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GADAIN, A LIGNAN FROM *JATROPHA GOSSYPIFOLIA*

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Key Word Index—*Jatropha gossypifolia*, Euphorbiaceae, lignan, gadain

Abstract—The isolation of a new lignan, gadain, from *Jatropha gossypifolia* is reported The structure and stereochemistry of this compound have been determined from spectral analysis, partial synthesis from jatrophan (a lignan of known absolute configuration) and from its transformation reactions

INTRODUCTION

In continuation of our work [1] on the constituents of *Jatropha gossypifolia* L, we isolated a new lignan, gadain (**1a**) In this paper we report the structure of this new compound, its interesting chemistry, as well as its partial synthesis from jatrophan (**2**) Several reactions of jatrophan (**2**) are also discussed

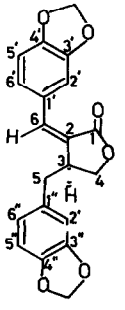
RESULTS AND DISCUSSION

Lignan **1a**, $C_{20}H_{16}O_6$ ([M]$^+$ *m/z* 352), mp 145° (C_6H_6), $[\alpha]_D^{25}$ +86° ($CHCl_3$), exhibited UV absorption [λ_{max}^{EtOH} nm (log ε) 337 (4 20), 293 (4 05) and 235 (4.12)] characteristic of lignans containing a dibenzylbutyrolactone skeleton with a double bond at the 2,6-position of the γ-butyrolactone ring [1–3] The IR spectrum showed characteristic signals of an α,β-unsaturated γ-lactone (1725 cm^{-1}), olefinic double bond (1620 cm^{-1}), aromatic nucleus (1590, 1490 and 1470 cm^{-1}) and methylenedioxy group (915 cm^{-1}) The 80 MHz ^{1}H NMR spectrum ($CDCl_3$) of **1a** revealed the presence of two methylenedioxy groups (δ5 97, 2H, *s* and 5 92, 2H, *s*), one highly deshielded aromatic proton (7 71, *s*) and five more aromatic and an olefinic proton (7 09–6 57, *m*) The deshielding of one of the six aromatic protons indicated its proximity to the carbonyl group H-3, H_2-4 and H_2-5 appeared as multiplets at *ca* δ3 32, 4 41–4 02 and 2 89–2 76, respectively Characteristic fragments were observed at *m/z* 352 [M]$^+$, 217, 189, 135 (base peak), 77 and 28 in the mass spectrum The peaks at *m/z* 217 and 135 resulted from benzylic cleavage at the 3,5-position The structure of gadain therefore appeared to be **1a** with the deshielded H-2'

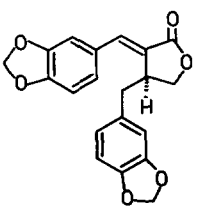
On the basis of its 100 MHz ^{13}C NMR and 300 MHz ^{1}H NMR spectra, the structure and stereochemistry of gadain could be unambiguously confirmed as **1a** The carbon chemical shifts were assigned from the additivity relationship as well as from a comparison with jatrophan (**2**) (Table 1) The values of the latter had not been reported earlier [1]

In the ^{13}C NMR spectrum, 20 resolved lines were obtained The APT experiment confirmed the presence of two $\succ CH_2$ groups, one next to oxygen (δ69 80) and one bonded only to carbon (δ40 73), a $-\overset{|}{C}H$ (C-3) group (δ44 22), two methylenedioxy carbons (δ101 42 and 101 02) together with seven protonated sp^2 carbons [olefinic carbon C-6 at δ140 33 and six aromatic doublets (C-2', δ108 36, C-5', 110 34, C-6', 125 18, C-2'', 107 87, C-5'', 109 27, C-6'', 122.69)] and seven non-protonated sp^2 carbons (C-1', δ131 37, C-1'', 127 89, C-3', 147 92, C-3'', 146 46, C-4', 148 97, C-4'', 147 55, C-2, 126 85) The δ169 26 shift is consistent with a conjugated lactone

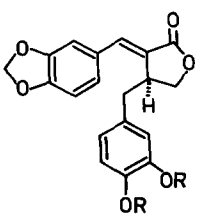
While studying the 300 MHz ^{1}H NMR spectrum of gadain in order to confirm the disposition of H-6, we observed an interesting *cis–trans* isomerization This conversion is possibly catalysed by the usual trace of hydrochloric acid in $CDCl_3$, the spectrum being run after leaving the compound in solution for 24 hr At this stage,



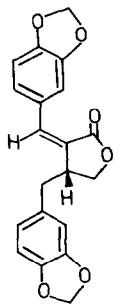
1a



1b



2 R = Me
3 R = H



Ic

Table 1 ^{13}C NMR spectral data of **1a** and **2** ($CDCl_3$, TMS as internal standard, δ values in ppm)

	1a	2
C-1	169 26	172 21
C-2	126 85	125 97
C-3	44 22	39 64
C-4	69 80	69 53
C-5	40 73	37 33
C-6	140 33	136 71
C-1′	131 37	130 17
C-2′	108 36	108 43
C-3′	147 92	148 80
C-4′	148 97	148 91
C-5′	110 34	112 03
C-6′	125 18	125 88
C-1″	127 89	127 91
C-2″	107 87	108 23
C-3″	146 46	147 84
C-4″	147 55	148 08
C-5″	109 27	111 33
C-6″	122 69	120 69
–OMe	—	55 60
$-OCH_2O-$	101 42, 101 02	101 51

two species were found to be present **1a** and **1b** in a ratio of 2 1 The reaction was not reversible and with time, the ratio of the peak intensities reversed The 30% component **1b** became 60% In fact, in keeping **1a** in hydrochloric acid (1 0 M) for 72 hr, it changed completely to **1b**, $C_{20}H_{16}O_6$ ($[M]^+$ *m/z* 352), mp 139° (C_6H_6) The two sets of ^1H NMR values are given in Table 2

As the presence of the two species caused crowding in the 300 MHz ^1H NMR spectrum, the 2D HOMCOR (COSY) experiment was carried out Both isomers exhibited the sequence $-CH_2-CH-CH_2-O-$ The aromatic region showed two ABX patterns, the minor one being more compact Of special significance was the shift of the olefinic proton by 0 95 ppm from δ6 59 to 7 54 The larger chemical shift is associated with the olefinic proton *cis* to the carbonyl and hence gadain must have the olefinic proton *trans* to the carbonyl, i e *cis* (*Z*) double bond [4] as in **1a** The upfield shift of the aromatic H-2′ (from δ7 75 to 7 07) in the more stable form **1b** accompanied with the

Table 2 300 MHz ^1H NMR spectral data of **1a** and **1b** ($CDCl_3$, TMS as internal standard, δ values in ppm, *J* in Hz)

	1a	1b
H-6	6 59, *d*, 1H *J* = 1 6	7 54, *d*, 1H *J* = 1 6
H-2′	7 75, *d*, 1H *J* = 1 5	7 07, *d*, 1H *J* = 1 5
H-5′	6 80, *d*, 1H *J* = 8 0	6 89, *d*, 1H *J* = 8 0
H-6′	7 17, *dd*, 1H J_1 = 8 0, J_2 = 1 5	7 11, *dd*, 1H J_1 = 8 0, J_2 = 1 5
H-2″	6 70, *d*, 1H *J* = 1 5	6 68, *d*, 1H *J* = 1 5
H-5″	6 66, *d*, 1H *J* = 8 0	6 64, *d*, 1H *J* = 8 0
H-6″	6 77, *dd*, 1H J_1 = 8 0, J_2 = 1 5	6 75, *dd*, 1H J_1 = 8 0, J_2 = 1 5
H_A-4	4 12, *dd*, 1H J_1 = 10 8, J_2 = 4 8	4 32–4 24, *m*, 2H
H_B-4	4 34, *dd*, 1H J_1 = 10 8, J_2 = 8 4	
H-3	3 31, *m*, 1H	3 72, *m*, 1H
H_A-5	2 82, *dd*, 1H J_1 = 16 8, J_2 = 10 8	2 60, *dd*, 1H J_1 = 16 8, J_2 = 12 0
H_B-5	2 92, *dd*, 1H J_1 = 16 8, J_2 = 8 4	3 02, *dd*, 1H J_1 = 16 8, J_2 = 4 8
$-OCH_2O-$	6 0, *s*, 2H	6 06, *s*, 2H
$-OCH_2O-$	5 96, *dd*, 2H J_1 = 3 0, J_2 = 1 2	5 93, *dd*, 2H J_1 = 3 0, J_2 = 1 2

downfield shift of the olefinic proton provided strong support for the *cis–trans* isomerization observed on keeping gadain in $CDCl_3$

The structure and stereochemistry of gadain received further confirmation from its synthesis from jatrophan (**2**) The latter on demethylation with boron tribromide afforded a hydroxylactone, **3**, $C_{19}H_{16}O_6$, mp 215° (C_6H_6) The presence of the hydroxyls was confirmed from the IR absorption peak at 3380 cm^{-1} and the broad two-proton signal at δ9 65 which disappeared on deuteration The chemical shifts for the other protons were almost similar to those of the corresponding protons in **2** On treatment with bromochloromethane in dry acetone in the presence of anhydrous potassium carbonate, compound **3** afforded **1b**, $C_{20}H_{16}O_6$ ($[M]^+$ 352), mp 142° (ν_{max}^{KBr} cm^{-1} 1730, 1630, 1610, 1485 and 915) It was found to be identical with the product isolated earlier from hydrochloric acid isomerization of the naturally-occurring lignan, gadain Irradiation of compound **1b** in acetone with a medium pressure mercury vapour lamp simultaneously at 313 and 336 nm for 12 hr afforded its isomer, mp 144°, $[\alpha]_D^{25}$ +86°, which was found to be identical with the natural product, gadain (**1a**), from its physical and spectral properties This synthesis established the 3*S*-configuration for **1a** This stereochemistry was also supported by the comparison of its physical and spectral properties to those of (−)-isohibalactone (**1c**) [3] formed by UV irradiation of (−)-hibalactone Gadain (**1a**) showed similar properties to (−)-isohibalactone (**1c**) (3*R*-configuration) with opposite optical rotation Hence gadain must be *cis*(*Z*)-2-piperonylidene-3-piperonyl-3-*S*-γ-butyrolactone

Both gadain (**1a**) and jatrophan (**2**) possess an α,β-unsaturated γ-lactone system and hence would be susceptible to metal hydride reduction On reduction with both lithium aluminium hydride in tetrahydrofuran and sodium borohydride in methanol, lignans **1a** and **2** afforded the corresponding diols **4** [$C_{20}H_{20}O_6$ ($[M]^+$ *m/z* 356), mp 135° (C_6H_6)] and **5** [$C_{21}H_{24}O_6$ ($[M]^+$ *m/z* 372), mp 119° (C_6H_6)], respectively Their IR spectra revealed the presence of hydroxyl groups (ν_{max}^{KBr} cm^{-1} for **4** 3375, for **5** 3380) but lacked the peak absorptions due to the α, β-unsaturated γ-lactone The ^1H NMR spectrum of **4** and **5** displayed a broad signal at δ2 27 (2H) and 2 16 (2H), respectively, which disappeared on deuteration They underwent allylic oxidation with manganese dioxide yielding gadain (**1a**) and jatrophan (**2**), respectively

Jatrophan (**2**) on oxidation with a mixture of 10% aqueous potassium hydroxide and 5% aqueous potassium permanganate yielded veratric acid (**6**), mp 181° (Et_2O) (lit [5] 181–182°) and piperonylic acid (**7**), mp 228° (Et_2O) (lit [6] 229°), while gadain (**1a**) gave only piperonylic acid (**7**), mp 228° (Et_2O)

Hydrogenation of the unsaturated lignans **1a** and **2** produced the dihydro-compounds **8** [$C_{20}H_{18}O_6$ ($[M]^+$ *m/z* 354), mp 132° (C_6H_6)] and **9** [$C_{21}H_{22}O_6$ ($[M]^+$ *m/z* 370), mp 125° (C_6H_6)], respectively The ^1H NMR spectra clearly showed the absence of H-6 in **8** and **9**

Gadain (**1a**) underwent an interesting oxidative cyclization with DDQ in refluxing benzene, affording the naturally-occurring arylnaphthalide lignan, justicidin E (**10**) [7], $C_{20}H_{12}O_6$ ($[M]^+$ *m/z* 348), mp 265° (C_6H_6) (lit [7] 265–269°) This obviously indicated that the naturally-occurring lignan gadain (**1a**) isomerized to the thermodynamically more stable **1b** prior to cyclization Under similar conditions, jatrophan (**2**) afforded retrochinensin (**11**) [8], $C_{21}H_{16}O_6$ ($[M]^+$ *m/z* 364), mp 232° (lit [8] 234–236°)

Osmic acid oxidation of jatrophan (**2**) converted it to a 2,3-dibenzylbutyrolactone lignan, **12**, $C_{21}H_{22}O_8$ ($[M]^+$ *m/z* 402), mp 175° (EtOH) possessing vicinal OH-2 and OH-6 (ν_{max}^{KBr} cm^{-1} 3560, and δ ($CDCl_3$) 2 63, 2H, *br s*, exchangeable with D_2O) Acidification of **12** with hydrochloric acid (12 M) and acetic acid (1 25) converted it into an aryltetralin lignan, **13**, $C_{21}H_{20}O_7$ ($[M]^+$ *m/z* 384), mp 245° (EtOH) (ν_{max}^{KBr} cm^{-1} 3520, and δ ($CDCl_3$) 2 58, 1H, *br s*, exchangeable with D_2O) When **13** was refluxed with 10% Pd–C in *p*-cymene for 2 hr, it was completely aromatized to a naturally-occurring arylnaphthalide lignan, justicidin B (**14**) [9], $C_{21}H_{16}O_6$, mp 235° (EtOH) (lit [9] 235–238°) The latter was also prepared directly from jatrophan (**2**) by NBS treatment

The reactions are summarized in Scheme 1

EXPERIMENTAL

Plant material Seeds, roots and stem of *J gossypifolia* L were collected from Nadia District, West Bengal, India Voucher specimens JG(se), JG(r) and JG(st) have been preserved in our laboratory

Isolation of gadain (**1a**) Air-dried and finely milled stem, roots and seeds (30 kg) were exhaustively extracted with petrol (60–80°) in a Soxhlet apparatus for 72 hr The extract was concd and chromatographed over silica gel, the column being eluted with solvents of increasing polarity The C_6H_6 eluate afforded gadain (yield 60 mg, 0 0002%), $C_{20}H_{16}O_6$, mp 145° (C_6H_6)

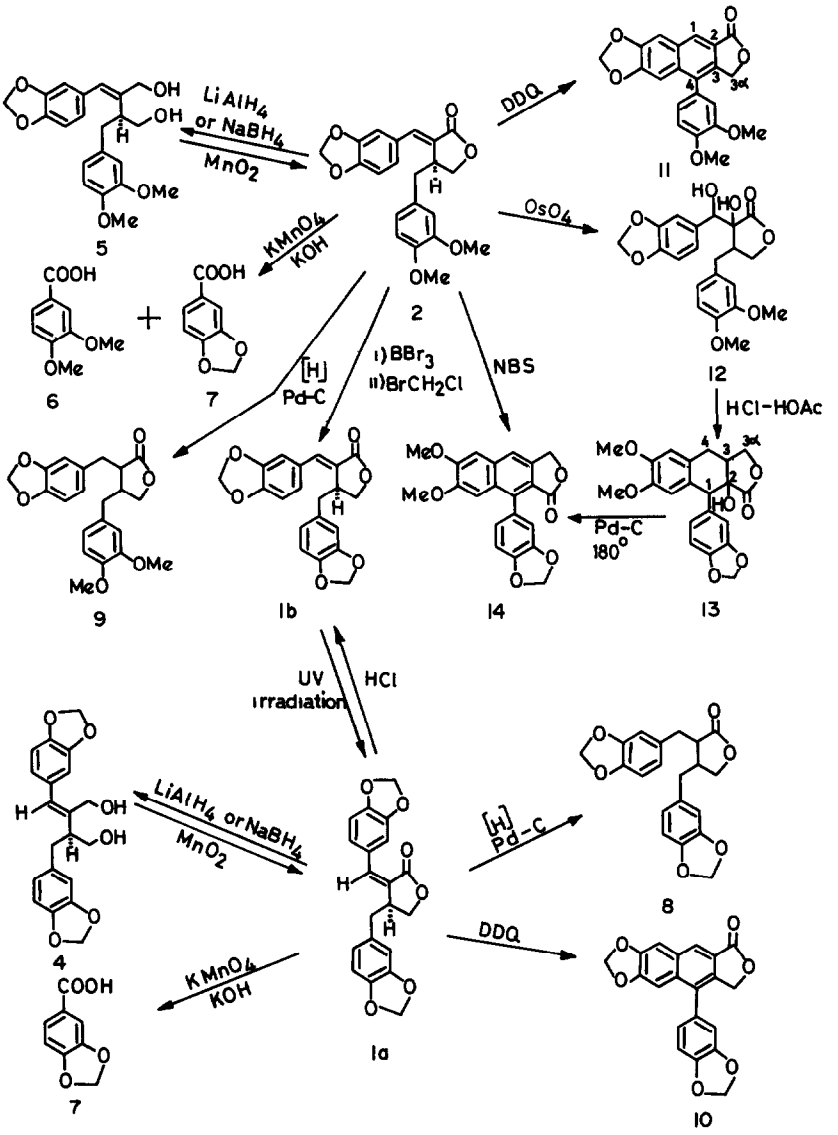
Reaction of **1a** *with* HCl Gadain (5 mg) was dissolved in $CHCl_3$ (0 5 ml) and a drop of HCl (1 0 M) added The mixture was kept at room temp for 72 hr It was then diluted with $CHCl_3$, washed with H_2O and dried (Na_2SO_4) The conc mass was purified by prep TLC on silica gel using C_6H_6–EtOAc (9 1) **1b** was obtained as white needles (3 mg), $C_{20}H_{16}O_6$, mp 139° (C_6H_6), IR ν_{max}^{KBr} cm^{-1} 1730 (α,β-unsaturated γ-lactone), 1630 (>C=C<), 1610, 1485 (aromatic >C=C<), 915 (–OCH_2O–)

Synthesis of **1a** (a) *Demethylation of* **2** To a soln of **2** (30 mg) in dry CH_2Cl_2 (20 ml) maintained at 0° to −5°, BBr_3 (1 ml) diluted with CH_2Cl_2 (10 ml) was added dropwise with vigorous stirring (2 hr) under N_2 The soln was then allowed to stand for 12 hr at room temp Excess BBr_3, and the boron complexes formed in the reaction, were decomposed with ice-cold H_2O and the CH_2Cl_2 layer was washed with 2% aq $NaHCO_3$ soln (4 × 20 ml) and H_2O, and finally dried (Na_2SO_4) The conc CH_2Cl_2 soln yielded the demethylated product **3** (14 mg), $C_{19}H_{16}O_6$, mp 215° (C_6H_6), IR ν_{max}^{KBr} cm^{-1} 3380 (–OH), 1725 (α,β-unsaturated γ-lactone), 1625 (>C=C<), 1590, 1480 (aromatic >C=C<), 910 (–OCH_2O–), ^1H NMR ($CDCl_3$) δ9 65 (2H, *br s*, exchangeable with D_2O, 2 –OH), 7 50 (1H, *s*, H-6), 7 0–6 5 (6H, *m*, Ar-H), 6 02 (2H, *s*, –OCH_2O–), 4 25 (2H, *d*, *J* = 4 1 Hz, H_2-4), 3 61 (1H, *m*, H-3), 3 03–2 64 (2H, *m*, H_2-5), MS *m/z* 340 $[M]^+$, 217, 189, 159, 123 (base peak), 77 and 28 (b) *Alkylation of* **3** *with* $BrCH_2Cl$ The demethylated product **3** (10 mg) was alkylated with $BrCH_2Cl$ (0 2 ml) in refluxing dry Me_2CO (20 ml) containing dry K_2CO_3 (200 mg) The filtrate on concn afforded a gummy residue which was crystallized from C_6H_6 to yield **1b** (5 mg), $C_{20}H_{16}O_6$, mp 142° (c) *UV irradiation of* **1b** **1b** (4 mg) was dissolved in Me_2CO (5 ml) and irradiated with UV light (313 and 336 nm) with a medium pressure Hg vapour lamp for 12 hr The light yellow soln showed two spots on TLC [R_f 0 49 and 0 53, silica gel, C_6H_6–EtOAc (9 1)] The more polar spot corresponded to **1b** and the less polar spot to gadain (**1a**) The compounds were separated by prep TLC on silica gel using C_6H_6–EtOAc (9 1), and crystallization of the product from the band of higher R_f *gave* gadain (**1a**, 2 mg), mp 144° (C_6H_6), $[\alpha]_D^{25}$ +86° ($CHCl_3$)

$LiAlH_4$ *reduction of* **2** A soln of **2** (30 mg) in dry THF (50 ml) was added dropwise to a slurry of $LiAlH_4$ (20 mg) in THF at 0° under dry conditions with vigorous stirring (6 hr) Excess reagent was decomposed with EtOAc and ice-cold H_2O The soln was filtered and the residue washed with hot EtOAc The EtOAc soln was concd to yield the diol **5** (19 mg), $C_{21}H_{24}O_6$, mp 119° (C_6H_6), UV λ_{max}^{EtOH} nm 257 (log ε 3 82), IR ν_{max}^{KBr} cm^{-1} 3380 (–OH), 1595, 1485 (aromatic residue and >C=C<), 920 (–OCH_2O–), ^1H NMR ($CDCl_3$) δ7 42 (1H, *s*, H-6), 6 64–6 46 (6H, *m*, Ar-H), 5 89 (2H, *s*, –OCH_2O–), 4 42–4 04 (4H, *m*, H_2-1 and H_2-4), 3 81 and 3 71 (each 3H, *s*, 2-OMe), 3 50 (1H, *m*, H-3), 2 72–2 40 (2H, *m*, H_2-5) and 2 27 (2H, *br s*, exchangeable with D_2O, 2-OH), MS *m/z* 372 $[M]^+$, 354, 221, 203, 151 (base peak), 77, 28

$NaBH_4$ *reduction of* **2** A MeOH suspension of **2** (30 mg) was cooled in ice and treated with $NaBH_4$ (20 mg) in small portions The reaction was monitored by TLC At the end of the reaction, MeOH was removed and H_2O (20 ml) added to the reaction mixture The soln was kept overnight and finally extracted with $CHCl_3$ The $CHCl_3$ soln was concd when the diol **5** (16 mg), $C_{21}H_{24}O_6$, mp 119° (C_6H_6), was obtained It was found to be identical to the $LiAlH_4$ reduction product of **2** from mmp, co-TLC and superimposable IR spectra

The above two reactions were repeated with **1a** (10 mg) Both produced the diol (**4**), $C_{20}H_{20}O_6$, mp 135° (C_6H_6), yield 6 5 mg ($LiAlH_4$ reduction) and 6 mg ($NaBH_4$ reduction), IR ν_{max}^{KBr} cm^{-1} 3375 (–OH), 1600, 1490 (aromatic residue and >C=C<), 920 (–OCH_2O–), ^1H NMR ($CDCl_3$) δ7 61 (1H, *s*, Ar-H), 6 82–6 54 (6H, *m*, Ar-H and H-6), 5 97 and 5 90 (each 2H, *s*, 2–OCH_2O–), 4 48–4 02 (4H, *m*, H_2-1 and H_2-4), 3 50 (1H, *m*, H-3), 2 82–2 46 (2H, *m*, H_2-5) and 2 16 (2H, *br s*, exchangeable with D_2O, 2-OH),



Scheme 1 Reactions of jatrophan (**2**) and gadain (**1a**)

MS *m/z* 356 $[M]^+$, 338, 221, 203, 135 (base peak), 77, 28

Oxidation of diols **4** *and* **5** *with* MnO_2 **4** and **5** were oxidized with MnO_2 to gadain (**1a**) and jatrophan (**2**), respectively, according to the following procedure The diol (**4** or **5**, 5 mg) in dry Me_2CO (20 ml) was stirred for 20 hr with freshly precipitated MnO_2 (30 mg) The mixture was filtered and the filtrate evapd to a gummy material which was crystallized from C_6H_6 The products were identified by mmp, co-TLC and superimposable IR spectra with authentic **1a** and **2** Yields for the oxidations of **4** and **5** were 3 5 and 4 0 mg, respectively

Oxidations of **2** *and* **1a** *with* $KMnO_4$ A mixture of **2** (30 mg), 10% aq KOH (10 ml) and 5% aq $KMnO_4$ (20 ml) was refluxed at 100° (2 hr) The reaction mixture was cooled and decolourized with Na_2SO_3 soln The soln was filtered, acidified with H_2SO_4 (2 N) and extracted with Et_2O (5 × 50 ml) The extract was dried and concd The mixture was subjected to fractional crystallization from Et_2O when two products, veratric acid (**6**, 4 5 mg), mp 181° (Et_2O) (lit [5] 181–182°) and piperonylic acid (**7**, 12 5 mg), mp 228° (Et_2O) (lit [6] 229°) were obtained Both compounds were identified by mmp, co-TLC and superimposable IR spectra with authentic samples

Gadain (**1a**, 10 mg) was also oxidized with alkaline $KMnO_4$ soln following the above procedure to furnish piperonylic acid (**7**, 6 0 mg), mp 228° (Et_2O) (lit [6] 229°)

Hydrogenation of **2** *and* **1a** Jatrophan (**2**, 20 mg) was dissolved in EtOH (20 ml) and the soln saturated with H_2 over 10% Pd–C for 4 hr The filtrate on concn afforded a gummy residue which crystallized from C_6H_6 as a white solid, **9** (16 mg), $C_{21}H_{22}O_6$, mp 125° (C_6H_6), IR ν_{max}^{KBr} cm^{-1} 1775 (γ-lactone), 1598, 1518, 1490 (aromatic ≻C=C≺), 1190 (–OMe) and 930 (–OCH_2O–), ^1H NMR ($CDCl_3$) δ7 06–6 43 (6H, *m*, Ar-H), 6 02 (2H, *s*, –OCH_2O–), 4 12 (2H, *br s*, H_2-4), 3 84 and 3 82 (each 3H, *s*, 2 –OMe), 3 33–2 26 (6H, *m*, H-2, H-3, H_2-5 and H_2-6), MS *m/z* 370 $[M]^+$, 219, 191, 151, 135, 77, 28

Gadain (**1a**, 5 mg) was hydrogenated following the same procedure to the dihydro-compound **8** (4 mg), $C_{20}H_{18}O_6$, mp 132° (C_6H_6), IR ν_{max}^{KBr} cm^{-1} 1775 (γ-lactone), 1610, 1592, 1490 (aromatic ≻C=C≺) and 940 (–OCH_2O–), ^1H NMR δ7 12–6 54

(6H, *m*, Ar-H), 5 98 and 5 95 (each 2H, *s*, 2 $-OCH_2O-$), 4 05 (2H, *br s*, H_2-4), 3 43–2 28 (6H, *m*, H-2, H-3, H_2-5 and H_2-6), MS *m/z* 354 $[M]^+$, 203, 175, 135, 77, 28

Reactions of **2** *and* **1a** *with DDQ* Jatrophan (**2**, 20 mg) was dissolved in dry C_6H_6 (20 ml), and DDQ (20 mg) added The mixture was refluxed for 24 hr The ppt formed was filtered off and the filtrate on concn afforded retrochinensin (**11**, 16 mg), which was purified by prep TLC on silica gel using C_6H_6–EtOAc (9 1), mp 232° (C_6H_6) (lit [8] 234–236°), UV λ_{max}^{EtOH} nm (log ε) 248 (4 60), 312 (3 96) and 348 (3 56), IR ν_{max}^{KBr} cm^{-1} 1760 (γ-lactone), 1625, 1510, 1470 (aromatic >C=C<), 900 ($-OCH_2O-$); ^1H NMR ($CDCl_3$) δ8 26 (1H, *s*, H-1), 7 39–6 83 (5H, *m*, Ar-H), 6 08 (2H, *s*, $-OCH_2O-$), 5 19 (2H, *s*, H_2-3α), 3 97 and 3 88 (each 3H, *s*, 2–OMe), MS *m/z* 364 ($[M]^+$, base peak), 349, 335, 307, 249, 227, 163 The physical and spectral properties were indistinguishable from those reported for retrochinensin [8] Direct comparison of the ^1H NMR spectrum of **11** with that of authentic retrochinensin confirmed the above identification

Following the above procedure, **1a** (10 mg) was also cyclized with DDQ to justicidin E (**10**, 7 mg), mp 265° (C_6H_6) (lit [7] 265–269°), IR ν_{max}^{KBr} cm^{-1} 1762 (γ-lactone), 1620, 1510 (aromatic >C=C<), 930 ($-OCH_2O-$), ^1H NMR ($CDCl_3$) δ8 27 (1H, *s*, H-1), 7 62–6 84 (5H, *m*, Ar-H), 6 12 and 6 16 (each 2H, *s*, 2 $-OCH_2O-$), 5 18 (2H, *s*, H_2-3α), MS *m/z* 348 ($[M]^+$, base peak), 319, 291, 261, 233, 205, 176 The physical and spectral properties of **10** were identical to those reported for justicidin E [7]

Reaction of **2** *with osmic acid* To a soln of jatrophan (**2**, 20 mg) dissolved in pyridine (0 5 ml), OsO_4 (20 mg) was added with stirring and the reaction continued for 24 hr A mixture of $NaHSO_3$ (35 mg), H_2O (5 ml) and pyridine (0 5 ml) was added and the reaction mixture stirred for 3 hr The product was extracted with $CHCl_3$ Concn of the organic layer afforded **12** (14 mg), $C_{21}H_{22}O_8$, mp 175° (EtOH), IR ν_{max}^{KBr} cm^{-1} 3560 (–OH), 1765 (γ-lactone), 1605, 1590 (aromatic >C=C<) and 912 ($-OCH_2O-$), ^1H NMR ($CDCl_3$) δ7 27–6 57 (6H, *m*, Ar-H), 6 04 (2H, *s*, $-OCH_2O-$), 4 95 (1H, *s*, H-6), 4 55–4 10 (2H, *m*, H_2-4), 3 92 and 3 88 (each 3H, *s*, 2 –OMe), 3 49–2 78 (3H, *m*, H-3 and H_2-5), 2 63 (2H, *br s*, exchangeable with D_2O, 2-OH), MS *m/z*, 402, 251, 233, 205, 175, 151 (base peak), 28

Cyclization of **12** *to* **13** Compound **12** (10 mg) was added to a mixture of HCl (12 M) and HOAc (1 25) and the mixture stirred for 12 hr The cyclization product **13**, $C_{21}H_{20}O_7$, was extracted with $CHCl_3$ and purified by crystallization from EtOH, mp 245°, yield 6 5 mg, IR ν_{max}^{KBr} cm^{-1} 3520 (–OH), 1770 (γ-lactone), 1610, 1590 (aromatic >C=C<) and 910 ($-OCH_2O-$), ^1H NMR ($CDCl_3$) δ7 22–6 78 (5H, *m*, Ar–H), 6 04 (2H, *s*, $-OCH_2O-$), 4 79–4 14 (2H, *m*, H_2-3α), 4 43 (1H, *s*, H-1), 3 85 and 3 92 (each 3H, *s*, 2 –OMe), 3 57–2 76 (3H, *m*, H-3 and H_2-4), 2 58 (1H, *br s*, exchangeable with D_2O, –OH), MS *m/z* 384, 366 (base peak), 351, 333, 289, 182, 28

Aromatization of **13** To a suspension of 10% Pd–C (10 mg) in *p*-cymene (10 ml), **13** (5 5 mg) was added The resulting suspension was heated under reflux with stirring for 2 hr under N_2 The mixture was cooled, filtered and the solvent removed in *vacuo* The residue on crystallization from EtOH furnished justicidin B (**14**, 4 mg), mp 235° (lit [9] 235–238°), IR ν_{max}^{KBr} cm^{-1} 1760 (γ-lactone), 1615 (aromatic >C=C<), 930 ($-OCH_2O-$), ^1H NMR ($CDCl_3$) δ7 73–6 92 (6H, *m*, Ar-H), 6 08 (2H, *s*, $-OCH_2O-$), 5 38 (2H, *s*, H_2-3α), 3 83 and 4 06 (each 3H, *s*, 2 –OMe), MS *m/z* 364 ($[M]^+$, base peak), 335, 321, 307, 277, 163, 28 The physical and spectral properties were indistinguishable from those reported for justicidin B [9]

NBS treatment of **2** Jatrophan (**2**, 20 mg) and NBS (20 mg) in dry CCl_4 (10 ml) were refluxed for 2 hr The ppt formed was removed by filtration The filtrate was evapd and the residue crystallized from EtOH to justicidin B (**14**, 15 mg), mp 235° The compound was identical to the aromatization product of **13** (mmp, co-TLC and superimposable IR spectra)

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