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STRUCTURES OF THREE NEW 6β-HYDROXY DI- AND TRI-OXYGENATED FRIEDELANE TRITERPENES FROM *KOKOONA ZEYLANICA* THW. (CELASTRACEAE)[1]

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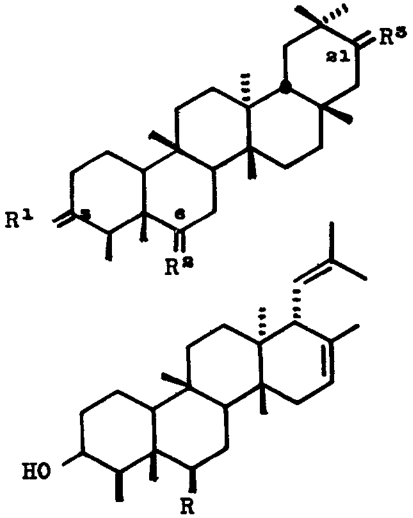
Summary: Three new triterpenes zeylanol, zeylanonol and zeylandiol isolated from *Kokoona zeylanica* have been identified as 6β-hydroxyfriedelan-3-one, 6β-hydroxyfriedelan-3,21-dione and 6β,21β-dihydroxyfriedelan-3-one, respectively by spectroscopic methods and chemical interconversions.

Recently we reported three new friedelane triterpenes, kokoonol, kokoononol and kokoondiol from *Kokoona zeylanica* Thw.[2] Three further triterpenes, zeylanol, zeylanonol and zeylandiol isolated from this plant have been identified as 6β-hydroxyfriedelan-3-one (1), 6β-hydroxyfriedelan-3,21-dione (2) and 6β,21β-dihydroxyfriedelan-3-one (3), respectively from the evidence presented below. This constitutes the first report of the natural occurrence of friedelanes with an oxygen substituent at C-6 and a hydroxy substituent at C-21 with a β-axial configuration. Occurrence of 6-hydroxyfriedelanes in Celastraceae is significant as 6-oxofriedelanes could be the possible biogenetic precursors of 24-norfriedelanes peculiar to this family.[3]

Spectroscopic and chemical evidence suggested zeylanol,[4] $C_{30}H_{50}O_2$, to be a keto-alcohol [ν, 3490 and 1715 cm^{-1} ; δ 3.66(1H,*m*,$W_{\frac{1}{2}}$ 20Hz)][5], zeylanonol, $C_{30}H_{48}O_3$, to be a diketo-alcohol [ν, 3490 and 1715 cm^{-1} ; δ 3.66(1H,*m*,$W_{\frac{1}{2}}$ 20Hz)] and zeylandiol, $C_{30}H_{50}O_3$, to be a keto-diol [ν, 3490 and 1715 cm^{-1} ; δ 3.73(D^6 - acetone + $CDCl_3$)(1H,*m*,$W_{\frac{1}{2}}$ 18Hz), 3.30 (1H,br*s*,$W_{\frac{1}{2}}$ 2Hz)] . All three compounds were related to friedelin by transformations depicted in the Scheme. Removal of OH groups in zeylanol and zeylandiol was achieved by Ph_3SnH reduction of the derived thiobenzoates (5) and (6), respectively. This recent deoxygenation method of Barton *et.al.*[6] was found to be superior to other conventional



(14) R = OH

(15) R = H

(1) $R^1 = O$; $R^2 = \beta\text{-OH}, \alpha\text{-H}$; $R^3 = H_2$

(2) $R^1 = R^3 = O$; $R^2 = \beta\text{-OH}, \alpha\text{-H}$

(3) $R^1 = O$; $R^2 = R^3 = \beta\text{-OH}, \alpha\text{-H}$

(4) $R^1 = R^3 = O$; $R^2 = H_2$

(5) $R^1 = O$; $R^2 = \beta\text{-O-}\overset{\overset{\text{S}}{\|}}{\text{C}}\text{-Ph}, \alpha\text{-H}$; $R^3 = H_2$

(6) $R^1 = O$; $R^2 = R^3 = \beta\text{-O-}\overset{\overset{\text{S}}{\|}}{\text{C}}\text{-Ph}, \alpha\text{-H}$

(7) $R^1 = R^3 = O$; $R^2 = \beta\text{-O-}\overset{\overset{\text{S}}{\|}}{\text{C}}\text{-Ph}, \alpha\text{-H}$

(8) $R^1 = R^2 = R^3 = O$

(9) $R^1 = R^2 = \beta\text{-OH}, \alpha\text{-H}$; $R^3 = O$

(10) $R^1 = R^2 = O$; $R^3 = H_2$

(11) $R^1 = R^3 = H_2$; $R^2 = O$

(12) $R^1 = [CH_2]_2O_2$; $R^2 = \beta\text{-OH}, \alpha\text{-H}$; $R^3 = O$

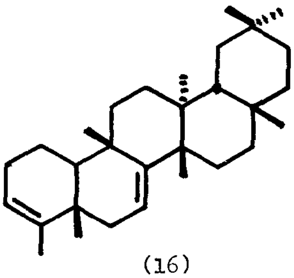
(13) $R^1 = R^2 = \beta\text{-OH}, \alpha\text{-H}$; $R^3 = H_2$

$$\begin{tikzcd}
& \begin{array}{c}\text{Zeylanol (1)}\\ \left[\begin{array}{l}\text{m.p.}274\text{-}76^\circ,\\ (\alpha)_D + 17.0\end{array}\right]\end{array} \arrow[dl, "iv"'] \arrow[d, "vi"] \arrow[dr, "ii,vi"] & (12) \arrow[l, "ii,iii"'] & \begin{array}{c}\text{Zeylanonol (2)}\\ \left[\begin{array}{l}\text{m.p.}272\text{-}74^\circ,\\ (\alpha)_D + 112.5\end{array}\right]\end{array} \arrow[l, "i"'] \arrow[r, "vi"] \arrow[d, "iv"] & (8) & \begin{array}{c}\text{Zeylandiol (3)}\\ \left[\begin{array}{l}\text{m.p.}276\text{-}78^\circ,\\ (\alpha)_D + 41.5\end{array}\right]\end{array} \arrow[l, "vi"'] \arrow[d, "vii"'] \arrow[dr, "iv"] & \\
(5) \arrow[d, "v"'] & (10) & (11) & (7) \arrow[r, "v"] & (4) & (9) & (6) \arrow[dllllll, "v"'] \\
\text{Friedelin} & & & & & &
\end{tikzcd}$$

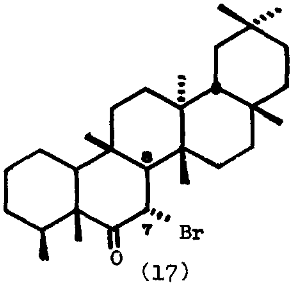
__Reagents:__ (i), $(CH_2OH)_2$/p-TSA/C_6H_6/reflux, 8h; (ii), $NH_2NH_2\text{-}H_2O$ (98-100%)/$(CH_2OH)_2$/150-60°C, 5h and 220°C for 10h; (iii), p-TSA/acetone/reflux, 12h; (iv), (a) $Ph.C(Cl)=\overset{+}{N}Me_2Cl^-/CH_2Cl_2$/THF, (b) H_2S/pyridine ; (v), Ph_3SnH/toluene/N_2/reflux, 2h; (vi), CrO_3/pyridine/25°C.

SCHEME

methods,[7,8] and has been applied for the first time to triterpene alcohols. More significantly, the method was successful in removing two oxygen atoms in one reaction as exemplified by the conversion of zeylandiol (3) to friedelin. Deoxygenation of zeylanon *via* the thiobenzoate (7) afforded friedelan-3,21-dione (4)[2] (m.m.p., Co-T.L.C., IR and MS). Since oxidation of both zeylanonol and zeylandiol gave the same triketone (8), zeylandiol should have an OH at C-21 with β-configuration ($W_{\frac{1}{2}}$ 2Hz). Removal of the 21-oxo function of zeylanonol yielded zeylanol (see Scheme). Therefore, it remained to determine the attachment of the OH substituent in zeylanol and zeylanonol.



(16)



(17)

Irradiation [125W, in refluxing dioxan, 18h][1] of the keto-diol (9), m.p. 280-82°, obtained from zeylanonol gave the non-conjugated diene (14). The ^{1}H n.m.r. spectrum of (14) was superimposable with that of (15)[2,9] except for the presence of a multiplet at 3.40 due to the additional $>$C$\underline{H}$OH. Therefore, the OH group is not in rings D or E. Presence of dioxygenated ring A was ruled out as the diketone (10), m.p. 305-6°, derived from zeylanol did not show any enol structure.[10,11] Zeylanol (1) on $NaBH_4$ reduction [CH_3OH/25°C/5 min.] gave the diol (13) which on treatment with $POCl_3$/pyridine[12] afforded a mixture of dienes. The major diene, m.p. 213-15°, had physical and spectral data compatible with the structure (16)[12]. As the diketone (10) was different from putranjivadione,[13] the OH group is not at C-7. However, the diene (16) could also arise from 3,6-dihydroxyfriedelane as a result of the rearrangement of 6(7)-olefin to more stable 7(8)-olefin under the above reaction conditions.

The monoketone (11), m.p. 276-78°, obtained from zeylanol by Huang-Minlon reduction and subsequent oxidation, showed in its ^{1}H n.m.r. spectrum a clear AMX pattern[14] due to 7-H_2 and 8-H [δ, 2.73 and 2.03(H-7), 1.63(H-8); $\underline{J}_{AM}$ 14Hz, $\underline{J}_{MX}$ 12Hz and $\underline{J}_{AX}$ 4Hz]. Addition of Eu(fod)$_3$ caused a low field shift of the signals due to these protons. ^{13}C n.m.r. spectrum of (11)[15] further supported the 6-keto assignment. The bromoketone

(17), m.p. 218-20°, prepared from (11) showed in its ^1H n.m.r. spectrum among other signals a dd due to 7-H and 8-H (δ,4.10 and 2.67 respectively, J 6Hz) further supporting the 6-keto assignment. ^1H n.m.r. spectra of all three natural compounds were in agreement with β-configuration for the OH group at C-6 (see above).

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