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THREE NEW DITERPENOIDS, JOLKINOLIDES C, D, AND E, ISOLATED FROM EUPHORBIA JOLKINI BOISS. (EUPHORBIACEAE)

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Further investigation of constituents in title plants gave three new diterpenoids, named jolkinolides C, D, and E. In this report structural elucidation of those compounds was described.

Previously[1)], we reported the structures of two diterpenoids, jolkinolide A and jolkinolide B possessing the novel functional groups, isolated from the title plants in the study on the irritant substances[2-9)] of Euphorbia species. Now we wish to report the structure of three new components, additionally isolated as minor constituents, which were elucidated by spectral data and chemical reactions.

Physical constants and spectral data of jolkinolides C, D, and E are as follows.

Jolkinolide C (1)

$C_{20}H_{26}O_3$: m$^+$ 314.1877 (calcd. 314.1882); m.p. ca.300 (decomp.); $[\alpha]_D^{20}$= -27 (c, 0.75, $CHCl_3$); UV (MeOH) 285 nm (ε, 2200); IR (KBr) 3400, 1790, 1640, 1620, 1500 cm^{-1}; NMR (δ, $CDCl_3$, 60 MHz) 0.95 (3H, s), 0.97 (3H, s), 1.20 (3H, s, 18-H), 1.63 (3H, d, J= 7.5 Hz, 16-H), 2.5-3.0 (2H, m, 7-H), 3.83 (1H, q, J= 7.5 Hz, 15-H), 4.7-5.0 (1H, br.s, exchangeable with D_2O), 6.53 (1H, s, 11-H).

Jolkinolide D (2)

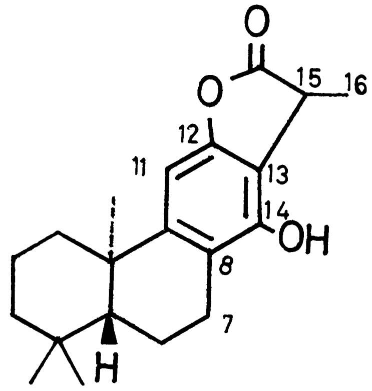
$C_{20}H_{28}O_3$: m$^+$ 316.2053 (calcd. 316.2038); m.p. 200-201°; $[\alpha]_D^{20}$= +360 (c, 0.28, $CHCl_3$); UV (MeOH) 223 nm (ε, 6600); IR (KBr) 3450, 1750, 1660, 1630, 870, 820 cm^{-1}; NMR (δ, $CDCl_3$, 60 MHz) 0.80 (3H, s), 0.88 (3H, s), 0.90 (3H, s), 1.9-2.2 (1H, br.s, exchangeable with D_2O), 4.45 (1H, br.s, 12-H), 5.15 (1H, br.s, 14-H), 5.82 (1H, s, 16-Ha), 6.22 (1H, s, 16-Hb).

Jolkinolide E (3)

$C_{20}H_{28}O_2$; m$^+$ 300.2092 (calcd. 300.2089); m.p. 182-183°; $[\alpha]_D^{20}$= +340 (c, 0.45, $CHCl_3$); UV (MeOH) 278 nm (ε, 22000); IR(KBr) 1750, 1665, 1605 cm^{-1}; NMR 0.85 (3H, s), 0.93(6H, s), 1.82 (3H, d, J= 1.5 Hz, 16-H), 2.56 (1H,m, 9-H), 4.85 (1H, d of d, J_{AX+BX}= 19 Hz, 12-H), 6.20 (1H, br.s, 14-H).

Spectral data of jolkinolide C (1) were similar to those of an aromatic compound (4) [$C_{20}H_{26}O_2$ (m^+ 298); IR ($CHCl_3$) 1810, 1635, 1490 cm^{-1}], which was obtained from jolkinolide B (5) with Zn-HCl gas in ether at room temperature. In the nmr spectra of these compounds the difference of jolkinolide C from the compound (4) was the presence of one hydroxy group instead of one proton on an aromatic ring. This showed that the hydroxy group of jolkinolide C was attached at C-11 or C-14 in the aromatic ring of compound (4). The location for the hydroxy group at C-14 was unambiguously confirmed by the transformation from jolkinolide A (6) to jolkinolide C. Jolkinolide A was converted to a keto compound (7) with BF_3-etherate in dry benzene for one hour at room temperature: (7) $C_{20}H_{26}O_3$ (m^+,314); IR ($CHCl_3$) 1770, 1700, 1655, 1630 cm^{-1}. The aromatization of this compound (7) with p-toluenesulfonic acid in benzene at 50° afforded[10)] jolkinolide C (1), whose structure was determined to be <u>1</u> because jolkinolide A was correlated to (-)-ferruginol (8)[1,11)], while a configuration at C-15 was unsettled.

With aid of catalyst and the use of ethyl acetate as the solvent, jolkinolide D consumed one equivalent of hydrogen and gave dihydrojolkinolide D (9): $C_{20}H_{30}O_3$ (m^+ 318); m.p. 191-193°; IR ($CHCl_3$) 3450, 1775, 1655, 820 cm^{-1}; NMR (δ, $CDCl_3$) 0.80 (3H, s), 0.89 (3H, s), 0.90 (3H, s), 1.20 (3H, d, J= 7.5 Hz, 16-H), 1.75 (1H, br.s, exchangeable with D_2O), 2.82 (1H, q, J= 7.5 Hz, 15-H), 4.40 (1H, br.s, 12-H), 5.32 (1H, s, 14-H). The nmr spectrum of the compound (9) showed that an exocyclic double bond conjugated with the carbonyl group of γ-lactone in jolkinolide D was lost and a secondary methyl group was newly formed. Further, a dehydration of the compound (9) with 50% aq. H_2SO_4-benzene afforded jolkinolide E (3), whose structure was in turn established by the correlation with jolkinolide A. Hydrogenation of jolkinolide A (Pd-C in ethyl acetate) gave tetrahydrojolkinolide A (10) [$C_{20}H_{30}O_3$ (m^+ 318); m.p. 250-252; IR ($CHCl_3$) 3600, 3450, 1745, 1680 cm^{-1}]. Dehydration of the derivative (10) in 50% aq. H_2SO_4-benzene afforded a compound, which was identical with the compound derived from jolkinolide E by treatment with potassium t-butoxide in t-butanol. From above experiments the structure of jolkinolide E and the framework of jolkinolide D were determined. There remained problems of the situation of one tertiary hydroxy group which was not acetylated with acetic anhydride-pyridine, and the trisubstituted double bond in jolkinolide D. The position of the tertiary hydroxy group at C-13 was supported from the consideration of the next findings. In the nmr spectra of jolkinolide D and dihydrojolkinolide D signals of the protons on C-12 were appeared as broad singlets (half band width 5 Hz and 5 Hz, respectively), which had to be assigned to equatorial protons. Only in the case that C-13 was sp^3 carbon atom, the proton on C-12 was permitted to be equatorial. Since the signal assigned to the proton on C-15 appeared as a sharp quartet in the nmr spectrum of dihydrojolkinolide D (9), the tertiary hydroxy group was present at C-13. That the trisubstituted double bond



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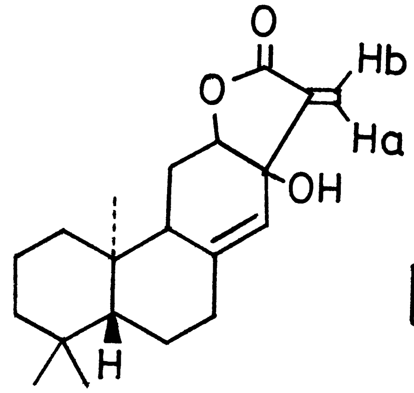

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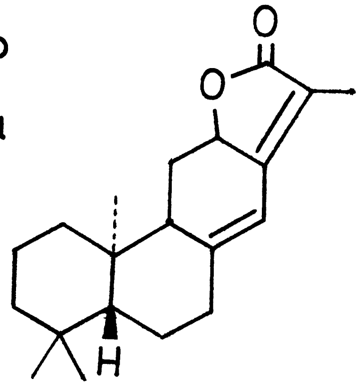

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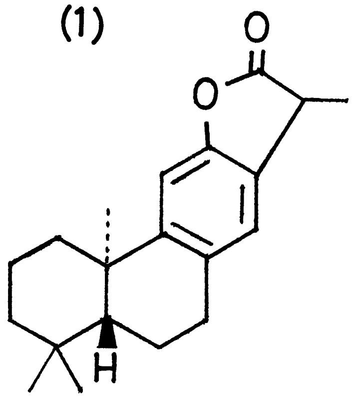

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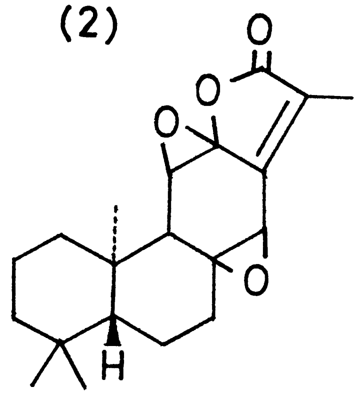

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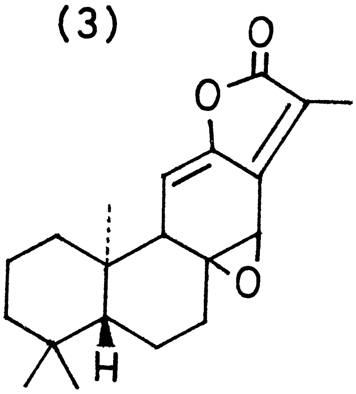

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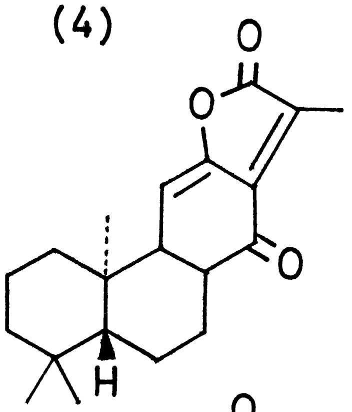

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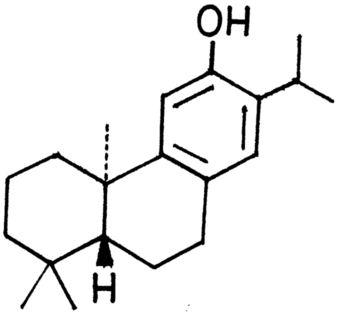

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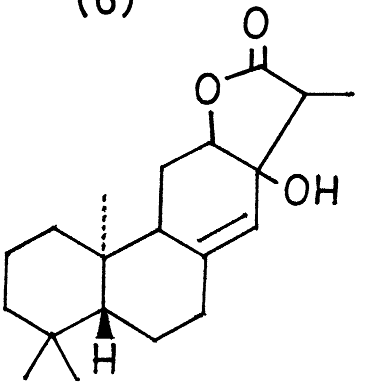

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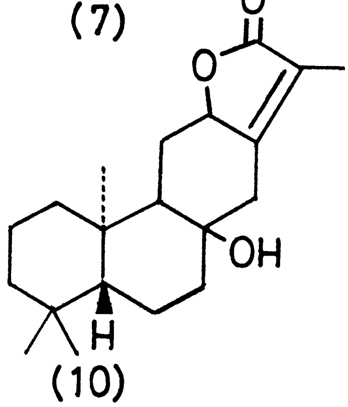

(10)

corresponding to the absorptions at 1665 and 820 cm^{-1} in the ir spectrum of dihydrojolkinolide D (9) was present between C-8 and C-14 was consistent with the appearance of a signal of the proton on C-14 as a broad singlet and the presence[12)] of long-range coupling between signals of protons on C-12 and C-14 in the nmr spectrum of dihydrojolkinolide D. Also easy dehydration of dihydrojolkinolide D to jolkinolide E suggested this conclusion. Therefore, the structures of jolkinolides D and E were shown as 2 and 3, respectively.

Investigation to determine the stereochemistry of jolkinolide is in progress.

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10) In this reaction another compound was obtained, which was considered to be C-15 epimer. The same treatment of natural jolkinolide C gave jolkinolide C and this compound.

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