

THE STRUCTURE OF KANSUININE A, A NEW MULTI-OXYGENATED DITERPENE

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Previously^{1,2)}, we described the structures of the 13-oxyingenol derivative and 20-deoxy-ingenol derivatives isolated from Chinese herb "Kansui" (Euphorbia kansui Liou).

Further investigation afforded a new toxic (LD₅₀ 30 mg/kg) compound, named kansuinine A, which had also analgesic and anti-writhing activities (0.5 mg/kg).

Now we wish to report the structure of kansuinine A. Physical and spectral data of kansuinine A are as follows.

Kansuinine A: C₃₇H₄₆O₁₅ [M⁺ 730.2840 (calcd. 730.2836)]; m.p. 218-220° (ether-petroleum ether); [α]_D²³ = +28 (c, 0.25 in methanol); IR (KBr) 3550, 1745, 1680, 1605, 1590, 1220-1280 cm⁻¹; UV (MeOH) 230 nm (ε, 12000); NMR Fig. 1.

The nmr spectrum of kansuinine A indicates that this compound has five acetates and one benzoate. This observation suggested that the parent alcohol of this compound is C₂₀H₃₂O₉, a multi-oxygenated diterpene. Since no further information was obtained from the nmr spectrum, we tried the following reactions to obtain properties of functional groups.

Kansuinine A (1) gave a diol (2) by the oxidation with osmium tetroxide followed by the treatment with sodium bisulfite. In the nmr spectrum of the diol (2) the signal of two protons assigned to -CH₂OH appeared as an AB quartet centered at δ 3.40. Furthermore, the diol (2) was converted to a p-bromobenzoate (3) and a keto compound (4). Also the acetylation of kansuinine A by the ordinary method (acetic anhydride-pyridine) did not occur, but this compound gave a methyl ether (5) with silver oxide and methyl iodide, in which no more alcohol groups are present. Kansuinine A was converted to compound (6) by the reduction with sodium borohydride in THF, from which kansuinine A was regenerated by oxidation with chromium trioxide

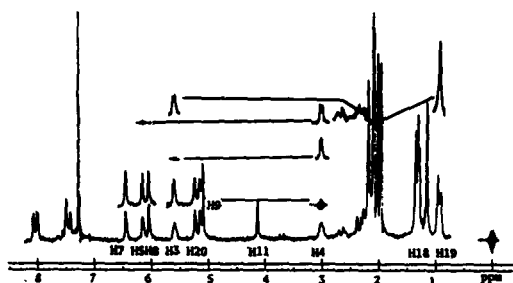


Figure 1. NMR spectrum (100 MHz, $CDCl_3$) of kansuicine A

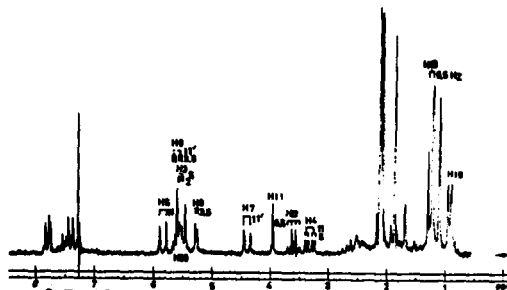
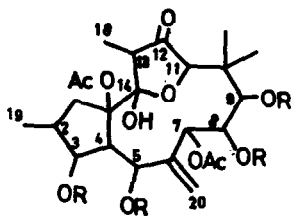
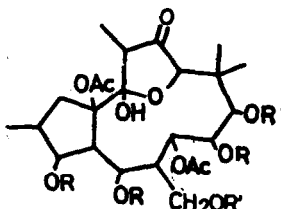


Figure 2. The NMR spectrum (100 MHz, $CDCl_3$) of compound (8)

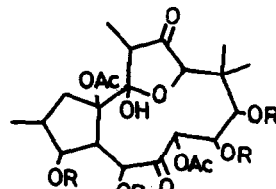


Kansuicine A (1)

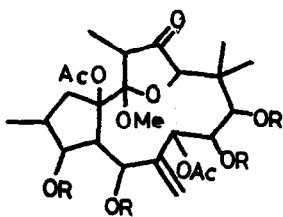


(2) $R' = H$

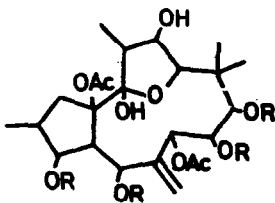
(3) $R' = p\text{-bromobenzoyl}$



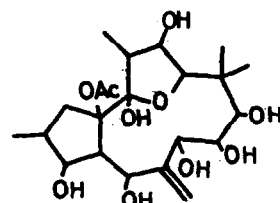
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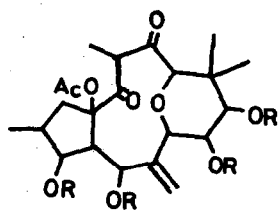
(5)



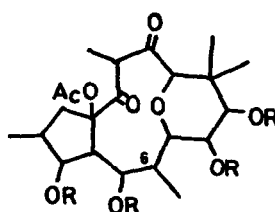
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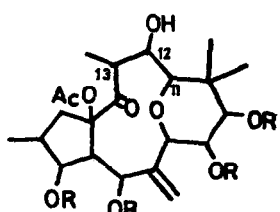
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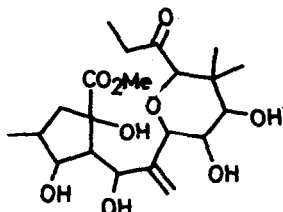
(8)



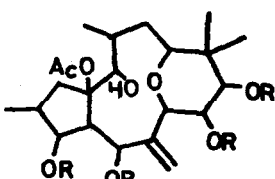
(9)



(10)



(11)

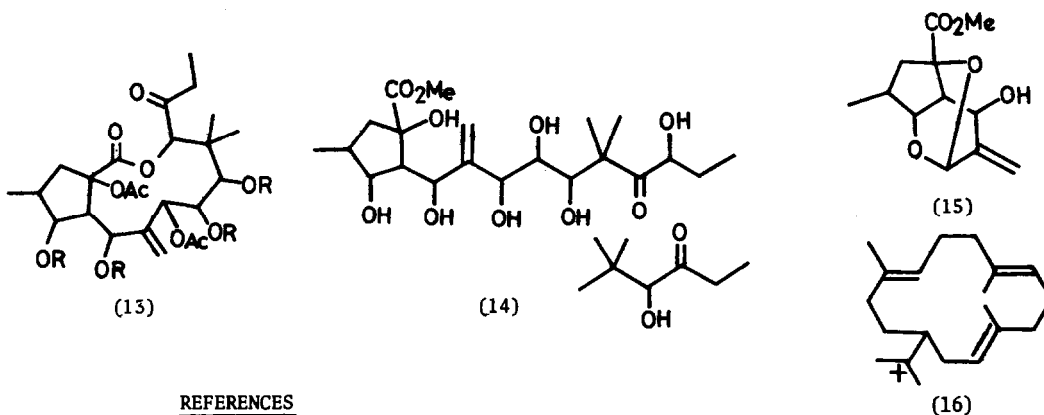


(12)

$R = \text{benzoyl X1, acetyl X3}$

Furthermore, we could detect the derivative possessing eleven carbon atoms of the parent diterpene skeleton by the next reaction. Kansuinine A yielded a lactone (13) with sodium hydride in THF at 50° for 30 minutes by a novel retro-aldol reaction. In the nmr spectrum of compound (13) the presence of protons [δ 1.08 (3H, t, $J = 7$ Hz), 2.50 (2H, q, $J = 7$ Hz)] due to the ethyl ketone group and the proton [δ 4.94 (1H, s)] on the carbon attached at ethereal oxygen of the lactone were shown. The lactone (13) was converted to the methyl esters (14), which gave compound (15) on oxidation with periodic acid in acetone-water. The structure of compound (15) was fully established by spectral data: compound (15) [$C_{12}H_{16}O_5$; IR(CHCl₃) 3550, 1735, 1600, 920 cm^{-1} ; NMR (δ , CDCl₃) 1.16 (3H, d, $J = 6$ Hz, 2-CH₃), 1.9-2.3 (3H, m, H-1 and H-2), 2.36 (1H, d of d, $J_{3,4} = 3$ Hz, $J_{4,5} = 3$ Hz), 3.78 (3H, s, COOCH₃), 4.16 (1H, d of d, $J_{2,3} = 3$ Hz, $J_{3,4} = 3$ Hz, H-3), 4.68 (1H, m, 5-H), 5.16 (1H, s, H-7), 5.22 (1H, d, $J_{5,20} = 2.5$ Hz, H-20), 5.28 (1H, d, $J_{5,20} = 2$ Hz, H-20); Mass 240 (m^+), 212 ($m^+ - 18$), 181 ($m^+ - 18 - 59$)].

As a result we established the structure of kansuinine A except the stereochemistry, which is described in the following paper. Kansuinine A possesses the jatrophone skeleton³⁾, and those compounds may be biosynthetically formed via casbene type compounds⁴⁾, or via a cation (16) directly.



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