*Phytochemistry*, 1980, Vol. 19, pp. 1175–1181. © Pergamon Press Ltd. Printed in England. 0031-9422/80/0601-1175 $02.00/0

# NEW PHYSALINS FROM *PHYSALIS ANGULATA* AND *PHYSALIS LANCIFOLIA*. STRUCTURE AND REACTIONS OF PHYSALINS D, I, G AND K

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(*Revised received* 7 *September* 1979)

**Key Word Index**—*Physalis angulata; P. lancifiolia;* Solanaceae; physalins D, I, G and K; structural elucidation.

**Abstract**—The structures of physalins I, G and K are established respectively as 5,6-dihydro-5α-methoxy-6β-hydroxy, 4,5-dehydro-5,6-dihydro-4β-hydroxy and 5,6-dihydro-4α,5α-epoxy-6α-hydroxy derivatives of physalin B. The chemistry of physalin D, and the synthesis of physalins D and I from physalin F and physalin K from physalin G are described.

## INTRODUCTION

The isolation of several new physalins E, F, G, H and I from *P. angulata* and *P. lancifolia* and the structural elucidation of physalins E, F, H and J were reported in previous papers [1, 2] We now describe the isolation of another new physalin K from *P. angulata,* along with physalin B, and the structural elucidation of physalins G (**15**), I (**10**) and K (**17**) are reported. Mulchandani *et al.* [3] proposed the structure (**1**) for physalin D on the basis of spectral data, but its chemistry was not studied satisfactorily. Its isolation from *P. angulata* has provided us the opportunity to study this compound and to compare it critically with its isomer, physalin E (**2**).

## RESULTS AND DISCUSSION

### *Physalin D*

In many respects, physalin D (**1**) resembles physalin E (**2**). With $Me_2CO$–conc $H_2SO_4$, both give rise to dehydrophysalin B (**8**) [4], suggesting that they differ only in the position of the two secondary hydroxyls. They give rise to monoacetates (**1a** and **2a**) and also yield two monoketones (**3** and **4**) on oxidation with Jones' reagent. The $^1$H NMR spectra of the parent compounds, their acetates and their ketones have been very helpful in confirming the structure of physalin D (**1**) as 5α,6β-dihydroxy-5,6-dihydrophysalin B. The $^1$H NMR spectral data for the 2-, 3- and 6-H of **1** and **1a** were similar to those of the known 5α,6β,17,20-tetrahydroxy-1-oxowitha-2,14,24-trienolide and its acetate, respectively [5]. The $^1$H NMR signals of the 6α-H (δ 3.85 *m*) on the secondary hydroxyl in physalin D (**1**) and the 7β-H (3.52 *m*) in physalin E (**2**) were shifted to lower field showing a narrow half-width at 4.80 *m* ($W_{1/2}$ = 6 Hz) and 4.76 *m* ($W_{1/2}$ = 7 Hz), respectively, in their monoacetates **1a** and **2a**, indicating their equatorial nature [5, 6]. The 7-$CH_2$ protons in physalin D-ketone (**3**) appeared as a *dd* at 3.73 ($J$ = 10, 4 Hz) and as an overlapped signal at ~3.2 like those of isophysalin F-7-one [2], while the 6-$CH_2$ and 8-CH protons of **4** appeared as a multiplet at 3.7–3.9 (1H) and as an overlapped signal at ~3.0 (2H). The results exclude the alternative 4,5-glycol structure (**1b**) for physalin D, as it is not possible to secure an α-methylene ketone during oxidation.

Physalin D (**1**) also differed from physalin E (**2**) very significantly in its reactions with boiling HOAc and $POCl_3$–Py. In the former case, physalin D (**1**) yielded the 6-acetate (**1a**), while in physalin E (**2**) the 5α-hydroxyl was readily lost to yield anhydrophysalin E (**5**), apparently indicating that the 6β-hydroxyl in physalin D (**1**) is obstructing the dehydration of the 5α-hydroxyl. With stronger reagents like $Me_2CO$–conc $H_2SO_4$, however, both **1** and **2** underwent facile dehydration to dehydrophysalin B (**8**) [1]. Even $POCl_3$–Py, which is known to yield isoanhydrophysalin E (**6**) from physalin E (**2**) [1], had an entirely unexpected effect on physalin D (**1**). The product (**7**) has no longer the 5α-hydroxyl but contained a chlorine atom with the 6β-hydroxyl intact. In its $^1$H NMR spectrum, the 4-$CH_2$ (δ 3.14, *m*) and also the 6α-CH (δ 4.16, *m*) protons appeared at a considerably lower field due, perhaps, to the halogen [7]. Furthermore, in the MS, the molecular peak at *m/e* 562 (plus an isotope peak at 564) and [M − 36 (HCl)] peak at *m/e* 526 clearly confirmed the chlorine in the molecule. The peak at *m/e* 143 was assigned to the structure (**9**) by analogy with a similar peak at *m/e* 125 obtained from withanolides [8] and physalin E (**2**) [1].

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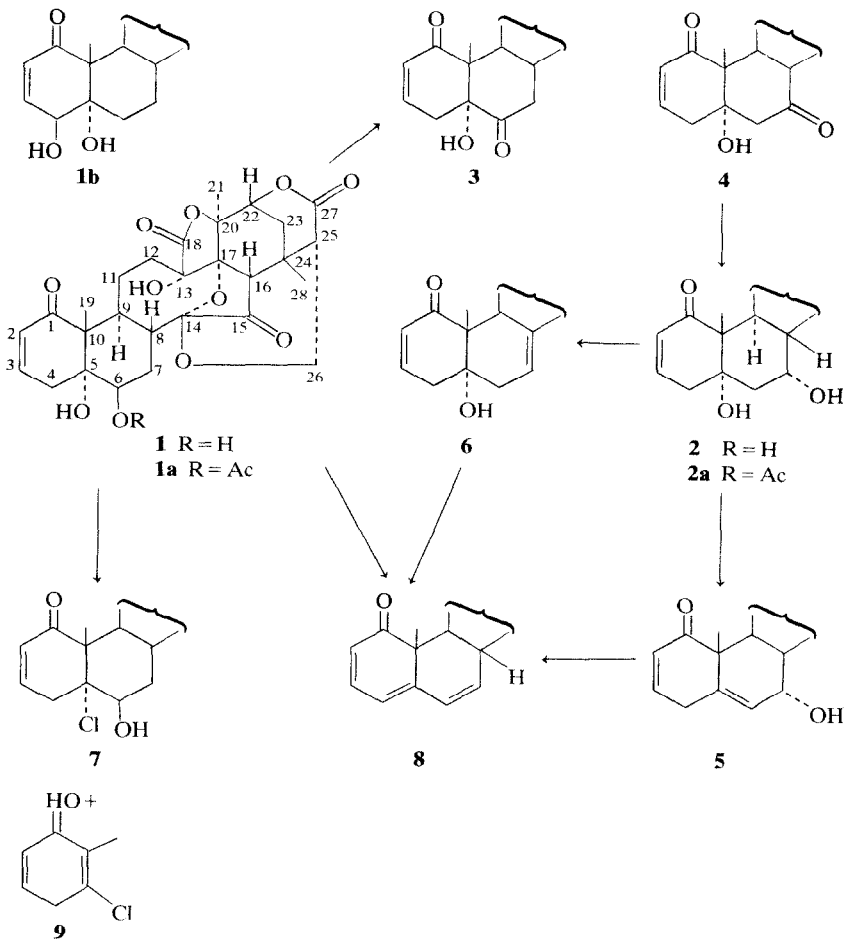



The CD band and ORD Cotton effects of physalin D (**1**) and the chloro-compound (**7**) were negative like other A/B-*trans* physalins [1, 2] and withanolide-2-ene-1-ones [5, 9], this being consistent with the 5α-configuration for **1**. The CD spectrum of the ketone **3** also showed negative values for the $n-\pi^*$ bands near 310 and 330 nm, similar to those of some withanolides having a 5α-hydroxy-1,6-dioxo-2-ene structure [5]. This also supported the 5α-configuration for **1**, although it has been reported 5α- and 5β-hydroxycholestanones both contribute to negative CD bands [10].

*The structure of physalin I* (**10**)

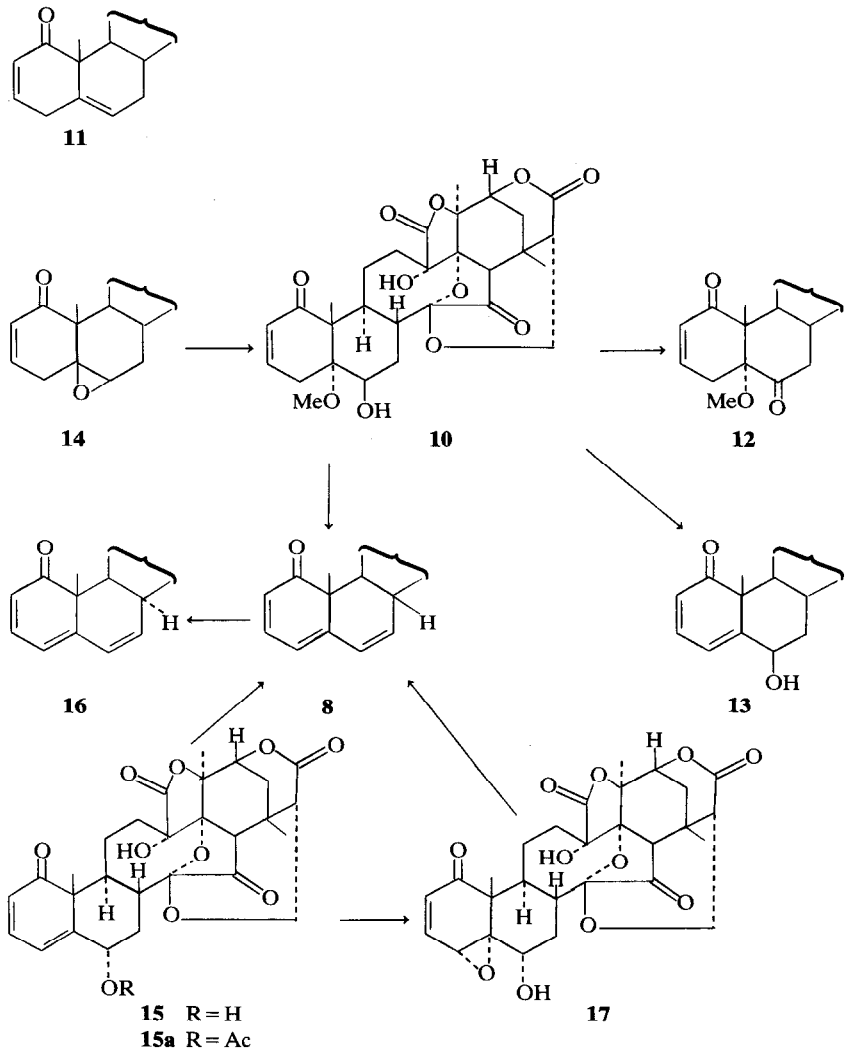
Physalin I (**10**) (mp 305–306°, $[\alpha]_D+12°$, $C_{29}H_{34}O_{11}$) contained a secondary hydroxyl and a methoxyl (δ 2.94, *s*) besides a methylene oxide bridge as in physalin B (**11**) [4]. Its correlation to physalin B (**11**) was established by the formation of dehydrophysalin B (**8**) [4] with $Me_2CO$–conc $H_2SO_4$. Physalin I readily yielded a ketone (**12**) with Jones' reagent. The $^1H$ NMR resonances of the proton (δ 3.84, *m*) geminal to the secondary hydroxyl in physalin I (**10**) and of the 7-proton (3.83, *m*) in the ketone (**12**) resembled those of physalin D (**1**) and its 6-one (**3**), respectively, thus supporting its location at C-6. Attempts to acetylate physalin I (**10**) with $Ac_2O$–Py at 100° resulted in the formation of a conjugated dienone (**13**), $\lambda_{max}^{EtOH}$ 325 nm (ε 9200), which contained three olefinic protons (δ 5.82, *dd*, $J=10$, 2 Hz for 2-H; 6.81, *dm*, $J=10$ Hz for 3-H; 6.32, *d*, $J=5$ Hz for 4-H). The 6-H remained at 3.80, *m* and, therefore, the dienone was given the structure **13**. The loss of a methoxyl was facile and can be due to its tertiary character, strongly suggesting its location at C-5. The neighbouring active 4-$CH_2$ in ring A readily loses a proton to form the dienone in this reaction. These experiments confirmed that physalin I was 5α-methoxy-6β-hydroxy-5,6-dihydrophysalin B (**10**).

The CD and ORD spectra of physalin I (**10**) and its 6-ketone (**12**) were very informative. The negative Cotton effect curve of **12** contained peaks at 360 nm (broad) and at 318 nm assignable to $n-\pi^*$ transitions of 1- and 6-keto groups, respectively. The results emphasize the A/B-*trans* configuration as in physalin I (**10**).

Finally, the structure of physalin I was confirmed by its synthesis from physalin F (**14**) [2] by the action of perchloric acid in methanolic solution following a similar procedure to that used for Jaborosa lactone A production [8]. The product was found to be identical to natural physalin I (**10**).

*The structure of physalin G* (**15**)

Physalin G (**15**) [mp 295–196°, $[\alpha]_D+17°$, $C_{28}H_{30}O_{10}$, $\lambda_{max}^{EtOH}$ 312 nm (ε 4000)] gave a monoacetate (**15a**). The $^1H$ NMR spectrum of physalin G (**15**)




was similar to that of dehydrophysalin B (**8**), showing the presence of the 14–25-methylene oxide bridge and the 13-tertiary hydroxyl as well as the 2,4-dien-1-one system (Table 1). There was an additional doublet at $\delta$ 5.08 ($J = 2$ Hz), which disappeared on shaking with $D_2O$. This signal was therefore assigned to a secondary hydroxyl in physalin G (**15**). The proton geminal to the secondary hydroxyl occured at 4.54, *m*, which changed to 5.50, *m* in physalin G acetate (**15a**). This resonance (4.54, *m*) of the proton was located at a much deshielded position unlike physalin E (**2**) (7 CH—OH, 3.52, *m*) and physalin D (**1**) (6 CH—OH, 3.85, *m*), indicating that it should be at an allylic position (C-6).

The presence of the 2,4-dien-1-one system was confirmed by decoupling experiments with physalin G acetate (**15a**). Both the C-2 (6.02 *d*) and C-4 protons (6.36, diffused *d*) became singlets on irradiation of the C-3 proton (7.04, *dd*), and the diffused doublet of the C-4 proton became sharper on irradiation at the C-6 proton (5.50 *m*). The latter decoupling result showed that there was a weak long-range coupling between the C-4 and C-6 protons. The structure **15** thus assigned for physalin G is epimeric to compound **13**. Since there is little possibility that epimerization at the C-6 position occurred during the formation of compound **13** from physalin I (**10**), physalin G is given structure **15**, having a 6$\alpha$-equatorial hydroxyl.

Supporting structure **15**, physalin G, like physalin D (**1**) and physalin I (**10**), readily gave rise to dehydrophysalin B (**8**) with the usual protonic reagents such as $Me_2CO$–conc $H_2SO_4$,$POCl_3$–Py, HOAc–conc HCl and DDQ–OH. A curious observation was made during the purification of **8** by chromatography on a Si gel column. When the column was left inadvertantly for 2 days, all the dehydrophysalin B (**8**) was converted into *epi*-dehydrophysalin B (**16**) [4]. Following this observation, the dehydrophysalin B (**8**) was refluxed with Si gel in $C_6H_6$–EtOAc (1:1), where upon the isomerization to **16** was found to be complete within 1 hr. In attempts to obtain a 1,6-diketone from physalin G (**15**), oxidation with Jones' reagent or with activated manganese dioxide always resulted in the formation of a complex mixture. Often the compound was destroyed and no isolable product could be secured, unlike the isomeric 7$\beta$-hydroxyphysalin B (physalin H) which readily furnished physalin B-7-one [1].

Table 1. $^1$H NMR values of relevant protons in new physalins and their derivatives*

| Compound | 2-H | 3-H | 4-H | 6-H | 7-H | 22-H | 26-$H_a$ | 26-$H_b$ | 13-OH | Other groups | *Tert.* Me |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **1** | 5.73*dd* (10.,4) | 6.61*dm* (10) | — | 3.85*m* | — | 4.55*m* | 4.20*m* | 3.60*d* (14) | 5.68*s* | 5-OH 4.19*s* 6-OH 4.85*d* (4) | 1.10*s*, 1.17*s* 1.83*s* |
| **1a** | 5.72*d* (10) | 6.63*dm* (10) | — | 4.80*m* | — | 4.56*m* | 4.27*dd* (14,4) | 3.59*d* (14) | 5.80*s* | 5-OH 4.80*s* 6-OAc 2.80*s* | 1.13*s*, 1.17*s* 1.83*s* |
| **8**† | 5.87*d* (19) | 7.03*dd* (19,6) | 6.08*d* (6) | 6.30*m* | 6.30*m* | 4.56*m* | 4.38*dd* (13,4) | 3.67*d* (13) | 6.47*s* | — | 1.16*s*, 1.21*s* 1.77*s* |
| **10** | 5.91*dd* (10,3) | 6.65*dm* (10) | — | 3.84*m* | — | 4.58*m* | 4.29*dd* (14,4) | 3.60*d* (13) | 5.70*s* | 6-OH 4.94*d* (4) 5-OMe 2.94*s* | 1.20*s* (6 H) 1.84*s* |
| **12** | 5.83*d* (10) | 6.70*dm* (10) | — | — | 3.83*m* | 4.64*m* | 4.28*dd* (14,4) | 3.60*d* (14) | 6.06*s* | 5-OMe 2.97*s* | 0.94*s*, 1.20*s* 1.78*s* |
| **15** | 5.94*d* (10) | 7.04*dd* (10,6) | 6.17*d*‡ (6) | 4.54*m* | — | 4.54*m* | 4.29*dd* (14,4) | 3.63*d* (13) | 6.36*s* | 6-OH 5.08*d* (2) | 1.20*s*, 1.26*s* 1.75*s* |
| **15a** | 6.02*d*‡ (10) | 7.06*dd* (10,6) | 6.36*d*‡ (6) | 5.50*m* | ;74.54*m* | 4.28*dd* | 3.60*d* (12,4) | 6.44*s* (13) | 6-OAc | 1.11*s*, 1.16*s* 2.00*s* | 1.72*s* |
| **17** | 7.05*dd* (8,2) | 6.73*dd* (8,6) | 4.66*dd* (6.2) | 3.85*m* | — | 4.58*m* | 4.30*dd* (12,4) | 3.62*d* (12) | 6.54*s* | 6-OH 5.69*d* (6) | 1.04*s*, 1.16*s* 1.82*s* |

* Spectra were taken in DMSO-$d_6$ solution; chemical shifts are $\delta$ values; coupling constants ($J$) in parentheses are given in Hz.

† Ref. [4].

‡ Diffused doublet.

*The structure of physalin K* (**17**)

Physalin K (**17**) is a minor component in *P. angulata* and could be isolated from the eluant fraction containing physalin G by careful fractional crystallization as colourless shining needles, mp 280–282°, $C_{28}H_{30}O_{11}$, $\lambda_{max}^{EtOH}$ 228 nm (ε 6500). From its spectral characteristics, it appeared to be unidentical to any known physalin. Thus, the name physalin K was given in conformity with this series of compounds. Its structure was established as **17** on the basis of its spectral properties and chemical reactions.

The spectral data showed that physalin K had the same skeletal arrangement including the 2-en-1-one system as physalin B (**11**). Of the two additional oxygen functions, one was a secondary hydroxyl (*d* 5.69, *d*, $J$ = 6 Hz, —CH—OH and 3.85, *m*, —CH—OH, decoupled each other) easily exchangeable with $D_2O$, and the other was present as an epoxide. A doublet of doublets at 4.66 ($J$ = 6, 2 Hz) was assigned to a proton on the epoxide ring located between C-4 and C-5, from its couplings with the C-2 and C-3 protons. The unusual chemical shifts of the C-2 (7.05) and C-3 (6.73) protons compared to those of the known physalins are probably due to a distortion of the ring A having an epoxide ring. Thus, physalin K may have the structure 4α,5α-epoxy-6α-hydroxy-5,6-dihydrophysalin B (**17**).

Physalin K (**17**) was readily converted into dehydrophysalin B (**8**), when refluxed with acetone in the presence of sulphuric acid. The structure **17** was confirmed by its synthesis from physalin G (**15**). When physalin G was treated with monoperphthalic acid at room temperature for 24 hr, a single product was obtained which was identical with physalin K (**17**). This synthesis led us to conclude that the 6-hydroxyl had the α-configuration. Finally, the α-configuration of the 4,5-epoxide was given on the basis of the negative CD bands and Cotton effect for physalin K [1, 2].

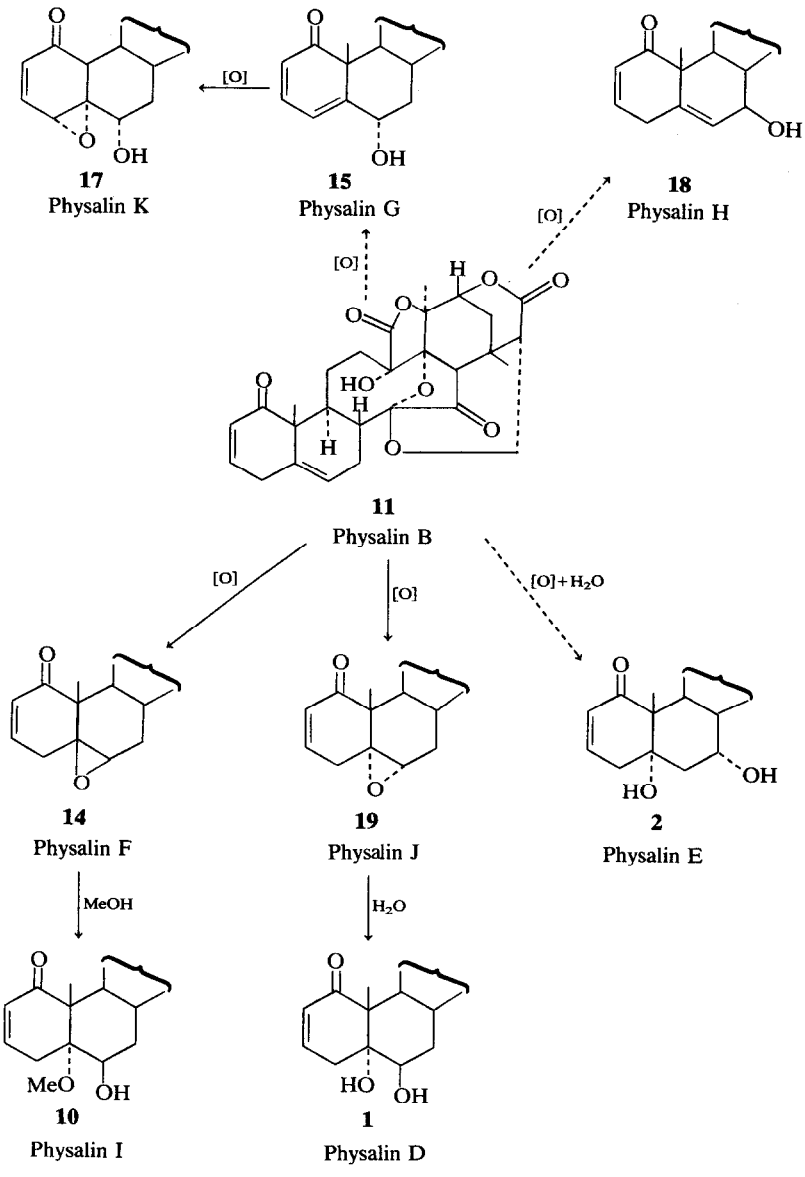
The chemical examination of *P. angulata* and *P. lancifolia* revealed as many as nine physalins, namely physalins B, D, E, F, G, H, I, J and K. Physalin B (**11**) seems to be the biogenetic precursor of all other physalins. Their plausible biogenetic interrelationship is presented in Scheme 1.

## EXPERIMENTAL

Mps were determined on a Micro Boittus apparatus and are uncorr. The compounds were dried for microanalysis at room temp. or at 100°/0.2 mmHg for 6 hr. $^1$H NMR spectra were determined in DMSO-$d_6$ containing TMS as int. standard. CD and ORD spectra were recorded in dioxane soln. MS were determined at 75 eV. TLC was carried out on chromatoplates of Si gel C and spots were visualised with MeOH–conc $H_2SO_4$ (19:1). The solvent systems are indicated at appropriate places.

*Extraction of the leaves of* P. angulata (*Copenhagen*). The seeds of *P. angulata* (Solanaceae) were secured from Copenhagen (Denmark) and the plants grown in the Botanic Farm, Andhra University, Waltair, India. The dry leaves were collected and extracted successively with *n*-hexane, $CHCl_3$ and EtOAc as described previously [1]. The last two extracts were fractionated on a Si gel column using several eluants to give compounds listed in Table 2. The stems of *P. angulata* (Lucknow) and the aerial parts of *P. lancifolia* were similarly extracted and the compounds were identified [1, 2].

*Physalin D* (**1**). Crystallization of fractions 80–95, showing a single TLC spot, from $Me_2CO$ gave physalin E (**2**) as




Scheme 1. Possible biosynthetic relationships of physalins. ⟶ Chemical conversion achieved. ------→ Chemical conversion not achieved.

colourless shining plates, mp 306–308°, identical with the sample isolated earlier. The mother liquor was evapd and the solid recrystallized from $Me_2CO$–MeOH (1 : 1) to give physalin D (**1**) as colourless shining plates, mp 286–287°, and mmp 279–280° on admixture with physalin E. [Found C, 61.10; H, 6.12; $M^+$, 544. $C_{28}H_{32}O_{11}$ requires: C, 61.82; H, 5.92%.] $\lambda_{max}^{EtOH}$ nm: 227 ($\varepsilon$ 6500); $\nu_{max}^{KBr}$ $cm^{-1}$: 3400, 1792, 1757, 1742, 1665; ORD (dioxane): $[M]_{355nm}$ −3500° (min), $[M]_{315}$ + 3300° (max), $[M]_{246}$ − 6500° (min), $[M]_{218}$ + 24 300° (max); CD (dioxane): $\lambda_{max}$: nm 344 ($\Delta\varepsilon$ −2.28), 339 (−2.26), 333 (−2.35), 266 (−0.03), 222 (−6.11) (strongly positive at shorter wavelengths). The acetate (**1a**) ($Ac_2O$/Py, 100°, 1 hr) was obtained as colourless needles from MeOH, mp 242–244°. [Found: C, 61.05; H, 5.98; $M^+$, 586. $C_{30}H_{34}O_{12}$ requires: C, 61.43; H, 5.85%.] $\lambda_{max}^{EtOH}$ nm: 224 ($\varepsilon$ 6700); $\nu_{max}^{KBr}$ $cm^{-1}$: 3400, 1792, 1760, 1742, 1728, 1665; MS: *m/e* (rel. int.) 586 ($M^+$, 31), 568 (23) (M−$H_2O$), 558 (57.3) (M−CO), 550 (20) (M−2$H_2O$), 540 (17.3) (M−CO−$H_2O$), 526 (35) M−MeCOOH), 522 (11) (M−CO−2$H_2O$), 332 (100), 125 (44).

*Oxidation of physalin D* (**1**) *to physalin D-6-one* (**3**). Physalin D (70 mg) in aldehyde-free $Me_2CO$ (40 ml) was treated with Jones' reagent (1 g $CrO_3$ + 7 ml $H_2O$ + 0.9 ml conc $H_2SO_4$; 8 drops) for 15 min. Excess reagent was destroyed using MeOH (1 ml). The mixture was concd, poured into cold $H_2O$ and extracted with $CHCl_3$ (30 ml × 3). The combined extracts were washed with N HCl followed by $H_2O$, dried ($MgSO_4$) and evapd. The residue crystallized from MeOH as shining needles, mp 294–295° (35 mg). [Found: C, 61.82; H, 5.38; $M^+$, 542. $C_{28}H_{30}O_{11}$ requires: C, 62.06; H, 5.43%.] $\lambda_{max}^{EtOH}$ nm: 228 ($\varepsilon$ 7200); $\nu_{max}^{KBr}$ $cm^{-1}$: 1780, 1767, 1730, 1710 (6-membered-ring ketone), 1665; $^1$H NMR: $\delta$ 5.75 (*dm*, $J$ = 10 Hz, 2-H), 6.69 (*dm*, $J$ = 10 Hz, 3-H), 4.60 (*m*, 22-H), 4.30 (*dd*, $J$ = 14, 4 Hz, 26-$H_a$), 3.60 (*d*, $J$ = 14 Hz, 26-$H_b$), 6.04 (*s*, 13$\alpha$-OH), [ 5.82 (*s*, 5$\alpha$-OH); ORD (dioxane): $[M]_{360nm}$ − 6800° (min), $[M]_{338}$ − 3500° (max), $[M]_{326}$ −

Table 2. Isolation of new physalins from the leaves of *P. angulata*

| Fraction (500 ml) | Eluant ($C_6H_6$–EtOAc) | Compounds | $R_f$ value* | Yield† (g) |
|---|---|---|---|---|
| 9–11 | 85:15 | Physalin B | 0.87 | 0.85 |
| 12–24 | 85:15 | Physalin F | 0.77 | 1.00 |
| 25–34 | 85:15 | Physalin H | 0.73 | 0.45 |
| 35–47 | 75:25 | Physalin K | 0.71 | 0.10 |
| 48–60 | 75:25 | Physalin K + Physalin G | — | 0.25 |
| 61–79 | 75:25 | Physalin G | 0.65 | 1.20 |
| 80–95 | 70:30 | Physalin D + Physalin E | 0.47 | 0.50 |
| 95–120 | 70:30 | Physalin E | 0.47 | 1.50 |

* Si gel TLC, $C_6H_6$–EtOAc (3:7).

† Yield after crystallization.

6800° (min), $[M]_{320}$ −6800° (min), $[M]_{315}$ −8100° (min), $[M]_{284}$ +12 500° (max), $[M]_{240}$ +680° (min); CD (dioxane) $\lambda_{max}$ 346 nm ($\Delta\varepsilon$ −2.13), 334 (−1.61), 308 (−6.06), 258 (−0.26), 232 (−3.28), 216 (+1.23); MS *m/e* (rel. int.): 542 ($M^+$, 80), 524 (80) (M−$H_2O$), 514 (100) (M−CO), 506 (50) (M−2$H_2O$), 496 (98) (M−CO−$H_2O$), 486 (5.5) (M−2CO), 478 (50) (M−CO−2$H_2O$), 125 (100).

*Action of glacial* HOAc *on physalin D* (**1**). Physalin D (50 mg) in glacial HOAc (10 ml) was refluxed on an oil bath for 24 hr. The product was worked up and the residue crystallized from MeOH as shining needles (45 mg), mp 280–281°, identical with physalin D-6-acetate (**1a**) (IR and co-TLC).

*Dehydration of physalin D* (**1**) *to dehydrophysalin B* (**8**). To a soln of physalin D (50 mg) in dry $Me_2CO$ (25 ml) was added conc $H_2SO_4$ (4 drops) and the mixture was heated on a steam bath for 15 min. After evapn *in vacuo*, the mixture was poured into cold $H_2O$ and extracted with (30 ml×3) $CHCl_3$. After usual work-up, the extract was crystallized from $Me_2CO$ as bright yellow glistening plates, mp 230–232° (40 mg), identical with dehydrophysalin B (**8**) (mmp, IR, $^1$H NMR) obtained earlier from physalin E (**2**) [1].

*Action of* $POCl_3$/Py *on physalin D* (**1**). Physalin D (50 mg) in dry Py (1 ml) was treated with freshly distilled $POCl_3$ (4 drops) for 15 min on a steam bath. The product was worked up and the residue crystallized from MeOH as shining colourless needles of 5α-chloro-6β-hydroxy-5,6-dihydrophysalin B (**7**) mp 260–262°. $R_f$ value 0.52 ($C_6H_6$–EtOAc, 3:7), $M^-$, 562 ($C_{28}H_{31}O_{10}Cl$). $\lambda_{max}^{EtOH}$ nm: 226 (ε 7000); $\nu_{max}^{Nujol}$ cm$^{-1}$: 3400, 1790, 1765, 1740, 1665, 830; ORD (dioxane): $[M]_{362\,nm}$ −5100° (min), $[M]_{358}$ −5000° (max), $[M]_{352}$ −5600° (min), $[M]_{310}$ +3500° (max), $[M]_{266}$ −2800° (min), $[M]_{225}$ −3500° (min); CD (dioxane) $\lambda_{max}$ nm: 400 ($\Delta\varepsilon$ = 0), 390 (0), 380 (0), 343 (−1.21), 341 (−2.17), 332.5 (−2.39), 275 (0), 265 (0) and 226 (0); $^1$H NMR: δ 6.67 (*m*, 3-H), 5.78 (*dm*, *J* = 10 Hz, 2-H), 5.90 (*s*, 13-OH), 4.58 (*m*, 22-H), 4.98 (*m*, 6-OH), 4.16 (*m*, 6-H); 3.14 (*d*, *J* = 8 Hz, 4-H), 4.31 (*dd*, *J* = 14, 4 Hz, 26-$H_a$), 3.63 (*d*, *J* = 14 Hz, 26-$H_b$), 2.90 (*d*, *J* = 4 Hz, 25-H), 2.84 (*s*, 16-H); MS *m/e* (rel. int.): 562 ($M^+$, 15), 544 (15) (M−$H_2O$), 534 (27) (M−CO), 526 (25) (M−HCl), 516 (12.5) (M−CO−$H_2O$), 508 (65) (M−HCl−$H_2O$), 498 (45) (M−CO−HCl), 490 (60) M−HCl−2$H_2O$), 171 (100), 143 (37.5), 36 (65) (HCl).

*Physalin I* (**10**). Crystallized from MeOH as shining colourless needles, isolated from *P. angulata* (Copenhagen) stems [1], mp 305–307° [Found: C, 61.23; H, 5.99; $M^+$, 558. $C_{29}H_{34}O_{11}$ requires: C, 61.82; H, 5.92%]. $[\alpha]_D$ +12° (*c* 0.5, $Me_2CO$). $\lambda_{max}^{EtOH}$ nm: 226–228 (ε 7200) → 218 nm with NaOEt: $\nu_{max}^{Nujol}$ cm$^{-1}$: 3400, 2890 (—OMe), 1790, 1772, 1745, 1662; ORD (dioxane): $[M]_{360\,nm}$ −3900° (min), $[M]_{352}$ −4100° (min), $[M]_{312}$ +1700° (max), $[M]_{250}$ −7200° (min); CD (dioxane) $\lambda_{max}$ 346 ($\Delta\varepsilon$ −1.53), 340 (−1.51), 334 (−1.60), 272 (−0.003), 234 (−6.42); MS *m/e* (rel. int.): 558 ($M^+$, 45), 530 (51) (M−CO), 526 (20) (M−MeOH), 508 (43) (M−MeOH−$H_2O$), 139 (43).

*Physalin B* (**11**). Crystallized from MeOH as colourless needles, mp 268–270°, identified by comparison with an authentic sample (mmp and IR) [4].

*Oxidation of physalin I* (**10**) *to physalin I-6-one* (**12**). Physalin I (70 mg) in aldehyde-free $Me_2CO$ (40 ml) was treated with Jones' reagent (8 drops) for 15 min. Excess reagent was destroyed using MeOH (1 ml). The mixture was concd and poured into cold $H_2O$ and, after usual work-up, the product was crystallized from MeOH as colourless shining needles, mp 280–282° (45 mg). [Found: C, 62.30; H, 6.20; $M^+$, 556. $C_{29}H_{32}O_{11}$ requires: C, 62.42; H, 6.13%.] $\lambda_{max}^{EtOH}$ nm: 229 (ε 6400), $\nu_{max}^{KBr}$ cm$^{-1}$: 3400, 2820 (—OMe), 1790, 1760, 1740, 1710 (6-membered-ring ketone), 1665; ORD (dioxane): Negative Cotton effect, $[M]_{370\,nm}$ −6100° (min), $[M]_{360}$ −6100° (min), $[M]_{354}$ −6100° (min), $[M]_{342}$ −4200° (max), $[M]_{330}$ −7800° (min), $[M]_{324}$ −6400° (max), $[M]_{318}$ −8300° (min), $[M]_{290}$ +12 500° (max), $[M]_{256}$ +800° (min), $[M]_{216}$ +1800° (max); CD (dioxane): $\lambda_{max}$ nm: 348 ($\Delta\varepsilon$ −1.99), 338 (−1.45), 326 (−1.93), 312 (−6.20), 264 (−0.20), 250 (+2.26), 218 (+1.09), 209 (−2.52).

*Action of Py–*$Ac_2O$ *on physalin I* (**10**). At 100° for 3 hr, **10** gave product **13** crystallized from MeOH as colourless shining needles, mp 284–285°. [Found: C, 62.98; H, 5.98; $M^+$, 526. $C_{28}H_{30}O_{10}$ requires: C, 63.87; H, 5.74%.] $\lambda_{max}^{EtOH}$ nm: 325 (ε 6500); $\nu_{max}^{Nujol}$ cm$^{-1}$: 3400, 1790, 1768, 1738, 1668; $^1$H NMR: δ 6.81 (*dm*, *J* = 10 Hz, 3-H), 5.80 (*dd*, *J* = 10, 2 Hz, 2-H), 4.55 (*m*, 22-H), 5.47 (*d*, *J* = 5 Hz, 6-OH), 6.20 (*s*, 13-OH), 6.32 (*d*, *J* = 2 Hz, 4-H), 3.80 (*m*, 6-H), 4.25 (*dd*, *J* = 14, 4 Hz, 26-$H_a$), 3.53 (*d*, *J* = 14 Hz, 26-$H_b$), 2.78 (*s*, 16-H), 2.92 (*d*, *J* = 4 Hz, 25-H).

*Dehydration of physalin I* (**10**) *to anhydrophysalin I* (*dehydrophysalin B* (**8**)). Physalin I (**10**) dissolved in dry $Me_2CO$ (30 ml) was mixed with conc $H_2SO_4$ (5 drops) and refluxed on an $H_2O$ bath for 15 min. After usual work-up, the residue was crystallized from $CHCl_3$ as bright yellow plates, mp 230–232°, identical with dehydrophysalin B (**8**) (IR, mmp).

*Action of* $HClO_4$–MeOH *on physalin F* (**14**). Physalin F (**14**) (50 mg) dissolved in dry MeOH (30 ml) was mixed with $HClO_4$ (3 drops) and heated on a steam bath for 1 hr. The soln was concd, poured into cold $H_2O$ (50 ml) and extracted with $CHCl_3$ (3×30 ml). After usual work-up, the product, physalin I (**10**), crystallized from MeOH–$Me_2CO$ (1:1) as colourless needles, mp 304–305° (40 mg), identical (mmp, IR) with the natural sample isolated from *P. angulata* by Row *et al.* [1].

*Physalin F* (**14**). Crystallized from MeOH–$Me_2CO$ (1:1) as colourless stout needles, mp 295–296°, identified by direct comparison with an authentic sample (mmp, IR and co-TLC) [2].

*Physalin G* (**15**). Crystallized from $Me_2CO$ as colourless thin needles, mp 295–296°, $[\alpha]_D$ +17° (*c* 0.5, $Me_2CO$), $R_f$ 0.65 (EtOAc–$C_6H_6$, 7:3). [Found: C, 63.52; H, 5.90; $M^+$, 526. $C_{28}H_{30}O_{10}$ requires: C, 63.87; H, 5.74%.] $\lambda_{max}^{EtOH}$ nm: 312 (ε 4000); $\nu_{max}^{KBr}$ cm$^{-1}$: 3400, 1790, 1765, 1740, 1665; ORD (dioxane): $[M]_{450\,nm}$ +662° (max), $[M]_{420}$ +1760° (max), $[M]_{415}$ +1760° (max), $[M]_{395}$ −220° (max), $[M]_{390}$ −880° (max), $[M]_{379}$ −3800° (max), $[M]_{376}$ −5000° (min), $[M]_{361}$ −9500° (max), $[M]_{357}$ −11 000° (min), $[M]_{347}$ −14 300° (min), $[M]_{339}$ −15 500° (min), $[M]_{317}$ −9700° (min), $[M]_{297}$ +3089° (max), $[M]_{285}$ +5300° (max), $[M]_{274}$ +3750°

(min), $[M]_{250}$ − 1800° (min), $[M]_{215}$ + 1700° (min), $[M]_{212}$ + 1700° (max); CD (dioxane): $\lambda_{max}$ nm: 415 ($\Delta\varepsilon$ + 0.78), 403 (+1.43), 380 (+2.14), 375 (+2.14), 355 (+1.43), 319 (−4.01), 312 (−4.80), 310 (−4.87), 307 (−4.87), 264 (−0.64), 241 (2.65), 213 (+0.64) and 209 (+0.78). The acetate (**15a**) (Py–$Ac_2O$ for 1 hr at 100°) crystallized from MeOH into small shining needles, mp 257–259°, $R_f$ value 0.83 ($C_6H_6$–EtOAc, 3:7). [Found: C, 63.20; H, 5.70; $M^+$, 568. $C_{30}H_{32}O_{11}$ requires: C, 63.42; H, 5.68%.] $\lambda_{max}^{EtOH}$ nm: 312 ($\varepsilon$ 4000); $\nu_{max}^{KBr}$ $cm^{-1}$: 3400, 1790, 1765, 1740, 1720 (acetate), 1665, 1625; MS *m/e* (rel. int.): 568 ($M^+$, 25), 560 (15) (M − $H_2O$), 508 (75) (M − MeCOOH), 462 (10) (M − MeCOOH − CO − $H_2O$).

*Dehydration of physalin G* (**15**) *to dehydrophysalin B* (**8**). Physalin G (50 mg) in dry Py (1 ml) was treated with freshly distilled $POCl_3$ (4 drops) for 15 min on a steam bath. The mixture was worked up as usual and the residue crystallized from $CHCl_3$ as bright yellow glistening plates, mp 230–232° (30 mg), identified as dehydrophysalin B (**8**) by mmp, IR and $^1H$ NMR. The same compound was also obtained when physalin G (**15**) was treated with $Me_2CO$–$H_2SO_4$, HOAc–HCl or DDQ–MeOH. [Found: C, 65.85; H, 5.72; $M^+$, 508. $C_{28}H_{28}O_9$ requires: C, 66.1; H, 5.6%.] $\lambda_{max}$ nm: 328 ($\varepsilon$ 50 000); $\nu_{max}^{Nujol}$ $cm^{-1}$: 3400, 1785, 1760, 1750, 1660, 1630; MS *m/e*: 508 ($M^+$), 490 (M − $H_2O$).

*Isomerization of anhydrophysalin G* (*dehydrophysalin B*) *on Si gel to yield* epi-*dehydrophysalin B* (**16**). Dehydrophysalin B (**8**) (35 mg) was adsorbed on Si gel G (100–200 mesh, 1.5 g) and the column 1.5″ × 1″) was wet with $C_6H_6$. The column was eluted with $C_6H_6$–EtOAc (3:1). Several fractions (100 ml each) were collected. The residue (30 mg) from fractions showing a single spot on TLC was crystallized from MeOH as orange–red needles, mp 250–252°, $R_f$ value 0.76 ($C_6H_6$–EtOAc, 3:7) (30 mg), identical with an authentic sample of *epi*-dehydrophysalin B (**16**) [4]. [Found: C, 65.9; H, 5.9; $M^+$, 508. $C_{28}H_{28}O_9$ requires C, 66.1; H, 5.6%.] $\lambda_{max}$ nm: 340 ($\varepsilon$ 6000); $\nu_{max}$ $cm^{-1}$: 3410, 1790, 1750, 1735, 1665, 1630, 1535; $^1H$ NMR: $\delta$ 5.88 (*d*, *J* = 10 Hz, 2-H), 7.08 (*dd*, *J* = 10, 6 Hz, 3-H), 6.06 (*d*, *J* = 6 Hz, 4-H), 6.30 (*d*, *J* = 10 Hz, 6-H), 6.17 (*dd*, *J* = 10, 3 Hz, 7-H), 6.56 (*s*, 13-OH), 4.60 (*m*, 22-H), 4.25 (*dd*, *J* = 12, 4 Hz, 26-$H_a$), 3.68 (*d*, *J* = 12 Hz, 26-$H_b$), 2.94 (*s*, 16-H), 3.02 (*d*, *J* = 2 Hz, 25-H), 1.17 (s, 24-Me), 1.38 (s, 10-Me), 1.66 (20-Me); MS *m/e*: 508 ($M^+$), 490 (M − $H_2O$).

*Oxidation of physalin G* (**15**). Physalin G (60 mg) was dissolved in aldehyde-free $Me_2CO$ (40 ml) and treated with Jones' reagent (8 drops). After 15 min at room temp., MeOH (1 ml) was added to destroy excess reagent. The soln was concd (10 ml), poured into cold $H_2O$ (50 ml) and extracted with $CHCl_3$. The $CHCl_3$ extract was washed with N HCl followed by $H_2O$, dried ($MgSO_4$) and evapd to a residue showing several spots on TLC, mp 271–272° and being unseparable, $\lambda_{max}^{EtOH}$ nm: 228 ($\varepsilon$ 10 900); $\nu_{max}^{KBr}$ $cm^{-1}$: 3400, 1790, 1765, 1740, 1665.

*Physalin H* (**18**). Crystallized from MeOH as colourless buttons, mp 238–240°, identified by comparison with an authentic sample (mmp, IR and co-TLC) [1].

*Physalin K* (**17**). Crystallized from $Me_2CO$–MeOH (1:1) as colourless shining needles, mp 280–282°. This compound was sparingly soluble in MeOH, $Me_2CO$ and $Et_2O$, and moderately in $CHCl_3$. $R_f$ value 71 ($C_6H_6$–EtOAc, 3:7). [Found: C, 61.90; H, 5.40; $M^+$, 542. $C_{28}H_{30}O_{11}$ requires C, 62.06; H, 5.43%.] $\lambda_{max}^{EtOH}$ nm: 228 ($\varepsilon$ 6500); $\nu_{max}^{KBr}$ $cm^{-1}$: 3400, 1785, 1760, 1740, 1668, 1080, 1068; ORD (dioxane): Negative Cotton effect, $[M]_{344nm}$ − 16 100° (min), $[M]_{333}$ − 7900° (max), $[M]_{330}$ − 6600° (min), $[M]_{317}$ + 3500° (max), $[M]_{330}$ − 6600° (min), $[M]_{317}$ + 3500° (max), $[M]_{306}$ + 6300° (max), $[M]_{282}$ + 3500° (max), $[M]_{274}$ + 1260° (min), $[M]_{247}$ − 3600° (min), $[M]_{244}$ − 3800° (min), $[M]_{238}$ − 3500° (max), $[M]_{230}$ − 2200° (min), $[M]_{225}$ − 3600° (min), $[M]_{218}$ + 5900° (max), $[M]_{215}$ + 6700° (min), $[M]_{209}$ + 3600° (max), $[M]_{208}$ + 4300° (max); CD (dioxane): $\lambda_{max}$ nm: 370 ($\Delta\varepsilon$ + 0.35), 365 (+0.38), 360 (+0.35), 336 (−4.59), 332 (−4.78), 326 (−5.16), 274 (−0.38), 270 (0.38), 265 (−0.38), 243 (−1.72), 238 (−2.10), 224 (−3.63) and 217 (−2.68); MS *m/e* (rel. int.): 542 ($M^+$, 7.4), 524 (15) (M − $H_2O$), 514 (11) (M − CO), 506 (22) (M − 2$H_2O$), 496 (44) (M − CO − $H_2O$), 486 (11) M − 2CO), 478 (14) (M − CO − 2$H_2O$).

*Dehydration of physalin K* (**17**) *to anhydrophysalin K* (*dehydrophysalin B* (**8**)). Physalin K (60 mg) dissolved in dry $Me_2CO$ (30 ml) was mixed with conc $H_2SO_4$ (5 drops) and refluxed on an $H_2O$ bath for 15 min. The mixture was worked up and the residue crystallized from $CHCl_3$ as bright yellow glistening plates, mp 230–232° (35 mg), identical with dehydrophysalin B (**8**) (mmp, IR and co-TLC) obtained from physalin G (**15**).

*Epoxidation of physalin G* (**15**) *to yield physalin K* (**17**). Physalin G (100 mg) in $CHCl_3$ (50 ml) was treated with a soln of monoperphthalic acid (100 mg) in 25 ml $Et_2O$. The mixture was kept for *ca* 24 hr at room temp. and diluted with $CHCl_3$. The total soln was washed with 2% aq. $NaHCO_3$ soln, N HCl and $H_2O$ successively. The organic layer was dried ($MgSO_4$) and evapd. The residue showed a single spot with some impurity on TLC, $R_f$ value 0.71 ($C_6H_6$–EtOAc, 3:7) and was crystallized from $Me_2CO$–MeOH (1:1) as colourless shining needles, mp 279–280°, which were identified as physalin K (**17**) by co-TLC, mmp and IR.

*Acknowledgements*—We thank Dr. K. G. Raja Rao, Department of Botany, Andhra University, for supplying the plant materials, Dr. Y. Morimoto, Fujisawa Pharmaceutical Co. Ltd., for measuring MS, and Mr. A. Takakuwa, Nihon Bunko Co. Ltd., for measuring ORD and CD spectra. One of the authors (K. S. R.) thanks the University Grants Commission for a Fellowship.

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