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Multidione, a novel diterpenoid from *Jatropha multifida* ☆

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ABSTRACT

A novel diterpenoid, multidione, has been isolated from the stems of *Jatropha multifida* and its structure has been settled from 1D and 2D NMR spectra. The compound possesses a phenolic moiety and a long side chain, structurally similar to the B ring of other lathyrane-diterpenoids in *seco*-form.The compound has possibly been derived biogenetically from a related lathyrane-diterpenoid.

Jatropha species (Euphorbiaceae) are a rich source of macrocyclic diterpenoids.[1–10] Some of these constituents possess interesting biological activities including *anti*-bacterial and *anti*-cancer properties. The constituents of *Jatropha* species are mainly of lathyrane-type diterpenoids. In continuation of our work[8,9] on these plants we have isolated a novel diterpenoid, multidione (**1**) from the stems of *Jatropha multifida*. The plant is reputed to exhibit various medicinal properties including antibiotic activity.[11] From the latex of the plant other workers reported some cyclic peptides, phenolics and glycosides.[12–14]

Multidione (**1**) is structurally interesting. It contains a phenolic moiety and a long side chain related to the B-ring of other lathyrane-diterpenoids in *seco*-form. The purification and structure elucidation of **1** are difficult. However, with our continuous efforts we were able to purify and characterize the molecule. Herein, we report its isolation and structure elucidation.

Multidione (**1**) was obtained as colourless liquid.[15] Its molecular formula was deduced to be $C_{20}H_{28}O_3$ from its HREIMS (*m*/*z* 317.2109 $[M+H]^+$). The IR spectrum showed the presence of hydroxyl and carbonyl groups as well as aromatic residue in the molecule.

The structure of the compound was settled from its ^1H and ^{13}C NMR spectroscopic data (Table 1) assigned in assistance with 2D NMR (^1H-^1H COSY, NOESY, HSQC and HMBC) and DEPT experiments. The spectra suggested that the compound contains a 2,4-disubstituted phenolic moiety having a methyl group at C-2 and a long side chain at C-4. In the ^{13}C NMR spectrum C-1 appeared at δ 158.8. The HMBC spectrum showed correlations between H-3 (δ 7.80, d, $J = 2.0$ Hz) and C-7 (δ 15.8) and Me-7 (δ 2.30, s)

Table 1
NMR spectral data of multidione (**1**) (500 MHz for ^1H NMR and 125 MHz for ^{13}C NMR, $CDCl_3$, 30 °C)

Position	^1H NMR	Multiplicity (*J* in Hz)	^{13}C NMR
1	–	–	158.8
2	–	–	124.2
3	7.80	d (2.0)	131.8
4	–	–	129.4
5	7.75	dd (8.4, 2.0)	128.3
6	6.83	d (8.4)	114.7
7	2.30	s	15.8
1′	–	–	203.8
2′	3.45	m	40.3
3′	(a) 1.42	m	
	(b) 1.68	m	29.01
4′	0.46	m	24.5
5′	–	–	17.3
6′	0.42	m	25.9
7′	(a) 1.55	m	19.1
	(b) 1.44	m	
8′	2.42	t (7.0)	44.1
9′	–	–	209.8
10′	2.15	s	29.9
11′	1.20	d (6.8)	17.4
12′	0.91	s	29.03
13′	0.89	s	14.7

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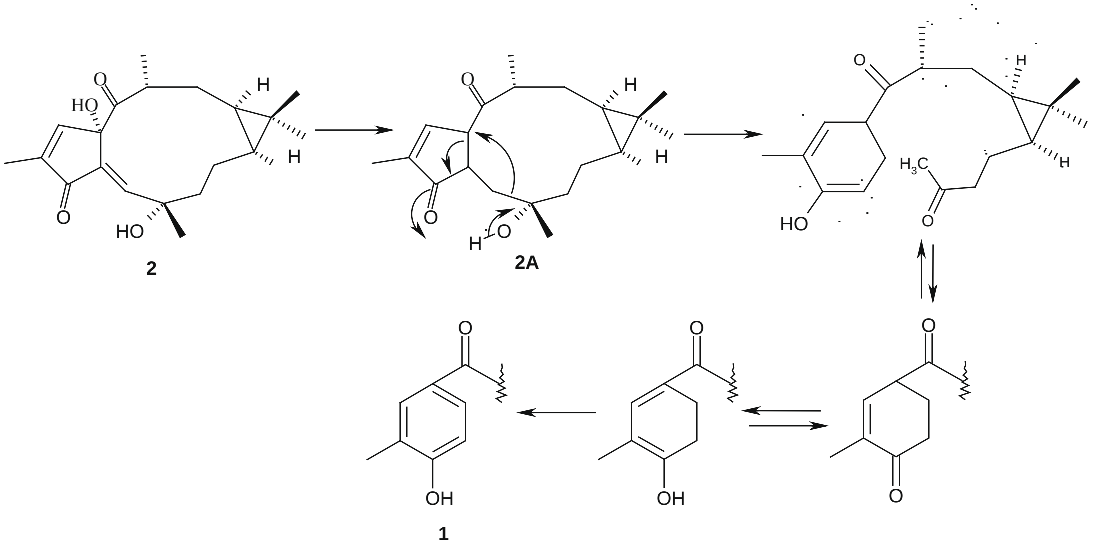
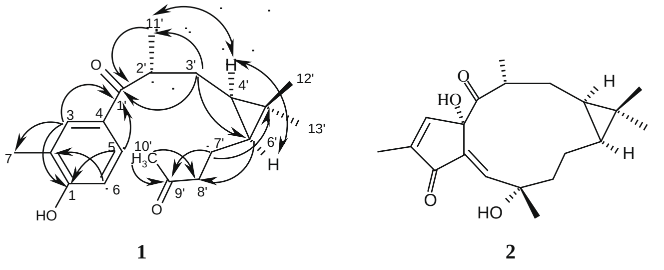


Scheme 1.

and C-3 (δ 131.8). The long side chain at C-4 is related to the B-ring of the known lathyrane-type diterpenoid, (4*E*)-jatrogrossidentadione (**2**)[4] (presently isolated from the same plant) in *seco*-form. This side chain contained four methyl groups, two carbonyl groups and a cyclopropane ring (Table 1). The presence of a carbonyl group at C-1′ (δ 203.8) was evident from the HMBC spectrum which revealed that both H-3 and H-5 (δ 7.75, dd, J = 8.4, 2.0 Hz) were related to this carbon. The ^{1}H-^{1}H COSY experiment showed the correlation sequence: H-2′–H-3′–H-4′–H-6′–H-7′–H-8′ and H-2′–Me-11′. The presence of three other methyl groups, Me-10′ (δ 2.15, s), Me-12′ (δ 0.91, s) and Me-13′ (δ 0.89, s) was also settled from the HMBC experiment. The NOESY experiment showed that the relative stereochemistry of the side chain of **1** was similar to that of the B-ring of **2**. H-4′ (δ 0.46, m) showed clear correlations with both H-6′ (δ 0.42, m) and Me-11′ (δ 1.20, s) indicating their α-configuration. Me-13′ (δ 0.89, s) showed correlations with H-4′ (δ 0.46, m) and H-6′ (δ 0.42, m). The stereochemistry has been further supported from interproton or heteronuclear coupling constant ($^3J_{H,H}$ or $^3J_{C,H}$).[16] In the ^{1}H NMR spectrum, of two protons at C-3′, one (H-3′a) appeared at the more upfield region (δ 1.42) compared to the other (H-3′b, δ 1.68). It has been observed that $^3J_{H\text{-}3'a\text{–}H\text{-}2'}$ is small (2 Hz) and $^3J_{H\text{-}3'b\text{–}H\text{-}2'}$ is large (10 Hz) while $^3J_{H\text{-}3'a\text{–}H\text{-}4'}$ is large (10 Hz) and $^3J_{H\text{-}3'b\text{–}H\text{-}4'}$ is small (2 Hz). On the other hand, $^3J_{C\text{-}1'\text{–}H\text{-}3'a}$ is large (8 Hz) and $^3J_{C\text{-}11'\text{–}H\text{-}3'a}$ is small (3 Hz). These data indicate that H-3′a is pro-*R* and H-3′b is pro-*S* and H-4′ and Me-11′ are in gauche orientation with H-3′b while C-1′ is in anti orientation with H-3′a. H-2′ and H-3′b are also in anti orientation. H-2′ (δ 3.45) showed NOESY correlation with H-3′a while H-3′b showed correlations with H-4′ (δ 0.46) and Me-11′ (δ 1.20). Thus H-4′ and Me-11′ were clearly decided[16] with α-configuration.



Selected **HMBC** (↷) and **NOESY** correlations (↔)

We are not certain about the biogenesis of **1** but it may possibly be derived from a related lathyrane-type diterpenoid like **2** (Scheme 1). The saturation of the double bond in ring B as well as dehydroxylation at the juncture of A and B rings (as shown in **2A**) is naturally well known.[5,6] However, **2A** may also be the precursor for both the compounds **1** and **2**.

Thus, multidione is a unique diterpenoid having a phenolic ring and a long side chain related to the B ring of lathyrane-diterpenoids in *seco*-form. From *Jatropha* species a large number of diterpenoids have been isolated[1–10] but both of these structural features have not yet been observed.

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15. *Isolation of multidione*: The stems of *Jatropha multifida* were collected from the Botanical Garden, Osmania University campus, Hyderabad and botanically

identified. The shade dried plant material (6 kg) was powdered and extracted thrice (72 h in each case) with $CHCl_3$–MeOH (1:1, 4 L) at room temperature. The total extract was concentrated to afford a thick brown mass (120.4 g). The residue (120 g) was subjected to column chromatography and the elution was carried out with solvents of increasing polarity using hexane and EtOAC. The separation of the components in the mixture was monitored by TLC. The latter fractions eluted with hexane–EtOAC (6:4) afforded a mixture of two products which were separated by rechromatography to yield 15-epi-(4*E*)-jatrogrossidentadione (122 mg)[4] and (4*E*)-jatrogrossidentadione (64 mg).[4] The fractions eluted with hexane–EtOAC (2:8) furnished a gummy mass which on rechromatography followed by preparative TLC (hexane–EtOAC, 1:1) afforded multidione (8 mg).

Multidione **(1)**: Colourless liquid, $[\alpha]_D^{25}$ −32.8 (c 0.5, $CHCl_3$); IR: 3362, 1708, 1665, 1594, 1262 cm^{-1}; ^{1}H and ^{13}C NMR: Table 1; HREIMS: *m*/*z* 317.2109 $[M+H]^+$ (Calcd for $C_{20}H_{29}O_3$: *m*/*z* 317.2111).

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