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JATRODIEN, A LIGNAN FROM STEMS OF *JATROPHA GOSSYPIFOLIA**†

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Key Word Index—*Jatropha gossypifolia*; Euphorbiacea; stems; lignan; jatrodien.

Abstract—A novel lignan, jatrodien, representing an intermediate in Haworth's biosynthetic scheme for the formation of lignans, has been isolated from the stems of *Jatropha gossypifolia*. The structure of the compound was derived from its spectroscopic data. Synthesis of the compound, starting from piperonal has been achieved.

INTRODUCTION

Jatropha gossypifolia, a small shrub, known for its reputed medicinal [1, 2] and pesticidal properties [1, 3], contains [2] mainly lignans and diterpenoids. We have recently isolated a new lignan, jatrodien (**1**) from the stems of this species. Here, we report on the structural elucidation and synthesis of the new compound.

RESULTS AND DISCUSSION

Jatrodien was isolated as a pale yellow viscous mass. Its mass spectrum showed a $[M]^+$ at m/z 426 in accordance with the molecular formula $C_{23}H_{22}O_8$. The compound was optically inactive. Its IR spectrum showed the presence of an α,β-unsaturated ester moiety (υ_{max}^{KBr} cm^{-1}: 1710). The structure of the compound was settled as **1** from its ^{1}H and ^{13}C NMR spectra. The ^{1}H NMR spectrum showed two sets of multiplet in the aromatic region involving six protons (δ7.06–6.89, 3H, *m* and 6.81–6.54, 3H, *m*). Two olefinic protons at C-7 and C-7′ appeared at δ7.76 and 7.72 (1H each, *s*). The spectrum also revealed the presence of one methylenedioxy (δ5.89, 2H, *s*) and four methoxyl groups (δ3.78, 3.68, 3.64 and 3.62, 3H each, *s*). Two of these methoxyl groups could be considered aromatic, and the other two as carbomethoxyls, after inspection of IR and ^{13}C NMR spectra. The latter showed signals at δ167.42 and 167.21 ($2\times >C=O$) and 55.54 and 55.39 ($2\times$Ar-$\underline{OMe}$) and 52.11 ($2\times$–$CO\underline{OMe}$). The presence of two trisubstituted double bonds, one methylenedioxy group and 12 aromatic protons were also suggested from the ^{13}C NMR spectrum (see Experimental). The deshielded olefinic protons at C-7 and C-7′ suggested [4, 5] the *trans* (E)-configuration for both double bonds present in the molecule. Structure **1** incorporates all the spectral features of the new lignan.

Synthesis of jatrodien (**1**) starting from piperonal (**2**) (Scheme 1) unambiguously settled its structure. Piperonal (**2**) underwent Stobbe condensation with dimethylsuccinate in the presence of sodium methoxide in methanol to produce compound **3**. The *trans* (E)-configuration of the olefinic double bond was evident from the appearance of the deshielded vinylic proton at δ7.82 in its ^{1}H NMR spectrum. Compound **3** was methylated with diazomethane in methanol to yield the diester **4**. The second Stobbe condensation of **4** with veratraldehyde in methanol in the presence of sodium methoxide yielded compound **5**. The two deshielded vinylic protons at δ7.88 and 7.84 in the ^{1}H NMR spectrum of **5** indicated the *trans* (E)-configurations for both the olefinic double bonds. Compound **5** was again methylated to produce a diester which was found to be identical to the naturally occurring lignan **1** in all respects.

Jatrodien (**1**) is an interesting molecule as it represents an intermediate in the Haworth's biosynthetic scheme for the formation of lignans [6]. The other lignans previously reported [4, 5] from *J. gossypifolia* were possibly formed biosynthetically from this intermediate. One other lignan diester, phebalarin [7], containing two conjugated double bonds was reported earlier from *Phebalium nudum*, but the authors expressed artefacts. Moreover, the *E*,*E*-configuration, of the olefinic double bonds of phebalarin was also not confirmed. Thus, jatrodien (**1**) may be considered as the first naturally occurring correctly established lignan diester containing two conjugated *E*,*E*-double bonds.

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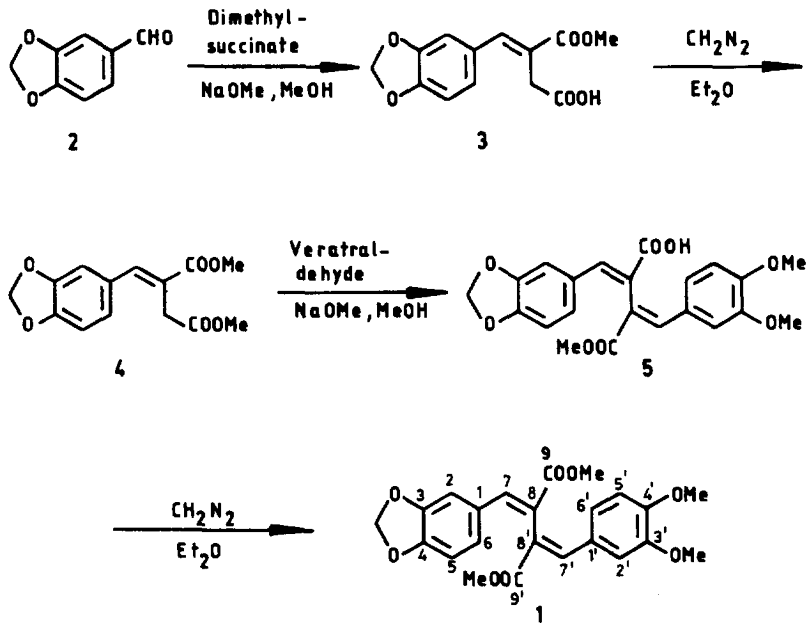

Scheme 1. Synthesis of jatrodien (1).

EXPERIMENTAL

General. Mps uncorr. CC: silica gel (BDH, 100–200 mesh). TLC: silica gel G. TLC spots were visualized by exposure of plates to I_2 vapour.

Plant material. Stems of *J. gossypifolia* L. were collected from West Bengal, India, in September 1993 and identified botanically. A voucher specimen (JG-S) is preserved in our laboratory.

Extraction and isolation. Stems (500 g) were dried, powdered and exhaustively extracted with petrol (60–80°) in a Soxhelt apparatus for 120 hr. The extract was filtered and concd by rotary evapn to produce a thick brown mass. This was chromatographed over silica gel and the column eluted with solvents of increasing polarity using hexane, benzene and EtOAc. The frs eluted with benzene–EtOAc were mixed and concd to give a gummy mass which showed some intense TLC spots with different R_f values. This was further purified by rechromatography over silica gel. Early frs from benzene–EtOAc (4:1) yielded jatrodien (**1**) as an yellow viscous mass, 22 mg. $[\alpha]_D^{25} \pm 0°$ (MeOH, *c* 0.517). IR υ_{max}^{neat} cm^{-1}: 1710, 1590, 1513, 1435. ^{13}C NMR (500 MHz, CDCl$_3$): δ 167.42, 167.21 (2 × -$\underline{C}$OOMe), 150.30 (C-4), 148.84 (C-4′), 148.50 (C-3), 147.77 (C-3′), 142.28 (C-7), 141.88 (C-7′), 128.57 (C-1), 127.21 (C-1′), 125.93 (C-6), 124.57 (C-8), 124.32 (C-6′), 123.75 (C-8′), 111.75 (C-5), 110.71 (C-5′), 108.45 (C-2), 108.18 (C-2′), 101.21 (– O$\underline{C}$H$_2$O–), 55.54 and 55.39 (2 × Ar-O$\underline{Me}$) and 52.11 (2 × – COO$\underline{Me}$). MS *m/z* (rel. int.): 426 [M]$^+$] (42), 395 (8), 394 (10), 335 (55), 273 (44), 165 (62), 151 (75), 135 (100). Frs eluted with benzene–EtOAc (1:1) contained jatrophan [4].

Synthesis of jatrodien (**1**). (1) *Stobbe condensation of piperonal with dimethylsuccinate.* Piperonal (1 g) and dimethylsuccinate (10 ml, d: 1.4 g m^{-1}) were added to a soln of NaOMe (0.5 g) in MeOH (50 ml). The mixt. was heated under reflux for 2 hr, cooled and acidified with HCl (IN). This was then extracted with Et$_2$O (3 × 50 ml). The Et$_2$O fr. was then re-extracted with aq. NaHCO$_3$ soln (3 × 50 ml). Acidifcation of the aq. NaHCO$_3$ extract with conc. HCl (12N) provided an oily layer. This was extracted with CH$_2$Cl$_2$ (3 × 50 ml) and the extract washed with H$_2$O (3 × 20 ml), dried and concd to yield compound **3** as a yellow solid. This was recrystallized from MeOH, 650 mg, mp 141–142°. IR υ_{max}^{Kbr} cm^{-1}: 3070, 1703, 1632, 1499, 1485. ^{1}H NMR (200 MHz, CDCl$_3$): δ7.83 (1H, $\underline{s}$, vinylic-$\underline{H}$), 6.93–6.78 (3H, *m*, Ar-$\underline{H}$), 6.01 (2H, $\underline{s}$, -OC$\underline{H}_2$O–), 3.84 (3H, *s*, -COO$\underline{Me}$) and 3.60 (2H, $\underline{s}$, -C$\underline{H}_2$-$\overline{C}$OOH). MS *m/z* (rel. int.): 264 (25), 232 (15), 220 (28), 189 (16), 160 (100), 102 (38). (2) *Methylation of compound* **3** *with diazomethane.* A soln of **3** (500 mg) in MeOH (10 ml) was added to an ice-cold soln of CH$_2$N$_2$-Et$_2$O. The mixt. was kept for 12 hr, filtered and concd to produce diester **4**. This was recrystallized from MeOH, 440 mg, mp 84–85°. IR υ_{max}^{Kbr} cm^{-1}: 1724, 1703, 1639, 1499, 1442. ^{1}H NMR (200 MHz, CDCl$_3$): δ 7.82 (1H, *s*, vinylic-$\underline{H}$), 6.92–6.82 (3H, *m*, Ar-$\underline{H}$), 6.02 (2H, *s*, -OC$\underline{H}_2$O–), 3.83 and 3.76 (3H each, *s*, 2 × -COO$\underline{Me}$), 3.57 (2H, *s*, -C$\underline{H}_2$-COOMe). MS *m/z* (rel. int.): 278 (100), 247 (10), 218 (28), 189 (65), 160 (45), 102 (35). (3) *Stobbe condensation of* **4** *with veratraldehyde.* Compound **4** (400 mg) on Stobbe condensation (following the abovementioned procedure) with veratraldehyde (350 mg) provided a light-yellow solid which was purified by recrystallization from MeOH to yield product **5**, 475 mg, mp 66–68°. IR υ_{max}^{KBr} cm^{-1}: 3200, 1710, 1690, 1590, 1510, 1440. ^{1}H NMR (200 MHz, CDCl$_3$) : δ 7.88 and 7.84 (1H each, *s*, 2 × vinylic – $\underline{H}$), 7.15–7.01 (3H, *m*, Ar-$\underline{H}$), 6.88–6.71 (3H, *m*, Ar-$\underline{H}$), 5.95 (2H, *s*, $-OC\underline{H}_2O-$), 3.85 (3H, *s*, Ar-O$\underline{Me}$), 3.74 (6H, *s*, Ar-O$\underline{Me}$ and $-\overline{C}OO\underline{Me}$). MS *m/z* (rel. int.): 412 (60), 380 (25), $\overline{264}$ (23), 220 (30), 160 (100). (4) *Methylation of compound* **5** *with diazomethane*. Compound **5** (200 mg) in Et_2O (20 ml) was methylated as described above with CH_2N_2-Et_2O to yield a yellow viscous mass, 180 mg, which was found to be identical to the naturally occurring jatrodien (**1**) in all respects (R_f, IR, ^1H NMR and MS).

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