Tetrahedron Letters No. 15, pp 1387 - 1390, 1972. Pergamon Press. Printed in Great Britain.

TWO NEW DITERPENOIDS, JOLKINOLIDES A AND B, OBTAINED FROM EUPHORBIA JOLKINI BOISS. (EUPHORBIACEAE)

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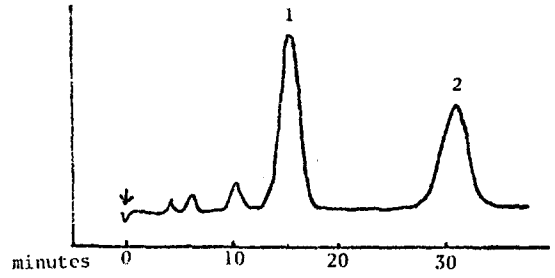
(Received in Japan 9 February 1972; received in UK for publication 2 March 1972)

In the course of our continuing search for irritant substances[1-6] in Euphorbia species, new several diterpenoids were isolated from E. Jolkini Boiss. (Japanese name, Iwataigeki). Now we wish to report the isolation and structures of new diterpenoids, named jolkinolides A and B.

The fresh roots crushed to pieces were washed with methanol and extracted with benzene. Benzene extracts were separated on silicic acid by column chromatography monitored by high speed liquid chromatography. Recrystallization from ether and methanol afforded jolkinolide A (1) [$C_{20}H_{26}O_3$: M^+ 314.1896 (calcd. 314.1882), m.p. ∿220° (decomp. in sealed tube), $[\alpha]_D^{25}$= +130° (c= 0.7, $CHCl_3$)] and jolkinolide B (2) (main component) [$C_{20}H_{26}O_4$: M^+ 330.1840 (calcd. 330.1831), m.p. ∿215° (decomp. in sealed tube), $[\alpha]_D^{25}$= +220° (c= 0.4, $CHCl_3$)], respectively. The high speed liquid chromatogram of one fraction containing both compounds descrived above is shown in Figure.



Column: 100 cm/ 1.8 mm i.d., Silicic acid (25-35 μ)
Flow : 20 ml/hr (2700 psi)
Solvent: 10% THF in isooctane
Detector: UV (254 nm)
Temperature: 35°

1. Jolkinolide A
2. Jolkinolide B

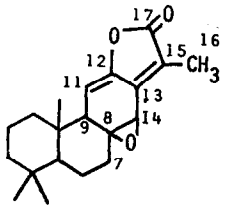
Figure

The structures of jolkinolides A and B were elucidated by the following spectral data and chemical evidence.

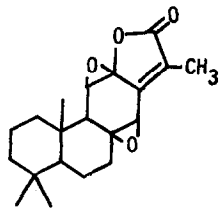
Jolkinolide A showed UV (MeOH) 288 nm (ε, 19300); IR ($CHCl_3$) 1770, 1670, 1660 cm^{-1}; NMR ($CDCl_3$, δ) 0.73, 0.87, 0.97 (9H, s, three CH_3), 2.08 (3H, s, 16-CH_3), 2.64 (1H, d, J= 6 Hz, 9-H),

3.74 (1H, br.s, 14-H), 5.47 (1H, d, J= 6 Hz, 11-H).

Jolkinolide B (2) showed UV (MeOH) 240 nm (ε, 16600); IR ($CHCl_3$) 1790, 1690 cm^{-1} ; NMR ($CDCl_3$, δ) 0.83, 0.87, 0.97 (9H, s, three CH_3), 2.10 (3H, s, 16-CH_3), 2.30 (1H, br.s, 9-H), 3.70 (1H, s, 14-H), 4.06 (1H, d, J= 1.5 Hz, 11-H).



(1)



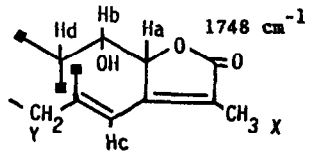
(2)

It was expected that epoxidation of jolkinolide A (1) would afford jolkinolide B (2) from the NMR spectral data of jolkinolides A and B: in the NMR spectrum of (2) one olefinic proton of (1) disappeared and instead a signal of one proton attached to carbon bearing oxygen appeared. Actually treatment of jolkinolide A (1) with m-chloroperbenzoic acid yieled jolkinolide B (2).

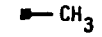
Catalytic hydrogenolysis of jolkinolide B (2) afforded tetrahydrojolkinolide B (3), m.p. 220-221°, which possesses molecular formula, $C_{20}H_{30}O_4$. The presence of an α,β-unsaturated γ-lactone [UV (MeOH) 225 nm (ε, 10400); IR ($CHCl_3$) 1750, 1680 cm^{-1}] and two hydroxy groups [IR ($CHCl_3$) 3400-3600 cm^{-1}; NMR ($CDCl_3$, δ)2.5-3.0 (2H, exchangeable with D_2O)] was evident in (3), which gave a monoacetate (4) [IR ($CHCl_3$) 3300-3650, 1755, 1690 cm^{-1}; NMR ($CDCl_3$, δ) 0.67, 0.80, 0.90 (9H, s, three CH_3), 1.80 (3H, br.s, 16-CH_3), 2.10 (3H, s, -$COCH_3$), 2.24 (1H, s, exchangeable with D_2O), 2.57, 2.72 (2H, m, 14-H), 4.98 (1H, d of d, J= 2.8, 5.6 Hz, 11-H), 5.60 (1H, m, 12-H)]. These spectral data of (4) support the presence of one tertiary hydroxy group and one secondary acetoxy group. And on treatment of (4) in ethanol in the presence of sodium borohydride (4) gave, without reduction, a product (5), which contained a γ-alkylidene-substituted α,β-unsaturated γ-lactone grouping [UV (MeOH) 282 nm (ε, 15000); IR ($CHCl_3$) 1765, 1665, 1655 cm^{-1})].

Dehydration of tetrahydrojolkinolide (3) in 50% aqueous sulfuric acid and benzene (1:1) gave a monohydroxy compound (6). The NMR ($CDCl_3$)[7], IR ($CHCl_3$), and UV (MeOH) spectra showed the following partial structures A and B for (6).

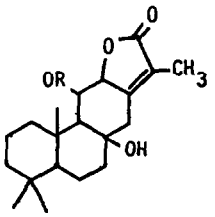
From the chemical shifts of three tertiary methyl groups and biogenetic consideration it was suggested that this compound (6) have an abietane skeleton, and the compounds (3), (4), (5), and (6) are figured as shown next.

A 

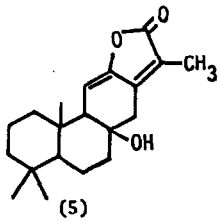
Ha 4.65 (1H, d of q, J_{aX}= 1.5 Hz J_{ab}= 9.3 Hz)
Hb 3.70 (1H, d of d, J_{bd}= 6.8 Hz, J_{ab}= 9.3 Hz)
Hc 6.20 (1H, br.s)
X 1.84 (3H, d, J_{aX}= 1.5 Hz)
Hd,Y 2.0-2.6 (3H, m)
279 nm (ε, 21500)

B 

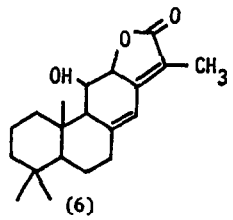
0.72 (3H, s), 0.82 (3H, s), 0.90 (3H, s)



(3) R= H
(4) R= $COCH_3$



(5)



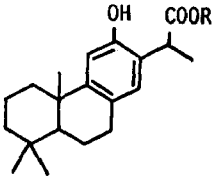
(6)

These results were supported by the following reactions. Hydrolysis of (6) with 5% aqueous potassium hydroxide and methanol (1:1), followed by treatment with 2N hydrochloric acid, yielded a hydroxy acid (7), which was converted to an aromatic methyl ester (8) [IR ($CHCl_3$) 3300-3600, 1700-1740 (broad band because of hydrogen bonding), 1620, 1495 cm^{-1}; NMR ($CDCl_3$, δ) 0.93 (6H, s, 18,20-CH_3), 1.17 (3H, s, 19-CH_3), 1.54 (3H, d, J= 7.5 Hz, 16-CH_3), 2.6-3.0 (2H, m, 7-H), 3.70 (3H, s, -$COOCH_3$), 3.82 (1H, q, J= 7.5 Hz, 15-H), 6.76, 6.80 (2H, s, 11,14-H)].

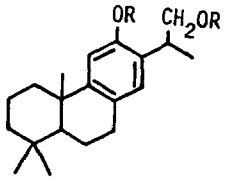
The structure of the methyl ester (8) was confirmed by the transformation of this compound to ferruginol (14)[8]. Lithium aluminum hydride reduction of (8) gave a diol (9), which was converted to dimethanesulfonate (10) with methanesulfonyl chloride in pyridine. Reaction of (10) with 1,5-diazabicyclo[5.4.0]undec-5-ene at 100° for 10 hours yielded a monomethanesulfonate (11) and an ether (12). Ether (12) would be produced by a cleavage of S-O bond[9] in phenol methanesulfonate, followed by cyclization. Catalytic hydrogenation of the monomethanesulfonate (11) gave (13), which was quantitatively converted with lithium aluminum hydride to (-)ferruginol (14): $[\alpha]_D^{25}$= -49° (c= 0.45, EtOH).

The location of the epoxide linkage in 11,12-position in (2) was determined by epoxidation of (1) with m-chloroperbenzoic acid to (2). And the presence of the epoxide linkage in 8,14-position in (2) was indicated by the signal [δ 3.70 (1H,s)] of one proton on C-14 in the NMR spectrum of (2).

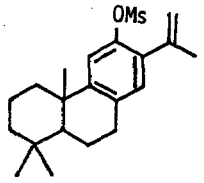
Investigation is in progress to determine the stereochemistry of jolkinolides A and B.



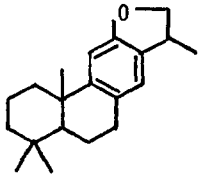
(7) R= H
(8) R= CH_3



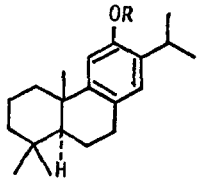
(9) R= H
(10) R= Ms



(11)



(12)



(13) R= Ms
(14) R= H

Acknowledgment

Our thanks are due to Professor H. Kakisawa (Tokyo Kyoiku University) for providing us with the IR spectrum of ferruginol.

Referrences and Footnotes

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7) This result was verified by the nuclear magnetic double resonance experiments (100 MHz).

8) C. W. Brandt and L. G. Neubauer, J. Chem. Soc., 1939, 1031.

9) Treatment of a methanesulfonate of β-naphthol with 1,5-diazabicyclo[5.4.0]undec-5-ene at 100° yielded β-naphthol, quantitatively.