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THE STRUCTURE OF PHASEOLLIDIN

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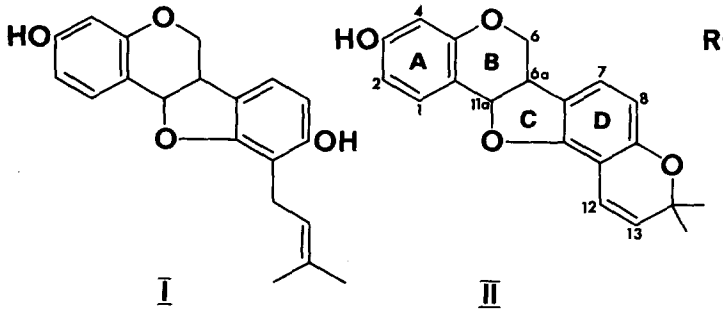
Phaseollidin, a second lipophilic antifungal compound from French bean (*Phaseolus vulgaris* L.), has recently been isolated, following its production in plant tissue subsequent to treatment by fungal inoculum, metabolic inhibitors and heavy metal ions (1). On the basis of physical evidence, structure (I) is proposed for phaseollidin and structure (II) is confirmed for phaseollin (2).††



I II III a R=H b R=CH_3

Molecular formulae, from mass spectra, were $C_{20}H_{20}O_4$ for phaseollidin and $C_{20}H_{18}O_4$ for phaseollin. The basic 10-substituted 3,9-dihydroxypterocarpan ring system in both compounds is evident from their NMR spectra (100 MHz, HA-100 Spectrometer, microcell, $CDCl_3$). Protons from the two aromatic rings and from the pterocarpan heterocyclic system form three isolated spin systems with very characteristic peak patterns. H-1 gives rise to a doublet ($J \sim 8.5$ Hz) coupled to the adjacent H-2 which, because of the additional *meta* coupling to H-4 ($J \sim 8.5$ Hz), shows up as a quartet. The resonance from H-4 is the expected narrowly split doublet. Protons on the central oxygen-heterocyclic rings (at 6, 6a, and 11a) form an ABMX system which gives a highly characteristic spectral pattern which has been studied for other pterocarpans by Pachler and Underwood (3). The very close similarity between the chemical shifts of these protons in phaseollidin, phaseollin and homopterocarpin (IIIb) is evident from the values listed in Table 1.

†† The nomenclature and numbering for pterocarpans follows the recommendation of the Editor, Chemical Society (Chem. Comm. 309, (1965)). Rings are lettered after Suginome (Experientia 15, 163, (1962)) in preference to the system used for flavanoid derivatives.

TABLE 1

Assignments of Chemical Shifts (δ in p.p.m.) in the NMR Spectra for Phaseollin, Phaseollidin and Model Compounds

Solvent $CDCl_3$

Compound	H-1	H-2	H-4	H-6	H-6a	H-7	H-8	H-11a	H-12	H-13	$(CH_3)_2$
Phaseollin	7.37	6.54	6.41	4.20, 3.64	3.50	6.92	6.32	5.55	6.48	5.54	1.49, 1.52
Phaseollidin	7.37	6.53	6.40	4.21, 3.63	3.54	6.93	6.36	5.44	3.36	5.28	1.76, 1.81
Homoptero-carpin	7.40	6.61	6.45	4.20, 3.60	3.44			5.45			
Gangetin				2,2-dimethylchromene					6.58	5.58	1.46, 1.50
				isopentenyl					3.37	5.33	1.79, 1.83

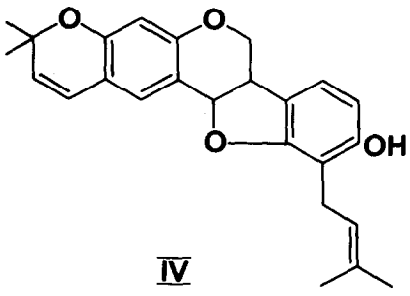
TABLE 2

Higher Mass Ions from the Mass Spectra of Phaseollin and Phaseollidin

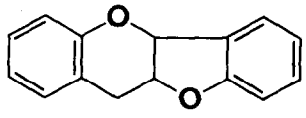
Phaseollin				Phaseollidin			
Mass	Intensity	Composition[a]	Parent ion	Mass	Intensity	Composition[b]	Parent ion
322[c]	73	$C_{20}H_{18}O_4$		324[d]	100	$C_{20}H_{20}O_4$	
321[c]	8	$C_{20}H_{17}O_4$		323	6	$C_{20}H_{19}O_4$	
307[c]	100	$C_{19}H_{15}O_4$	322[f]	322	4	$C_{20}H_{18}O_4$	
306[c]	2	$C_{19}H_{14}O_4$		309[d]	2	$C_{19}H_{17}O_4$	
279[c]	29	$C_{17}H_{11}O_4$	322	281[d]	5	$C_{17}H_{13}O_4$	
267[c]	6	$C_{16}H_{11}O_4$	322[e]	269[d]	41	$C_{16}H_{13}O_4$	324[e]
185	4	$C_{12}H_9O_2$		268[d]	86	$C_{16}H_{12}O_4$	324[f]
173	7	$C_{11}H_9O_2$		267[d]	18	$C_{16}H_{11}O_4$	
161[c]	6	Doubly charged 322		251	2	$C_{16}H_{11}O_3$	
153.5[c]	14	Doubly charged 307		239	2	$C_{15}H_{11}O_3$	
153[c]	21	Doubly charged 306		225	2	$C_{14}H_9O_3$	268[e]
147[c]	6	$C_9H_7O_2$	161[e]	162	2	Doubly charged 324	
				147[c]	10	$C_9H_7O_2$	
				134	8	Doubly charged 268	

[a] Computed from average of 3 scans
[b] Computed from an average of 7 scans
[c] Exchange with D_2O shows 1 exchangeable H
[d] Exchange with D_2O shows 2 exchangeable H's
[e] First Field Free region metastable observed
[f] Second Field Free region metastable observed

Although coupling constants for the ABMX systems were not extracted from the spectra reported here, the peak patterns were almost identical with that reported for homopterocarpin (3). The third NMR feature common to all three is the AB system from H-7 and H-8. The quartet from these protons contains a typical aromatic *ortho* coupling of ~ 8.5 Hz. The upfield doublet is assigned to H-8 because of the presence of an adjacent oxygen atom. There are four possible arrangements of the oxygen and other substituents on this aromatic ring which would produce an *ortho* AB-type system but the chemical shifts (Table 1) are consistent only with that shown in structures (I) and (II). The isopentenyl sidechain of phaseollidin and the dimethylchromene ring of phaseollin also produce characteristic NMR patterns for which many model compounds are available. Both systems occur in gangetin (IV) (4) and the appropriate chemical shifts are included in Table 1. The two methyl groups of the dimethylchromene ring in (IV) are non-equivalent and the ethylenic protons give an AB quartet (J ~ 10 Hz). In the isopentenyl sidechain of (IV) the methyl groups are allylic and resonate at lower field than those of the dimethylchromene ring. The remaining protons, $-CH_2-CH=$, form a typical "deceptively simple" ABX system, the methylene group absorbing as a broad doublet and the methine proton as a broad triplet.



IV



V

Confirmation of these structures was obtained from high resolution mass spectrometry (MS902, direct insertion probe, on-line Raytheon 706 computer) by interpretation of the higher mass ions listed in Table 2.

Both spectra are characterized by a paucity of intense peaks at lower mass values. This is typical for the pterocarpan ring system where retro-Diels-Alder reactions on electron bombardment do not lead to fragmentation (5,6). Significant peaks arising from retro-Diels-Alder fragmentations involving the 6-membered oxygen-heterocyclic ring are often observed in the mass spectra of other isoflavanoid and flavanoid ring systems (6,7) and would be expected for a derivative of (V).

The small peak of m/e 147 ($C_9H_7O_2$) observed for both phaseollin and phaseollidin may be formulated as a hydroxybenzopyrylium ion arising from rings A and B. The intense M-15 peak in the spectrum of phaseollin is consistent with the presence of a 2,2-dimethyl-chromene ring (8,9). In the spectrum of phaseollidin the peaks M-55 and M-56 are typical of either the *o*-hydroxy-isopentenyl grouping (10,11,12) or the isomeric 2,2-dimethylchroman ring (12,13). The open chain structure is indicated by the presence of two exchangeable hydrogen atoms in the molecule arising from two phenolic hydroxyls.

On the basis of the assigned structures many of the chemical properties of phaseollin and phaseollidin are readily understood. Absorption maxima corresponding to those of demethylhomopterocarpin are present in the uv spectrum of phaseollin and the extinction coefficients at these maxima are very similar. However, the small additional peak at 315 nm,

shown by phaseollin, and the reversal in the relative intensities of the maxima at 280 and 286 nm can be interpreted on the basis of structure (II). The chromene substitution on ring D can be expected to lead to changes because of the existence of a 2,6-dihydroxylated styrene chromophore. In (I), on the other hand, this conjugation is lacking so that the spectrum closely resembles that of demethylhomopterocarpin.

TABLE 3

Absorption Maxima [nm (logϵ)] in the Ultra-violet Spectra of Phaseollidin, Phaseollin and Demethylhomopterocarpin (in Ethanol)

Phaseollidin	208 (4.60)	237 (4.28) Shr.	281 (3.90)	286 (3.95)	
Phaseollin	207 (4.68)	230 (4.40)	280 (3.97)	286 (3.90)	315 (3.34)
Demethylhomopterocarpin (IIIa)			282 (3.84)	287 (3.89)	

The diazotised reagent Fast Blue Salt B reacts with most phenolic pterocarpans in alkaline solution to give an orange colour (λ_{max} 407 nm). With phaseollidin, on the other hand, a characteristic and much more intense orange-pink colour (λ_{max} 449 nm) is produced (1). We suggest that the difference arises from the phenolic group on ring D which leads to coupling of this ring with the diazotate.

Like most other representatives of naturally occurring pterocarpans, including homopterocarpin, demethylhomopterocarpin and gangetin (4), phaseollin (2) and phaseollidin (1) have large negative optical rotations (~ -150° to -250° at 578 nm), indicating that they have the same (6aR, 11aR) absolute configuration (4,14) and providing evidence that phaseollin and phaseollidin may have a close biogenetic relationship.

REFERENCES

1. I.A.M. Cruickshank, Dawn R. Perrin and D.R. Biggs, In preparation.
2. Dawn R. Perrin, Tetrahedron Letters No. 1, 29 (1964).
3. K.G. Pachler and W.G.E. Underwood, Tetrahedron, 23, 1817 (1967).
4. K.K. Purushothaman, V.M. Kishore, V. Narayaneswani and J.D. Connolly, J. Chem. Soc. (C), 2420 (1971).
5. A. Pelter and P.I. Amenechi, J. Chem. Soc. (C), 887 (1969).
6. A. Pelter, P. Stainton and M. Barber, J. Heterocyclic Chem. 2, 262 (1965).
7. A. Pelter, P. Stainton, A.P. Johnson and M. Barber, J. Heterocyclic Chem. 2, 256 (1965).
8. C.S. Barnes and J.L. Occolowitz, Aust. J. Chem. 17, 975 (1964).
9. B. Willhalm, A.F. Thomas and F. Gautschi, Tetrahedron, 20, 1185 (1964).
10. J.A. Ballantine, D.J. Francis, C.H. Hassall and J.L.C. Wright, J. Chem. Soc. (C), 1175 (1970).
11. E. Ritchie, W.C. Taylor and J.S. Shannon, Tetrahedron Letters No. 23, 1437 (1964).
12. S.J. Shaw and P.V.R. Shannon, Organic Mass Spectrometry, 3, 951 (1970).
13. H. Zilg and H. Grisebach, Phytochemistry, 7, 1765 (1968).
14. G.J.H. Rall, J.P. Engelbrecht and A.J. Brink, Tetrahedron, 26, 5007 (1970).