtusiloba Blume (Japanese name "Dankōbai"), we could isolate obtusilactone (I) with a novel lactone grouping.[1] We further made a considerable effort to find such a novel lactone as I. In the present paper, we wish to describe the isolation and structures of three new lactones [isoobtusilactone (II), obtusilactone A (III) and isoobtusilactone A (IV)].

The fresh leaves of the above plant were carefully extracted with a large amount of benzene.[2] According to essentially the same procedure as reported earlier,[1] the benzene extracts were rapidly chromatographed on silica gel (Mallinckrodt, 100 mesh) and then on florisil (Katayama Chemicals, 60 - 100 mesh) using $CHCl_3$ as an eluent. Further separation was carried out by repeated preparative TLC [1) Kieselgel 60 PF_{254}, 2) 10%$AgNO_3$-Kieselgel 60 PF_{254} and 3) Kieselgel 60 PF_{254}] using benzene-AcOEt (3 : 1) to afford three new oily substances, in each pure state, in addition to obtusilactone (I) as a main product[1] [II, 0.0022%; III, 0.017%; IV, 0.0066%]. The physical data of these three new lactones are shown below.

Isoobtusilactone (II) as colorless viscous liquid: $C_{17}H_{26}O_3$ [m/e 278(M^+), 250, 235 and 140][3]; $[\alpha]_D^{23°} = -56°$ in $CHCl_3$ (c = 0.67); ν_{max}($CHCl_3$) 3580, 3430, 3060, 1780, 1685sh., 1680, 1645 and 915cm^{-1}; λ_{max}(MeOH) 222nm (ε, 11000); δ ($CDCl_3$) 1.31 (14H, br.s), 2.06(2H, q, J= 6.5Hz), 2.49(2H, q, J= 7.8Hz), 2.49(1H, superimposed on the methylene signal, OH), 4.6 - 5.1(4H, complex), 5.25(1H, br.s), 5.77(1H, ddt, J= 17, 10 and 6.5Hz) and 7.04ppm(1H, td, J= 7.8 and 2.0Hz).

Obtusilactone A (III) as colorless viscous liquid: $C_{19}H_{32}O_3$ [m/e 308(M^+), 280, 265, 237, 153 and 140][3]; $[\alpha]_D^{23°} = -46°$ in $CHCl_3$ (c = 0.45); ν_{max}($CHCl_3$) 3630, 3400, 1785 and 1680cm^{-1}; λ_{max}(MeOH) 225nm (ε, 11300); δ ($CDCl_3$) 0.89(3H, t, J≃ 6Hz), 1.30 (22H, br.s), 2.78(2H, q, J= 7.5Hz), 2.78(1H, superimposed on the methylene signal, OH), 4.68(1H, dd, J= 3.0 and 1.5Hz), 4.88(1H, dd, J= 3.0 and 2.0Hz), 5.22(1H, br.s) and 6.68ppm(1H, td, J= 7.5 and 2.0Hz).

Isoobtusilactone A (IV) as colorless viscous liquid: $C_{19}H_{32}O_3$ [m/e 308(M^+), 280, 265, 237 and 140]; $[\alpha]_D^{23°} = -54°$ in $CHCl_3$ (c = 0.50); ν_{max}($CHCl_3$) 3580, 1785 and 1675cm^{-1}; λ_{max}(MeOH) 222nm (ε, 11700); δ ($CDCl_3$) 0.89(3H, t, J≃ 6Hz), 1.28(22H, br.s), 2.46(2H, q, J= 7.5Hz), 2.46(1H, superimposed on the methylene signal, OH), 4.73(1H, dd, J= 3.0 and 2.0Hz), 4.94(1H, dd, J= 3.0 and 2.0Hz), 5.26(1H, br.s) and 7.05ppm(1H, td, J= 7.5 and 2.0Hz).

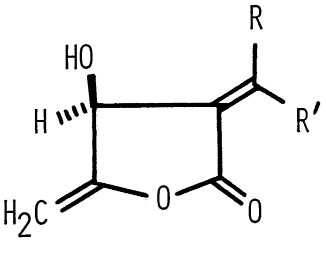
As shown above, isoobtusilactone (II) has the same molecular formula ($C_{17}H_{26}O_3$) as that of obtusilactone (I)[1], and can be regarded as an isomer of I. In fact, the former was proved to be different from I only at the position of the tri-substituted double bond conjugated to a lactone carbonyl, as discussed below.

The IR and UV spectra of isoobtusilactone are quite similar to those of obtusilactone (I)[1]. Furthermore, the NMR spectra[4] of both lactones are also similar to each other except for some remarkable differences of δ-values, as shown in the Table.

The Table. δ-Values of the methylene and olefinic protons attached to the tri-substituted double bond

Obtusilactone (I)	Isoobtusilactone (II)
2.76 (2H, q, J = 7.5Hz)	2.49 (2H, q, J = 7.8Hz)
6.64 (1H, td, J = 7.5 and 2.0Hz)	7.04 (1H, td, J = 7.8 and 2.0Hz)

From these data, the structure of isoobtusilactone should be represented by II. This is also confirmed by the following chemical evidence. On catalytic hydrogenation over 5%Pd-$BaSO_4$ in EtOH (room temp., 6hr), obtusilactone (I) was readily converted into the corresponding hexahydro-lactone (V)[5], mp 82-83°C (from n-hexane); $C_{17}H_{32}O_3$ [m/e 284(M^+), 129 and 116]; ν_{max}($CHCl_3$) 3500 and 1770cm^{-1}; δ ($CDCl_3$) 0.90(3H, t, J≃6.5Hz), 1.26(22H, br.s), 1.43(3H, d, J= 7.0Hz), 2.36(1H, br.s, OH), 2.58(1H, m) and 4.3 - 4.6(2H, complex). This reduction product was also

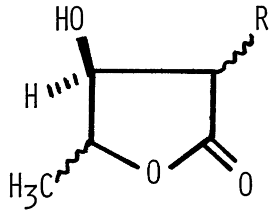


(I) R = H, R′ = $CH_2-(CH_2)_8-CH=CH_2$

(II) R = $CH_2-(CH_2)_8-CH=CH_2$, R′ = H

(III) R = H, R′ = $CH_2-(CH_2)_{11}-CH_3$

(IV) R = $CH_2-(CH_2)_{11}-CH_3$, R′ = H



(V) R = $CH_2-(CH_2)_{10}-CH_3$

(VI) R = $CH_2-(CH_2)_{12}-CH_3$

obtained from isoobtusilactone (II).

Obtusilactone A (III) and isoobtusilactone A (IV) both have the same molecular formula ($C_{19}H_{32}O_3$). The IR and UV spectra of them indicate that they have the same lactone grouping as those of I and II. Furthermore, on the basis of the exhaustive comparison of their spectral data, these two lactones must be geometrical isomers to each other at the position of the tri-substituted double bond conjugated to a lactone carbonyl, as seen in the cases of I and II. In particular, the structural assignments to these two lactones are based on δ-values of the methylene and olefinic protons attached to the tri-substituted double bond [III, δ 2.78 and 6.68ppm; IV, δ 2.46 and 7.05ppm].

Finally, the structures of these two lactones (III and IV) are confirmed by the following chemical evidence. Both lactones were subjected to catalytic hydrogenation over 5%Pd-$BaSO_4$ in EtOH - AcOEt (room temp., 5hr) to give the same tetrahydro-compound (VI)[5], mp 82.5-84°C (from n-hexane); $C_{19}H_{36}O_3$ [m/e 312(M^+), 129 and 116]; ν_{max}($CHCl_3$) 3630, 3430 and 1780cm^{-1}; δ($CDCl_3$) 0.90(3H, t, J$\simeq$6Hz), 1.28(26H, br.s), 1.45(3H, d, J= 6.5Hz), 2.60(1H, m) and 4.2 - 4.5ppm(2H, complex).

From a biogenetic point of view, these four lactones must be derived from a C_{14} or C_{16}-fatty acid and pyruvyl CoA.[1]

Chemical and structural studies on these novel lactones are further in progress.

REFERENCES AND FOOTNOTES

1. M. Niwa, M. Iguchi and S. Yamamura, Tetrahedron Lett. in press (1975) and references cited therein.
2. In the case of the air-dried leaves, these lactones have been detected only in quite low yields.
3. In the mass spectrum of I [m/e 278(M^+), 250, 235, 153 and 140], the prominent peaks corresponding to those of II are found in addition to the presence of a peak at m/e 153. This peak (m/e 153) is also present in the case of obtusilactone A (III), which has the same geometry as that of I at the position of the tri-substituted double bond.
4. Assignment of each signal has been carried out unambiguously with aid of double resonance experiments.
5. The stereostructures of V and VI remain unsettled.

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