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

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(Received in Japan 15 March 1975; received in UK for publication 11 April 1975)

Previously<sup>1,2)</sup>, we described the structures of the 13-oxyingenol derivative and 20-deoxyingenol derivatives isolated from Chinese herb "Kansui" (<u>Euphorbia kansui</u> Liou). Further investigation afforded a new toxic (LD<sub>50</sub> 30 mg/kg) compound, named kansuinine A, which had also analgesic and anti-writhing activities (0.5 mg/kg).

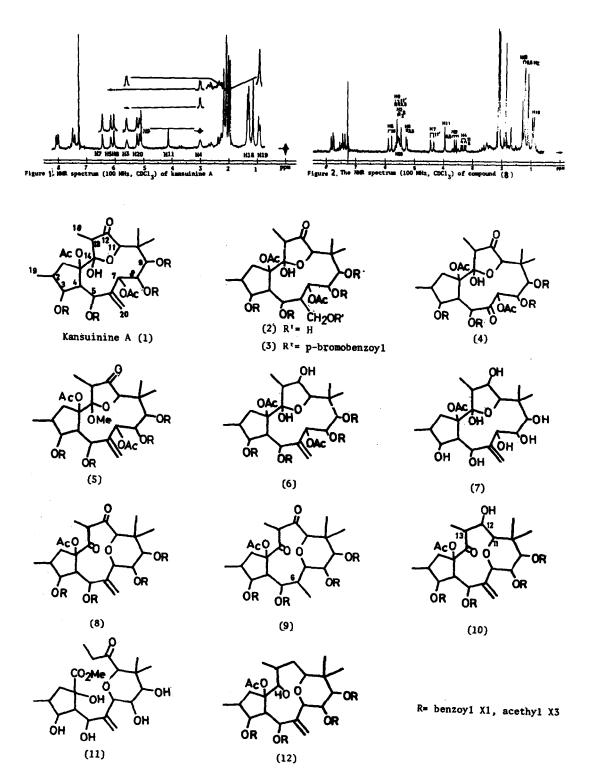
Now we wish to report the structure of kansuinine A. Physical and spectral data of kansuinine A are as follows.

Kansuinine A:  $C_{37}H_{46}O_{15}$  [M<sup>+</sup> 730.2840 (calcd. 730.2836)]; m.p. 218-220° (ether-petroleum ether);  $[\alpha]_D^{23} \approx +28$  (c, 0.25 in methanol); IR (KBr) 3550, 1745, 1680, 1605, 1590, 1220-1280 cm<sup>-1</sup>; UV (MeOH) 230 nm ( $\epsilon$ , 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  $C_{20}H_{32}O_9$ , 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  $-CH_2OH$  appeared as an AB quartet centered at  $\delta$  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 in pyridine. This result indicates the presence of a keto group in kansuinine A. Furthermore, the presence of a tertiary acetoxy group was deduced as follows. Hydrolysis of compound (6) afforded compound (7) containing one acetoxy group, whose nmr spectrum showed no low field proton signals originally present in (6) except those due to two protons assigned to the exocyclic methylene. Above data showed that the properties of nine oxygens present in kansuinine A are characterized as seven hydroxyls, one ketone, and one ethereal function. Consequently, the number of the ring system is three, including the ether ring. As shown in Fig.1, the values of coupling constants among the protons are small, so we tried to obtain derivatives better suited for structure elucidation by nmr spectral analysis.

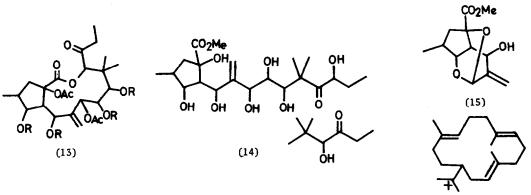
The treatment of kansuinine A with p-toluenesulfonic acid in benzene afforded a deacetoxy compound (8) in good yield [(8): C<sub>35</sub>H<sub>42</sub>O<sub>13</sub>; m.p. 206-207°; IR(CHCl<sub>3</sub>) 1740, 1685, 1640, 1600, 1585, 940 cm<sup>-1</sup>; Mass 670 (m<sup>+</sup>), 642]. The nmr spectrum of this compound (8) is shown in Fig.2; the assignment of each proton was clearly made on this compound (8) by decoupling procedures and the observation of INDOR spectra. Furthermore, hydrogenation of compound (8) afforded a dihydro compound (9) with Pd-C as catalyst. In the nmr spectrum of compound (9), the doublet signal of the newly formed secondary methyl group appeared at  $\delta$  1.38, and the irradiation of the signal assigned to proton at C-6 caused two broad doublets at  $\delta$  4.09 (H-7) and  $\delta$  5.20 (H-5) to become to sharp doublets, respectively. Based on the nmr spectral data of compounds (8) and (9), partial structures were able to be derived as shown in I, II, and III. The reduction of compound (8) with sodium borohydride gave compound (10). The findig that in the nmr spectrum of compound (10) the signal of the new proton appeared at 8 3.65 as a double doublet  $(J_{11,12} = 6 \text{ Hz}, J_{12,13} = 4 \text{ Hz})$ , and the presence of the  $\beta$ -diketone group in compound (8), which was proved by the formation of compound (11)  $[C_{21}H_{34}0_9; IR(CHC1_3) 3450,$ 1742, 1700, 1620, 940 cm<sup>-1</sup>; NMR 0.92 (3H, t, J= 7 Hz, H-18), 2.60 (2H, q, J= 7 Hz, H-13), 3.71 (3H, s, -COOCH<sub>2</sub>); Mass 412 (m<sup>+</sup>-18), 383 (m<sup>+</sup>-18-29), 355 (m<sup>+</sup>-18-29-28)] and (12), suggested another partial structure IV. These partial structures, I, II, III, and IV, coupled with the biogenetic consideration suggested the structure of kansuinine A as depicted in (1).



(16)

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 [ $\delta$  1.08 (3H, t, J= 7 Hz), 2.50 (2H, q, J= 7 Hz)] due to the ethyl ketone group and the proton [ $\delta$  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(CHCl<sub>3</sub>) 3550, 1735, 1600, 920 cm<sup>-1</sup>; NMR ( $\delta$ , CDCl<sub>3</sub>) 1.16 (3H, d, J= 6 Hz, 2-CH<sub>3</sub>), 1.9-2.3 (3H, m, H-1 and H-2), 2.36 (1H, d of d, J<sub>3,4</sub>= 3 Hz, J<sub>4,5</sub>= 3 Hz), 3.78 (3H, s, COOCH<sub>3</sub>), 4.16 (1H, d of d, J<sub>2,3</sub>= 3 Hz, J<sub>3,4</sub>= 3 Hz, H-3), 4.68 (1H, m, 5-H), 5.16 (1H, s, H-7), 5.22 (1H, d, J<sub>5,20</sub>= 2.5 Hz, H-20), 5.28 (1H, d, J<sub>5,20</sub>= 2 Hz, H-20); Mass 240 (m<sup>+</sup>), 212 (m<sup>+</sup>-18), 181 (m<sup>+</sup>-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 skeleton<sup>3)</sup>, and those compounds may be biosynthetically formed <u>via</u> casbene type compounds<sup>4)</sup>, or <u>via</u> a cation (16) directly.



## REFERENCES

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