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NEW PROPACIN ANALOGUES FROM A COLLECTION OF THE WHOLE PLANT OF *JATROPHA GOSSYPIFOLIA*[1]

RATNA DAS[a]*, K.V.N.S. SRINIVAS[b], R. RAMU[b], B. VENKATAIAH[b] and BISWANATH DAS[b]*

[a]Department of Chemistry, Gurudas College, Narkeldanga Main Road, Calcutta–700 054.
[b]Organic Chemistry Division–I, Indian Institute of Chemical Technology, Hyderabad–500 007.
e–mail: biswanathdas@yahoo.com; Fax: 91–40–7160512

ABSTRACT

From a collection of the whole plant of *Jatropha gossypifolia* two new propacin analogues, jatrocins A and B along with the known coumarino–lignans, propacin and cleomiscosin A were isolated. The structures of the new compounds were settled by extensive studies of their spectra (mainly 1D– and 2D– NMR).

Key words : New propacin analogues, Jatropha Gossypifolia

INTRODUCTION

Jatropha gossypifolia Linn (Euphorbiaceae), is a small shrub found in different parts of India. The plant is reputed[2,3] ethnomedically to treat cancerous growths. Earlier chemical investigation on the plant resulted in the isolation of various diterpenes and lignans.[4–10] In continuation of our work[7–10] on the bioactive constituents of the plant, a collection of the whole plant has been examined. Two new propacin analogues, jatrocins A(**1**) and B(**2**) together with the known coumarino–lignans, propacin (**3**)[11,12] and cleomiscosin A (**4**)[13] were isolated. Here, the isolation of these constituents and the structure elucidation of the new compounds, **1** and **2** has been reported.

EXPERIMENTAL

Melting points were measured in a Buchi 510 instrument and are uncorrected. Spectra were recorded with the following instruments: IR: Nicolet–740 spectrophotometer, ^{1}H– and ^{13}C–NMR: Varian Gemini 200 MHz and EIMS: VG Micromass 7070 H (70 eV). Optical rotations were determined with a Jasco DIP 360 Digital polarimeter.

The whole plants of *J. gossypifolia* were collected from the Osmania university campus in the month of May, 2000. The air dried plant material (2 kg) was extracted thrice with CH_2Cl_2–MeOH (1:1) (3 x 5 lit). Each extraction was continued for 3 days. The total extract was concentrated under reduced pressure to produce a thick brown gummy mass. The residue was subjected to column chromatography over silica gel (100–200 mesh) and the column was eluted

with solvents of increasing polarity using a mixture of hexane and EtOAc. The fractions eluted with hexane–EtOAc (2:3) were found (TLC) to contain the mixture of four compounds, which were separated by preparative TLC to afford jatrocin A (**1**, 12mg), jatrocin B (**2**, 15mg), propacin (**3**, 23 mg) and cleomiscosin A (**4**, 37 mg).

Jatrocin A (**1**): Viscous, $[\alpha]_D25 \pm 0$ (c 1.02, MeOH); IR: ν_{max} (KBr): 3417, 1710, 1612, 1584 cm^{-1}; ^1H– and ^{13}C– NMR: Tables 1 and 2; EIMS: m/z 356 (M^+), 312, 194, 164, 137; Found: C, 64.17; H, 4.43. $C_{19}H_{16}O_7$ requires: C, 64.04; H, 4.49%.

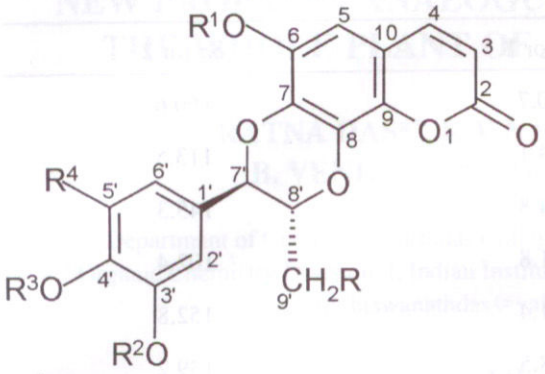
Jatrocin B (**2**): Viscous, $[\alpha]_D25 \pm 0$ (c 1.31, MeOH), IR: ν_{max} (KBr): 3406, 1710, 1618, 1595 cm^{-1}; ^1H– and ^{13}C– NMR: Tables 1 and 2; EIMS: m/z 400 (M^+), 356, 208, 194, 167; Found: C, 62.85; H, 5.09. $C_{21}H_{20}O_8$ requires: C, 63.00; H, 5.00%.

Propacin (**3**): White solid, m.p. 227–228°C; $[\alpha]_D25 \pm 0$ (c 1.12, MeOH). Spectral properties were similar to those reported[11, 12] earlier.

Cleomiscosin A (**4**): White solid, m.p. 244 –245°C $[\alpha]_D25 \pm 0$ (c 1.09, MeOH). Spectroscopic data were identical to the reported values.[13]

RESULTS AND DISCUSSION

Jatrocin A (**1**) was obtained as viscous mass and it was optically inactive. Its molecular formula was derived as $C_{19}H_{16}O_7$ from its elemental analysis and mass spectrum. The IR spectrum of the compound (vide Experimental) indicated the presence of hydroxy group, coumarin moiety and unsaturation in the molecule. The ^1H– and ^{13}C– NMR spectral data (Tables 1 and 2) were closely related to those of the known coumarino–lignan, propacin (**3**)[11,12] isolated together with **1**. The structural difference between the compounds **1** and **3** was observed that the former contained two hydroxyl groups (δ 8.52 and 8.48, each brs, 1H each) and a methoxyl (δ 3.85, 3H, s) but the latter contained one hydroxyl and two methoxy groups. 2D–NMR spectral studies on jatrocin A (**1**) showed that the proton of one of hydroxy group (δ 8.48) was related to C–5 (δ 101.8) and C–7 (δ 138.4) while the proton of other hydroxy group (δ 8.52) was related to C–3' (δ 149.4) and C–5' (δ 115.6) in the HMBC experiment. Thus one of the hydroxy groups of **1** is located at C–4' (like propacin) and the other at C–6 (instead of a methoxy group present in propacin). The HMBC experiment also showed the correlations between H–7' (δ 4.62, d, J = 8.0 Hz) and C–7 (δ 138.4) and again between H–8' (δ 4.28–4.16, m) and C–8 (δ 137.8) in **1**. The coupling constant between H–7' and H–8' was found to be 8.0 Hz indicating *trans* orientation of these two protons. However, as the molecule was optically inactive it was racemic like other coumarino–lignans.[14] In the mass spectrum the most prominent peak was observed at m/z 164 (100%) (as was observed in the mass spectrum of propacin) resulting from the retro–Diels Alder cleavage of the molecule. Considering all these spectral values, the structure of jatrocin A (**1**) was derived as 6–demethylpropacin.



1 : R = R^1 = R^3 = R^4 = H, R^2 = Me
2 : R^1 = R^2 = Me, R = R^3 = H, R^4 = OMe
3 : R^1 = R^2 = Me, R = R^3 = R^4 = H
4 : R^1 = R^2 = Me, R^3 = R^4 = H, R = OH

Table 1. ^{1}H–NMR spectral data of 1 and 2 in $CDCl_3$ + DMSO–d_6

Proton	δ_H for **1**	δ_H for 2
H–3	6.30 (d, *J* = 9.5 Hz)	6.33 (d, *J* = 9.5 Hz)
H–4	7.62 (d, *J* = 9.5 Hz)	7.57 (d, *J* = 9.5 Hz)
H–5	6.57 (s)	6.54 (s)
H–2', H–5', H–6'	7.02 – 6.78 (m)	6.81(s)*
H–7'	4.62 (d, *J* = 8.0 Hz)	4.61 (d, *J* = 8.0 Hz)
H–8'	4.28 – 4.16 (m)	4.31– 4.17 (m)
–Me	1.23 (d, *J* = 7.0 Hz)	1.28 (d, *J* = 7.0 Hz)
–OH	8.52 (brs) 8.48 (brs) 5.77 (brs)	8.49 (brs)
–OMe	3.85 (s)	3.82 3.84 (x 2)

* for H–2' and H–6' (2H), H–5' is absent (suggested from HMBC spectrum)

Table 2. ^{13}C–NMR spectral data of 1 and 2 in $CDCl_3$+DMSO–d_6

Carbon	δ_C for **1**	δ_C for **2**
C–2	160.7	160.6
C–3	114.1	113.5
C–4	144.8	145.3
C–5	101.8	102.4
C–6	151.4	152.8
C–7	138.5	139.2
C–8	137.8	137.6
C–9	142.4	141.7
C–10	112.2	111.9
C–1'	127.5	126.3
C–2'	111.2	106.5
C–3'	149.4	150.2
C–4'	148.2	135.4
C–5'	115.6	150.2
C–6'	120.8	106.5
C–7'	81.1	80.7
C–8'	73.4	72.8
–Me	17.7	18.3
–OMe	55.8	56.1 55.9

The second new compound, jatrocin B (**2**) was also isolated as viscous mass and it was optically inactive. Its molecular formula was deduced to be $C_{21}H_{20}O_8$ from elemental analysis and mass spectrum. The IR (vide Experimental), ^{1}H– and ^{13}C– NMR spectral data (Tables 1 and 2) clearly suggested that the structure of jatrocin B was related to that of propacin (**3**) as well as of jatrocin A (**1**). The former (**2**) was found to contain three methoxyls (δ 3.82 and 3.84 (x 2) in the ^{1}H–NMR spectrum and δ 55.9 and 56.1 (x 2) in the ^{13}C–NMR spectrum) instead of two methoxyls present in **3**. The two protons, H–2' and H–6' appeared as singlet (δ 6.81) indicating

that the positions C–3', C–4' and C–5' were substituted, 2D– NMR studies with the assistance of HMBC experiment suggested that in **2**, the proton of the hydroxyl group (δ 8.49, brs) was related to C–3' (δ 150.2) and C–5' (δ 150.2), both of which contained methoxy groups. That means, the hydroxy group is present at C–4'. The ^{1}H– and ^{13}C–NMR spectral values of all the protons and carbons respectively of the coumarin moiety of **2** were identical to those of the corresponding protons and carbons of propacin (**3**). The HMBC experiment on **2** also showed that H–7' (δ 4.61, d, J = 8.0 Hz) was correlated to C–7 (δ 138.2) and again H–8' (δ 4.31–4.17, m) to C–8 (δ 137.6). The coupling constant of H–7' and H–8' of the compound **2** was also 8.0 Hz supporting their *trans* orientation. However, the molecule was optically inactive and hence racemic in nature. The base peak in the mass spectrum appeared at m/z 194 (100%) due to retro–Diels Alder cleavage of the molecule. All these spectral data clearly established the structure of jatrocin B (**2**) as 5'–methoxypropacin.

The known coumarino–lignans, propacin (**3**)[11, 12] and cleomiscosin A (**4**)[13] were identified by comparison of their physical and spectral properties with those reported earlier.

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