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# TWO NEW ARYL NAPHTHALIDE LIGNANS FROM *POLYGALA CHINENSIS**

SHIBNATH GHOSAL, RAMABALLAV P. S. CHAUHAN and RADHEY S. SRIVASTAVA

Pharmaceutical Chemistry Research Laboratory, Department of Pharmaceutics, Banaras Hindu University, Varanasi-5, India

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**Key Word Index**—*Polygala chinensis*; Polygalaceae; chinensinaphthol; chinensinaphthol methyl ether; 1-aryl-2,3-naphthalide lignan.

**Abstract**—Chinensinaphthol and chinensinaphthol methyl ether, two new 1-aryl-2,3-naphthalide lignans, have been isolated from the title plant. Structures (**2**) and (**3**) have been established for them by chemical transformations and spectral evidence. Significant quantitative variations in the content of the cyclic and the acyclic lactonic lignans (**1**–**3**, **5**–**7**) of *P. chinensis* have been observed in plant material, collected from the same locality and examined in 3 consecutive years.

## INTRODUCTION

PREVIOUSLY, the isolation and structure elucidation of a new 1-aryl-2,3-naphthalide lignan, chinensin (**1**), from the whole plant of *Polygala chinensis* were reported.[1] The present paper reports the isolation and structure of two new 1-aryl-2,3-naphthalide lignans.

## RESULTS AND DISCUSSION

Extraction of the entire plant with light petroleum followed by crystallization and column chromatography of the extractives gave four crystalline lignans, viz, chinensin (**1**), suchilactone (**5**), chisulactone (**6**), and helioxanthin (**7**). Extraction of the defatted plant materials with EtOH followed by the usual processing of the extractives afforded a further crop of chinensin together with two new compounds chinensinaphthol and chinensinaphthol methyl ether.

### *Chinensinaphthol*

The molecular formula $C_{21}H_{16}O_7$ was established from elemental analyses and MS determination ($M^+$). It responded to Labat test indicating the presence of methylenedioxy group (which was subsequently established from its PMR spectrum), and showed a purple colour with conc. $H_2SO_4$, characteristic of arylnaphthalide lignans.[1] Zeisel determination showed the presence of two methoxyl groups. The UV spectrum was strikingly similar to that of diphyllin (**4**).[2] The IR spectrum showed major bands at $\nu$ 3520 (OH), 1745 (aromatic $\gamma$-lactone), 942 (methylenedioxy), 800 $cm^{-1}$ (1,2,4-trisubstituted benzene ring). The lactone

* Part III in the series "Chemical Constituents of the Polygalaceae". For Part II see Ref. 1.

[1] GHOSAL, S., CHAUHAN, R. B. P. S. and SRIVASTAVA, R. S. (1974) *Phytochemistry* **13**, In press.

[2] HORII, Z., OHKAWA, K. and IWATA, C. (1972) *Chem. Pharm. Bull. Japan* **20**, 624 and references cited therein.

carbonyl band exhibited an upward shift by 36 $cm^{-1}$ from that of diphyllin ($\nu_{O\,CO}$ 1709 $cm^{-1}$). In the corresponding *O*-methyl derivatives, however, this band appeared at the same position ($\nu$ 1762 $cm^{-1}$). These observations, together with the sparing solubility of chinensinaphthol in 5 per cent aqueous NaOH and the negative ferric chloride test indicated that the lactone carbonyl was located at the *meta* position to the naphthol OH as in diphyllin. Chemical evidence for the presence of the OH group was obtained from acetylation and methylation; the *O*-acetyl and *O*-methyl derivatives showed satisfactory combustion analyses.

The 60 MHz PMR spectrum in $CD_3COCD_3$ showed proton signals ascribable to a lactone methylene group ($\delta$ 5·34, 2H, *s*, non-shielded by the aryl nucleus perpendicular to the naphthalene ring of the arylnaphthalide lignan[3]), a methylenedioxy group ($\delta$ 6·05, 2H, *s*, attached to the upper aromatic ring-A), and two methoxyl groups ($\delta$ 3·78 and 3·89, 3H each, *s*, attached to the lower aromatic ring, $\Delta\delta$ being $<0{\cdot}2$),[4] and five aromatic protons ($\delta$ 7·42, 1H, *s*, 5-H; 6·80, 1H, *s*, 8-H; 6·90, 3H, ABX *m*, three C-ring protons). Addition of $D_2O$ did not cause any new shifts, the phenolic proton (OH) is presumably buried beneath the water impurity signal. The MS of chinensinaphthol showed, aside from the molecular ion peak at *m/e* 380 (100%), a fragmentation pattern reminiscent of chinensin,[1] in which each oxygen carrying a carbon (associated with the methylenedioxy/methoxy groups) is lost in turn. Controlled oxidation of chinensinaphthol with acetone–$KMnO_4$ gave 3,4-methylenedioxy-6-(3′,4′-dimethoxybenzoyl)benzoic acid. The acid was previously obtained from chinensin from similar cautious oxidation.[1]

On the above basis, chinensinaphthol is assigned structure (**2**) which is isomeric with diphyllin (**4**).

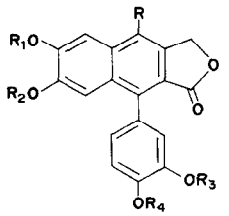
*Chinensinaphthol methyl ether*

The lignan, $C_{22}H_{18}O_7$ ($M^+$, 394), exhibited a UV spectrum closely similar to that of chinensinaphthol. The IR spectrum showed major bands at $\nu_{max}^{Nujol}$ 1762 (aromatic $\gamma$-lactone), 940, 923 (methylenedioxy), 798 $cm^{-1}$ (1,2,4-trisubstituted benzene ring), characteristic of 1-aryl-2,3-naphthalide lignans. The 60 MHz PMR spectrum in $CDCl_3$ showed four groups of signals ascribable to three methoxyl groups ($\delta$ 4·10, 3H, *s*, $C_4$–OMe, 4·0, 3H, *s*, 3·88, 3H, *s*), a lactone methylene group ($\delta$ 5·50, 2H, *s*, non-shielded by the aryl nucleus perpendicular to the naphthalene ring), a methylenedioxy group ($\delta$ 6·02, 2H, *s*), and five aromatic protons ($\delta$ 7·55, 1H, *s*, 5-H, 6·84, 1H, *s*, 8-H, 6·88, 3H, ABX *m*, three C-ring protons). The downfield methoxyl signal ($\delta$ 4·10) is assigned to $C_4$ by the close similarity of the chemical shift to the corresponding one of justicidin-A ($\delta$ 4·08).[5] The $\Delta\delta$ value of the remaining two methoxyl signals indicate that these are attached to the lower aromatic ring (C-ring).[4]

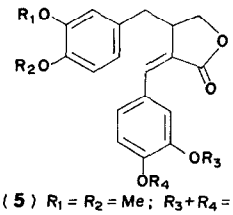
The chemical evidence for the presence of the lactone ring in this compound was provided by the reduction with $LiAlH_4$. The corresponding diol, $C_{22}H_{22}O_7$, m.p. 214–215°, showed IR spectrum: $\nu_{max}^{Nujol}$ 3400, 1038 $cm^{-1}$ (OH), and mass spectrum ($M^+$, 398), consistent with the transformation of the lactone ring to the diol. The mass spectrum of chinensinaphthol methyl ether showed a fragmentation pattern indicating a methylenedioxy–trimethoxy–1-aryl-2,3-naphthalide lignan structure. The further chemistry of the lignan, in

[3] HORII, Z., TSUJIUCHI, M. and MOMOSE, T. (1969) *Tetrahedron Letters* 1079.
[4] STEVENSON, R. and HOLMES, T. L. (1971) *J. Org. Chem.* **36**, 3450.
[5] OKIGAWA, M., MAEDA, T. and KAWANO, N. (1970) *Tetrahedron* **26**, 4301.

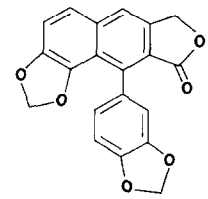
particular, its oxidation with acetone–$KMnO_4$ to give 3,4-methylenedioxy-6-(3′,4′-dimethoxybenzoyl)-benzoic acid, albeit in small yield, is readily explicable in terms of the formulation (**3**). Methylation of (**2**) gave (**3**), identical with the natural compound.



(**1**) R = H; $R_1+R_2$ = —$CH_2$—; $R_3=R_4$=Me
(**2**) R = OH; $R_1+R_2$ = —$CH_2$—; $R_3=R_4$=Me
(**3**) R = OMe; $R_1+R_2$= —$CH_2$—; $R_3=R_4$=Me
(**4**) R = OH; $R_1=R_2$=Me; $R_3+R_4$= —$CH_2$—



(**5**) $R_1=R_2$=Me; $R_3+R_4$= —$CH_2$—
(**6**) $R_1+R_2$= —$CH_2$—; $R_3=R_4$=Me



(**7**)

The co-occurrence of the three arylnaphthalide lignans (**1–3**), together with helioxanthin (**7**), in the same plant is biogenetically significant. One possible way of formation of the cyclic lignans could be by oxidative cyclization of an appropriate diarylidene butyrolactone intermediate.[2] Such a cyclization in the present case, involving a diarylidene butyrolactone precursor corresponding to suchilactone (**5**), would lead to diphyllin and justicidin-B. These two cyclic lignans have so far remained undetected in *P. chinensis* plant extracts. Further, while the other acyclic lignan, chisulactone (**6**), was so far obtained as a minor lignan from this plant, the yield of suchilactone (**5**) varied (inversely proportional) with those of the arylnaphthalide lignans (**2–3**) (Table 1).[1,6,7] Since the yield of chisulactone, the diarylidene equivalent of which could act as the precursor of the cyclic lignans (**1–3**), remained unchanged irrespective of the yield of the latter, the role of (**5** and **6**) in the biogenesis of (**1–3**) is not readily explicable. Additionally, suchilactone was recovered completely unchanged after air was bubbled through its acetone solution in direct sunlight for 2 hr. Thus, it would seem that suchilactone and chisulactone do not lie on the natural biosynthetic pathway to the cyclic lignans but accumulate as shunt products.

TABLE 1. RELATIVE % YIELD AND ABUNDANCE OF LIGNANS IN *Polygala chinensis**

| Lignan structure | Lignan total % yield August 1971 0·31% | August 1972 0·35% Relative abundance | September 1973 0·23% |
|---|---|---|---|
| **1** | 1·5 | 25 | 0·5 |
| **2** | 4 | 40 | 2·5 |
| **3** | 0·5 | 18 | 0·4 |
| **4** | — | | — |
| **5** | 66 | 0·3 | 73 |
| **6** | 4 | 2·8 | 3 |
| **7** | traces | — | traces |
| Unidentified lignans | 24 | 14 | 20 |

* Mean of two experiments is recorded.

[6] GHOSAL, S., KUMARSWAMY, C. and RAY, A. B. (1973) *Proc. 60th Indian Sci. Cong.*, III. 121.
[7] GHOSAL, S., KUMARSWAMY, C., CHAUHAN, R. B. P. S. and SRIVASTAVA, R. S. (1973) *Phytochemistry* **12**, 2550.

## EXPERIMENTAL

General methods are as reported in a recent paper.[1] The plant materials were collected from Varanasi, every year during August–September for 3 yr (1971–1973), and their identity was duly confirmed. Voucher specimens have been kept at the Department of Pharmaceutics, Banaras Hindu University. The usual procedure was followed for the isolation of the lignans. The relative % yield and abundance of the individual lignans, occurring in *P. chinensis* plants, collected in the three batches, are recorded in Table 1.

*Chinensinaphthol* (**2**). The lignan crystallized from MeOH–dioxan as colourless needles, m.p. 285–286°; $[\alpha]_D^{25}$ 0° (*c* 0·24, MeOH); UV: $\lambda_{max}$ 228, 262, 290–295 sh, 312, 325, 355 nm (log $\epsilon$ 4·42, 4·58, 3·95, 3·92, 3·94, 3·68); IR: $\nu_{max}^{Nujol}$ 3520, 1745, 1622, 1604, 1582, 1540, 1520, 1504, 1348, 1246, 1145, 1118, 1040, 1015, 942, 800 $cm^{-1}$; MS: *m/e* 380 ($M^+$, 100%), 365 (22), 351 (3), 350 (4), 337 (3), 335 (2), 322 (7), 305 (4), 291 (2), 279 (2), 277 (2), 238 (3), 203 (3), 190 (5), 149 (8), 102 (7); (Found: C, 66·18; H, 4·44; OMe, 15·8. $C_{21}H_{16}O_7$ requires: C, 66·31; H, 4·21; 2 OMe, 16·3). The acetate was obtained as needles, m.p. 210–212°; *m/e* 422 ($M^+$); IR: $\nu_{max}^{Nujol}$ 1760, 1748, 1240 $cm^{-1}$. The methyl ether ($Me_2SO_4/K_2CO_3$), crystallized from $CHCl_3$–MeOH as needles, m.p. and m.m.p. with chinensinaphthol methyl ether, 257–258°; co-TLC showed a single fluorescent spot having the same $R_f$ value; superimposable IR spectra.

*$KMnO_4$ oxidation of chinensinaphthol.* To a saturated boiling solution of chinensinaphthol (1·1 g) in $Me_2CO$ (500 ml), $KMnO_4$ (3 g) was added during 1 hr. The reaction was refluxed for 1 hr more and then the solvent was removed. The residue was suspended in $H_2O$, acidified with dil. $H_2SO_4$, and treated with $NaHSO_3$ till all the $MnO_2$ dissolved. The dull yellow solid was collected by filtration. It was digested with aq. NaOH soln (2%, 50 ml). The alkaline soln was acidified and the product was extracted with $CHCl_3$ (3 50 ml-portions). The residue from the $CHCl_3$ extract was dissolved in minimum quantity of MeOH (*ca* 5 ml) and chromatographed over silica gel column (28 × 1·4 cm). $C_6H_6$ and $CHCl_3$ were used as the eluents. The middle $CHCl_3$ eluates afforded 3,4-methylenedioxy-6-(3′,4′-dimethoxybenzoyl)-benzoic acid (43 mg), m.p. 205–207°. The identity was confirmed by direct comparison (co-TLC, superimposable IR spectra) with reference material.[1]

*Chinensinaphthol methyl ether* (**3**). The $CHCl_3$ eluates from the column chromatographic resolution of the phenolic-carboxylic acid fraction gave chinensinaphthol methyl ether as an amorphous solid. It crystallized from $CHCl_3$–MeOH as colourless needles, m.p. 257–258°; $[\alpha]_D^{25}$ 0° (*c* 0·34, $CHCl_3$); UV: $\lambda_{max}$ 235, 260, 295, 312, 324, 345 nm (log $\epsilon$ 4·24, 4·63, 3·78, 3·80, 3·74, 3·49); IR: $\nu_{max}^{Nujol}$ 1762, 1618, 1588, 1536, 1420, 1410, 1360, 1345, 1250, 1225, 1145, 1082, 1030, 940, 923, 798 $cm^{-1}$; MS: *m/e* 394 ($M^+$, 100%), 379 (5), 365 (7), 364 (17), 351 (16), 336 (3), 335 (4), 320 (24), 305 (4), 278 (3), 197 (4), 165 (5); (Found: C, 66·68; H, 4·26. $C_{22}H_{18}O_7$ requires: C, 67·00; H, 4·56). Oxidation of chinensinaphthol-methyl ether (0·38 g) with acetone (200 ml)–$KMnO_4$ (0·98 g), according to the procedure described for chinensinaphthol, furnished 3,4-methylenedioxy(3′,4′-dimethoxybenzoyl)-benzoic acid (18 mg). $LiAlH_4$ reduction furnished the diol as an amorphous solid. It crystallized from $Me_2CO$ as needles, m.p. 214–215°; *m/e* 398 ($M^+$); IR: $\nu_{max}^{Nujol}$ 3400, 1625, 1598, 1038 $cm^{-1}$. (Found: C, 65·92; H, 5·21. $C_{22}H_{22}O_7$ requires: C, 66·33; H, 5·52).

*Attempted photolytic oxidation of suchilactone* (**5**). Suchilactone (0·12 g) was dissolved in anhyd. acetone (100 ml) through which air was bubbled for 2 hr in direct sunlight. The solvent was removed and the residue co-chromatographed with suchilactone in 3 solvents. Only one fluorescent and $I_2$-positive spot, having the same $R_f$ as suchilactone, was detected. The residue crystallized from EtOH as colourless needles, m.p. and m.m.p. with suchilactone, 130–131°.

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