Phytochemistry, Vol. 23, No. 4, pp. 867–869, 1984.
Printed in Great Britain.

0031–9422/84 $3.00 + 0.00

A COUMARINO-LIGNAN FROM *JATROPHA GLANDULIFERA*

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(*Revised received* 19 *August* 1983)

Key Word Index—*Jatropha glandulifera*; Euphorbiaceae; roots; jatropholone-A; coumarino-lignan; fraxetin.

Abstract—An investigation of the roots of *Jatropha glandulifera* revealed the presence of a coumarino-lignan, along with jatropholone-A and fraxetin.

INTRODUCTION

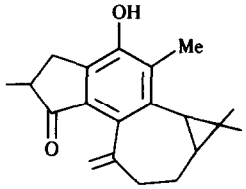
The methanol extract of roots of *Jatropha glandulifera* was chromatographed over a column of silica gel and was successively eluted with benzene, 3% ethyl acetate in benzene and ethyl acetate. The first fraction yielded compound A (jatropholone-A), the second compound B (coumarino-lignan) and the third compound C (fraxetin).

RESULTS AND DISCUSSION

Compound A, $C_{20}H_{24}O_2$ $[M]^+$ m/z 296 readily formed a monoacetate with acetic anhydride and pyridine and a mono methyl ether with dimethyl sulphate, suggesting it to be phenolic. The UV absorption maxima at 272 and 320 nm also showed bathochromic shifts expected of a phenolic compound. The IR spectrum showed a conjugated carbonyl (1670 cm^{-1}), aromatic (1565 cm^{-1}) and exocyclic methylene (885 cm^{-1}) absorptions. The ^1H NMR revealed two tertiary methyls (δ0.76 and 1.20), one secondary methyl (δ1.11, d, J = 7 Hz, 3H, CH–CH_3), an aromatic methyl (δ2.17), besides two vinylic protons (δ4.51 and 5.08). Compound A acetate could be hydrogenated to a dihydro derivative, the ^1H NMR of which revealed an additional secondary methyl (δ1.08) and no olefinic protons. Thus compound A appeared to be tetracyclic aromatic diterpene with one carbonyl and one phenolic hydroxyl group. These data are in agreement with jatropholones, recently reported from the roots of a related species *J. gossypifolia* [1] and from the position of the secondary methyl in the ^1H NMR spectrum it was inferred to be the epimer, jatropholone-A. In the earlier report the structure of jatropholone-B was based only on an X-ray study of its acetate and no chemical data was reported.

Compound B, $C_{20}H_{18}O_7$ $[M]^+$ m/z 370, gave a brown colour with ferric chloride. Its UV maxima at 257 and 334 nm and IR bands at 3380 and 1705 cm^{-1} suggested it to be a coumarin, which was confirmed by the appearance of two doublets in the ^1H NMR at δ6.25, 7.90 (J = 9 Hz), characteristic of the H-3 and H-4 protons of coumarins. Formation of a monoacetate with acetic anhydride and pyridine and a mono methyl ether with dimethyl sulphate suggested the presence of one free phenolic hydroxyl in compound B. Additional features of compound B that could be inferred from the study of its ^1H NMR and also of its derivatives were two methoxyls, a trisubstituted aromatic ring, a secondary methyl (δ1.20), a lone aromatic proton and two deshielded aliphatic protons forming an ABX_3 system with the secondary methyl. The remaining two oxygen atoms were probably present as ether links and this led to the conclusion that compound B is a coumarino-lignan involving a dioxan type link between a coumarin and a phenyl propane precursor, similar to the one found in the flavano-lignans silymarin [2, 3] and hydnocarpin [4]. In agreement with the postulates, compound B underwent pyridine–HBr fission [5] and the product was found to be identical with 6,7,8-trihydroxycoumarin (mp 260°; $[M]^+$ m/z 182), obtained by similar demethylation of fraxetin. The most abundant fragment ion at m/z 164 in the mass spectrum of compound B revealed the existence of the system $(OCH_3)(OH)C_6H_3$–CH–CH–CH_3.

Assuming compound B is a further elaboration of fraxetin with which it is co-occurring and the accepted biosynthesis of neolignans [6], structure **2** is preferred for



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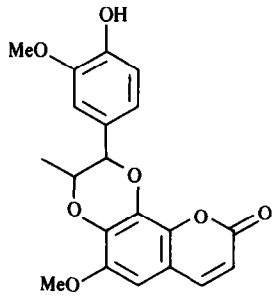


2

compound B. The *trans* diaxial arrangement of the substituents in the benzodioxan, is in conformity with the relatively low-field methyl signal and the relatively large J values (7 Hz) between the two vicinal oxymethine protons. We suggest that it is probably biosynthesized from eugenol (**3**) and fraxetin (**4**) as shown in Scheme 1.

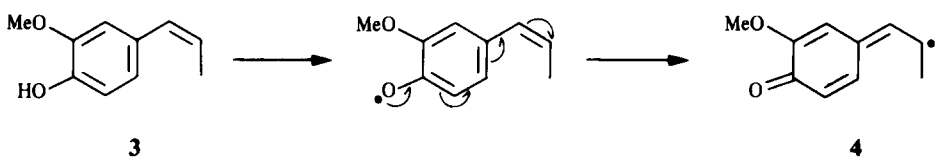
A preliminary study of the ^{13}C NMR spectral data also lends support to the above formulation. The assignments for various signals are included in the Experimental and are based on literature data [7, 8], intensity and additivity relationships. The three carbons of the lactone ring are located at δ 160.3, 113.8 and 145 assignable to C-2, C-3 and C-4 carbons, respectively, and the other three carbons of the phenyl propane moiety at δ 17.3, 73.7 and 80.6, the last two being deshielded by the two oxygens of the dioxan ring. The remaining signals account for the aromatic carbons and two methoxyl groups. The structure **2** proposed for the coumarino-lignan has been suggested earlier as one of the alternative structures for prapacin [9] and in addition to this four more coumarino-lignans namely cleomiscosin A and B [10], aquillochin [11] and daphneticin [12] have been characterized. Of these the first three are based on the fraxetin nucleus and the fourth on daphnetin. Compound C, obtained from ethyl acetate elutions, was identified as fraxetin (**5**) from its spectral data and direct comparison and by derivatization.

EXPERIMENTAL

Mps are uncorr. For TLC the following solvent systems were used (a) EtOAc–C_6H_6 (1:1); (b) EtOAc; (c) EtOAc–MeOH–H_2O (20:3.3:2.7). NMR spectra were recorded at 250 MHz and the values are expressed in δ units.

Isolation. Air-dried roots (10 kg) were chopped into small pieces and extracted with hot MeOH. Excess solvent was distilled under red. pres., and the concentrate (15 g) was adsorbed on silica gel (60–120 mesh, 20 g) and chromatographed on a silica gel column. The column was developed in C_6H_6. Elution with C_6H_6 afforded a colourless crystalline solid compound A (jatropholone-A). Subsequent elutions with 3% EtOAc in C_6H_6 and with EtOAc yielded compound B and compound C (fraxetin), respectively.

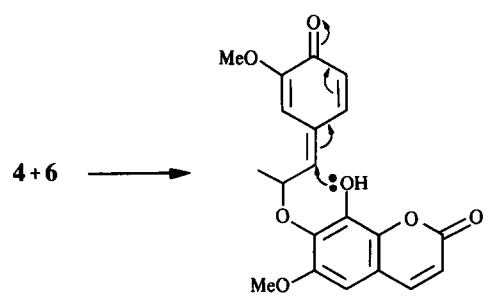
Jatropholone A. Crystallized from C_6H_6 as a colourless solid (90 mg), mp 237–238°. UV λ_{max}^{MeOH} nm: 222, 230, 272, 320; + alkali 290, 360; IR ν_{max}^{nujol} cm^{-1}: 3200, 2850, 1670, 1565, 885. ^1H NMR (DMSO-d_6): δ 0.76 (*s*, 3H, Me), 1.20 (*s*, 3H, Me), 1.11 (*d*, J = 7 Hz, CH–Me), 2.17 (*s*, 3H, Ar–Me), 4.51 (*s*, 1H, =CH_2), 5.08 (*s*, 1H, =CH_2); MS *m/z*: 296, 281, 253, 240, 227, 225. C, 80.7; H, 7.8%. $C_{20}H_{24}O_2$ requires C, 81%, H, 8.1%). ^{13}C NMR: 13.65 (sec. Me), 15.83, 16.7 (tert. Me), 18.7, 20.9, 30.5 (carbons of cyclopropane ring), 27.87 (Ar–Me), 114.75, 114.8 (H_2C=C), 131.0, 131.6, 131.9, 136, 137.8, 151.1 (aromatic carbons), 207.0 (carbonyl). Acetate (Ac_2O–pyridine, 100°, 1 hr) crystallized from MeOH, mp 220°. ^1H NMR ($CDCl_3$): δ 0.8 (*s*, 3H, Me), 1.20 (*s*, 3H, Me), 1.22 (*d*, J = 7 Hz, 3H, CH–Me), 2.12 (*s*, 3H, Ar–Me), 2.32 (*s*, 3H, OAc), 4.70 (*s*, 1H, =CH_2), 5.22 (*s*, 1H, =CH_2); MS *m/z* of acetate: 338, 337, 296, 295, 280, 252, 239. (C, 77.9; H, 7.5%. $C_{22}H_{26}O_3$ requires C, 78.07; H, 7.74%). Me ether (Me_2CO–K_2CO_3–Me_2SO_4) crystallized from C_6H_6, mp 186–187°. ^1H NMR ($CDCl_3$): δ 0.8 (*s*, 3H, Me), 1.20 (*s*, 3H, Me), 1.22 (*d*, J = 7 Hz, CH–Me), 2.23 (*s*, 3H, Ar–Me), 3.79 (*s*, 3H, OMe), 4.55 (*s*, 1H, =CH_2), 5.05 (*s*, 1H, =CH_2). (C, 80.8; H, 8.21%.



3 **4**

Scheme 1.

5 **6**



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$C_{21}H_{26}O_2$ requires C, 81.2; H, 8.44%.)

The acetate (20 mg), dissolved in dry MeOH, was subjected to hydrogenation over Pd–C (catalyst) (200 mg) at room temp. When there was no further absorption, the soln was filtered off from the catalyst and the solvent evapd to obtain a sticky solid, which could not be crystallized. ^{1}H NMR ($CDCl_3$): δ0.70 (*s*, 3H, Me), 1.15 (*s*, 3H, Me), 1.08 (*d*, J = 7 Hz, 3H, CH–Me), 1.30 (*d*, J = 7 Hz, 3H, CH–Me), 1.93 (*s*, 3H, OAc), 2.15 (*s*, 3H, Ar–Me).

Compound B. Crystallized from EtOAc–petrol as colourless needles, mp 245–248°, $[\alpha]_D$ −56°; UV λ_{max}^{MeOH} nm: 257, 334. IR ν_{max}^{KBr} cm^{-1}: 3380, 1705, 1610, 1570, 1500, 1380, 1035. ^{1}H NMR (DMSO-d_6): δ1.20 (*d*, J = 7 Hz, 3H, H-9′), 3.76 (*s*, 6H, 2 × OMe), 4.30 (*m*, 1H, H-8′), 4.70 (*d*, J = 7 Hz, H-7′), 6.25 (*d*, J = 9 Hz, 1H, H-3), 6.82 (*s*, 1H, H-5), 6.99 (*b*, 3H, H-2′, H-5′, H-6′), 7.90 (*d*, J = 9 Hz, 1H, H-4). ^{13}C NMR: δ17.3 (Me), 56.2 (OMe), 73.7 (C-8′), 80.6 (C-7′), 101.2 (C-5), 111.6 (C-2′), 112.6 (C-10), 113.8 (C-3), 115.8 (C-5′), 121.2 (C-6′), 127.3 (C-1′), 137.7, 138.1 (C-8 and C-7), 144 (C-9), 145 (C-4), 147 (C-4′), 148 (C-3′), 153 (C-6), 160.3 (C-2). (C, 64.5; H, 4.5%. $C_{20}H_{18}O_7$ requires C, 64.8; H, 4.9%.) Acetate (Ac_2O–pyridine, 100°, 1 hr) crystallized from MeOH, mp 185–186°. IR ν_{max}^{KBr} cm^{-1}: 1712, 1605, 1565, 1500, 1360, 830. ^{1}H NMR ($CDCl_3$): δ1.30 (*d*, J = 7 Hz, 3H, H-9′), 2.30 (*s*, 3H, OAc), 3.85 (*s*, 6H, 2 × OMe), 4.20 (*m*, 1H, H-8′), 4.70 (*d*, H-7′), 6.20 (*d*, J = 9 Hz, 1H, H-3), 6.45 (*s*, 1H, H-5), 6.92 (*b*, 3H, H-2′, H-5′, H-6′), 7.52 (*d*, J = 9 Hz, H-4), (C, 63.9; H, 4.5%. $C_{22}H_{20}O_8$ requires C, 64.07; H, 4.8%.) Me ether (Me_2CO–K_2CO_3–Me_2SO_4) crystallized from C_6H_6–petrol, mp 95–96°, ^{1}H NMR ($CDCl_3$): δ1.20 (*d*, J = 7 Hz, 3H, H-9′), 3.76 (*s*, 9H, 3 × OMe), 4.25 (*m*, 1H, H-8′), 4.62 (*d*, J = 7 Hz, H-7′), 6.25 (*d*, J = 9 Hz, H-3), 6.81 (*b*, 3H, H-2′, H-5′, H-6′), 7.0 (*s*, 1H, H-5), 7.90 (*d*, J = 9 Hz, H-4).

Compound B (25 mg) was thoroughly mixed with pyridine–HBr (300 mg) in a hard glass test tube and heated until molten. It was kept in a molten state for *ca* 3 min, taking care that the melt did not char. After cooling for a few min at room temp., the viscous mass was treated with dil HCl and crushed ice and extracted with EtOAc and worked up. The product (mp 260°, $[M]^+$ m/z 182) was found to be identical with the product obtained from identical treatment of fraxetin on TLC and mmp.

Compound C (fraxetin). Crystallized from MeOH, mp 231°. IR ν_{max}^{KBr} cm^{-1}: 3320, 1670, 1570, 1500, 1460, 1320, 1080, 930, 850. Acetate (Ac_2O–pyridine, 100°, 1 hr), crystallized from MeOH, mp 192–193° (lit. mp 194°). ^{1}H NMR ($CDCl_3$): δ2.28 (*s*, 3H, OAc), 2.32 (*s*, 3H, OAc), 3.78 (*s*, 3H, OMe), 6.22 (*d*, J = 9 Hz, 1H, H-3), 6.70 (*s*, 1H, H-5), 7.48 (*d*, J = 9 Hz, H-4). Me ether crystallized from C_6H_6–petrol, mp 102° (lit. mp 104°). ^{1}H NMR ($CDCl_3$): δ3.82 (*s*, 3H, OMe), 3.90 (*s*, 3H, OMe), 3.94 (*s*, 3H, OMe), 6.25 (*d*, J = 9 Hz, 1H, H-3), 6.70 (*s*, 1H, H-5), 7.62 (*d*, J = 9 Hz, 1H, H-4).

Acknowledgements—We are grateful to Dr. K. K. Purushotham, Captain Srinivasamurthy Research Institute, Madras, for providing the samples of Jatropholone A and B. One of us (K.P.S.) gratefully acknowledges D.A.E. for financial assistance.

REFERENCES

1. Kozhiparambil, K. Purushotham, S. C., Forbes, A., Cameron, J. Connolly, D., Labbe, C., Maitz, A. and Rycroft, D. S. (1979) *Tetrahedron Letters* **11**, 979.
2. Wagner, H., Horhammer, L. and Munster, R. (1968) *Arznoimittel-Forsch*, **18**, 688.
3. Pelter, A. and Hansel, R. (1968) *Tetrahedron Letters* 2911.
4. Ranganathan, K. R. and Seshadri, T. R. (1973) *Tetrahedron Letters* 3481.
5. Howard, G. and Mabry, T. J. (1970) *Phytochemistry* **9**, 2414.
6. Merlini, L. and Zanarotti, A. (1975) *Tetrahedron Letters* 3621.
7. Wenkert, E., Gottlieb, H. E., Gottlieb, O. R., Das Pereira, M. O. and Formiga, M. D. (1976) *Phytochemistry* **15**, 1547.
8. Cussans, N. J. and Huckerby, T. N. (1975) *Tetrahedron* **31**, 2587.
9. Das Gracas, M., Zoghbi, B., Roque, N. F. and Gottlieb, O. R. (1981) *Phytochemistry* **20**, 180.
10. Ray, A. B., Chattopadhyay, S. K., Konno, C. and Kino, H. H. (1982) *Heterocycles* **19**, 19.
11. Bhandari, P., Pushpa Pant and Rastogi, R. P. (1982) *Phytochemistry* **21**, 2147.
12. Gen, Z. L., Seligmann, O. and Wagner, H. (1983) *Phytochemistry* **22**, 617.