FLAVIDIN, A NOVEL 9,10-DIHYDROPHENANTHRENE DERIVATIVE OF THE ORCHIDS *COELOGYNE FLAVIDA*[1], *PHOLIDOTA ARTICULATA* AND *OTOCHILUS FUSCA*

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ABSTRACT.—The structure of flavidin (**1a**), a modified 9,10-dihydrophenanthrene, isolated from the orchids *Coelogyne flavida*, *Pholidota articulata* and *Otochilus fusca* has been established on the basis of spectral data.

Barring the isolation of the physiologically active alkaloids like dendrobine and some of its structural analogues from the orchids of the genus *Dendrobium* (1), the vast area of the Himalayan orchids has practically remained chemically unexplored. This has prompted us to undertake a systematic chemical investigation of a series of these orchids from which we have earlier reported (2–4) the isolation of a number of 9,10-dihydrophenanthrene derivatives. As a part of this program we report in this communication the isolation of yet another new phenolic compound, designated flavidin, from three Himalayan orchids, *Coelogyne flavida*, *Pholidota articulata* and *Otochilus fusca*.

RESULTS AND DISCUSSION

Flavidin, $C_{15}H_{12}O_3$ ($M^{+\cdot}$ 240), mp 210°, $[\alpha]D \pm 0°$ ($CHCl_3$) showed uv absorptions, λmax (EtOH) 214, 286 and 303 nm (log ε 4.52, 4.23 and 4.14) resembling those of 9,10-dihydrophenanthrenes (2–5). The characteristic color reactions and the alkali-induced bathochromic shift of the uv maximal positions, λmax (EtOH–0.1N NaOH) 219 and 309 nm (log ε 4.43 and 4.32) of flavidin indicated its phenolic nature, which was also supported by its ir spectrum showing absorption at νmax 3260 cm^{-1} besides the usual bands for aromatic nucleus. The presence of two phenolic hydroxyl groups in flavidin was indicated by the formation of a diacetyl derivative, $C_{19}H_{16}O_5$ ($M^{+\cdot}$ 324), mp 166°, and a dimethyl ether, $C_{17}H_{16}O_3$ ($M^{+\cdot}$ 268), mp 138°.

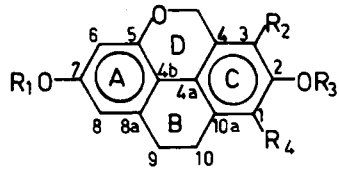
The 80 MHz ^1H nmr spectrum of flavidin showed a four-proton singlet at δ 2.77, which is typical (5,6) of the 9- and 10-methylene protons of a 9,10-dihydrophenanthrene; a two-proton singlet at δ 5.01, attributable to the protons of the system, Ar-O-CH_2-Ar; and a two-proton broad signal at δ 4.61 (disappearing on deuterium exchange) for two phenolic hydroxyl protons. The spectrum also revealed the presence of four aromatic protons, two of which appeared as a pair of doublets at δ 6.37 and 6.53 ($J = 3$ Hz), while the remaining two resonated at δ 6.25 as a broad signal. All the four aromatic protons of flavidin were shifted downfield by ~ 0.3–0.4 ppm in the pmr spectrum of its diacetyl derivative indicating that each of them was *ortho* to a phenolic hydroxyl group. On the basis of these spectral data the structure of flavidin was assigned as 2,7-dihydroxy-9,10-dihydro-5H-phenanthro[4,5-bcd]pyran[2] (**1a**), which is also consistent with its mass spectral data.

Contrary to expectation, flavidin was resistant to hydrogenolysis with 10% Pd-C under normal conditions. Such behaviour was also observed with coelogin (**1d**), a structurally similar compound recently isolated in our laboratory (2).

Further evidence in support of structure **1a** for flavidin was provided by ^{13}C

[1]A preliminary account of this work was presented at the fifth National Symposium on Organic Chemistry (NASOC–V), University of Calcutta, Calcutta, 1981, *Abstracts*, P. 35, p. 41.

[2]For ease of comparison of spectral results the phenanthrene numbering system has been used in this paper.



1a : $R_1 = R_2 = R_3 = R_4 = H$
1b : $R_1 = R_3 = Ac$, $R_2 = R_4 = H$
1c : $R_1 = R_3 = Me$, $R_2 = R_4 = H$
1d : $R_1 = H$, $R_2 = OH$, $R_3 = Me$, $R_4 = OMe$

nmr spectral analyses of its more soluble diacetyl derivative **1b**. The substitution profile of the carbon centers was determined by an off-resonance decoupling technique. The assigned carbon chemical shifts of **1b** (table 1) were in good agreement with the calculated values when the known additivity parameters (7) of the functional groups on the reported carbon chemical shifts of the parent 9,10-dihydrophenanthrene (7) were used. The observed upfield shift of C-4a by ~9 ppm from the calculated value was attributed to the γ-hetero atom (8) in the oxymethylene bridge. The carbon chemical shifts of **1b** also exhibited a striking resemblance to those of coelogin diacetate, the difference being due only to different substituents.

TABLE 1. The carbon chemical shifts of diacetyl flavidin (**1b**).

Carbon atoms	[a]Chemical shifts in δppm	Carbon atoms	[a]Chemical shifts in δppm
C-1	120.2	C-8	114.3
C-2	149.8	C-8a	134.6[a]
C-3	115.5	C-9	27.1[b]
C-4	129.9	C-10	27.2[b]
C-4a	123.7	C-10a	135.7[a]
C-4b	116.6	$-O-CH_2-$	67.8
C-5	153.2	$-OCOCH_3$	20.9
C-6	108.1	$-OCOCH_3$	169.3
C-7	150.6		

[a]The δ values are in ppm downfield from TMS;
$\delta(TMS) = \delta(CDCl_3) + 76.9$ ppm

[a,b]Values are interchangeable.

It is interesting to note that, like coelogin, flavidin is also optically inactive. Construction of Dreiding models showed that the energy barrier between the two possible conformers of flavidin obtained by flipping rings B and D was quite low and that the flip conformer was the optical antipode of the other. Thus, at ordinary temperature, the facile interconversion of one conformer into the other rendered flavidin optically inactive. This view was supported by the nmr signal of the oxymethylene protons which appeared as a singlet instead of an AB quartet.

Flavidin is thus a new member of a novel series of 9,10-dihydrophenanthrene derivatives bearing an additional ring formed by an oxymethylene bridge between C-4 and C-5. In view of the report of orchinol (9), a phytoalexin (10) having a structurally related 9,10-dihydrophenanthrene system, which, when formed in injured orchids, increases their immunity against bacterial infection, it would be worthwhile to study flavidin for similar biological activity.

EXPERIMENTAL[3]

PLANT MATERIALS.—All three plants, *Coelogyne flavida* Hook. F. ex Lindl, *Pholidota articulata* Lindl. in Wall, *Otochilus fusca* Lindl, were collected by M/s. Mukherjee & Co., Siliguri, India, from Kafer (6000'), Darjeeling, India, in November, 1980, and were duly identified by them. The identification has been further verified by Mr. R. C. Biswas, Botanist, Botanical Survey of India, India, by comparing the plant material with authentic herbarium specimens kept preserved in the Central National Herbarium, Botanical Survey of India, Indian Botanic Garden, India.

ISOLATION OF FLAVIDIN (**1a**).—Air-dried, powdered whole plant of *C. flavida* (1 kg) was successively extracted with petroleum ether and ethanol in a Soxhlet. The ethanol extract was concentrated under reduced pressure, diluted with water and exhaustively extracted with ether. The total ether-soluble material was extracted with 2N aq. NaOH soln. The aq. soln was acidified in the cold with concentrated HCl, and the liberated solid was extracted with ether, washed with water, and dried, and the solvent was removed. The residue was chromatographed. The petroleum ether-ethyl acetate (5:1) eluate gave flavidin (**1a**) (yield 0.02%), crystallized from petroleum ether-ethyl acetate mp 210°, (Calcd. for $C_{15}H_{12}O_3$: C, 75.00; H, 5.00. Found: C, 74.81; H, 5.12%); *m/e* 240 ($M^{+\cdot}$, 90), 239 (100), 238 (7), 237 (8), 181 (7), 152 (6), 120 (16) and 119 (8). Flavidin diacetate (**1b**) (prepared by treatment of **1a** with Ac_2O/Py in the cold), crystallized from petroleum ether-ethyl acetate, mp 166°, (Calcd. for $C_{19}H_{16}O_5$: C, 70.37; H, 4.94. Found: C, 70.16; H, 4.97%); λmax 216, 280, 293 and 297sh nm (log ε 4.57, 4.13, 4.10 and 4.07); νmax 1275 and 1750 cm^{-1} (OAc); δppm 2.29 (6H, s; $-OCOCH_3$), 2.90 (4H, s; H_2–9 and H_2–10), 5.13 (2H, s; Ar-OCH_2–Ar), 6.56 (2H, br. s; H–6 and H–8), 6.78 (1H, br. s; H–1) and 6.85 (1H, br. s; H–3); *m/e* 324 ($M^{+\cdot}$, 9), 282 (10), 280 (20), 279 (96), 240 (49), 167 (100), 150 (47), 149 (98), 113 (49) and 112 (40). Flavidin dimethyl ether (**1c**) (prepared by treatment of a methanolic soln of **1a** with an ethereal soln of CH_2N_2), crystallized from petroleum ether-ethyl acetate, mp 138°, (calcd. for $C_{17}H_{16}O_3$: C, 76.12; H, 5.97; Found: C, 76.25; H, 5.89%); λmax 215, 286 and 303 nm (log ε 4.50, 4.21 and 4.14); δppm 2.85 (4H, s; H_2–9 and H_2–10), 3.76 (6H, s, $ArOCH_3$), 5.06 (2H, s; Ar-OCH_2–Ar), 6.35 (2H, s; H–6 and H–8), 6.45 (1H, d, J=3 Hz; H–1) and 6.63 (1H, d, J=3 Hz; H–3); *m/e* 268 ($M^{+\cdot}$, 100), 267 (23), 254 (10), 253 (55) and 239 (6).

The same isolation procedure was used to obtain flavidin (**1a**) from *P. articulata* (yield 0.019%) and *O. fusca* (yield 0.0195%).

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[3]Mps were determined in a Kofler block and are uncorrected. Silica gel (60–100 mesh) was used for column chromatography, and silica gel G was used for tlc. Uv spectra were measured in 95% aldehyde-free EtOH, and ir spectra were run on a KBr disc in a Beckman Spectrophotometer (Model 20). Both ^1H and ^{13}C nmr spectra were recorded in a Varian CFT-20 instrument in $CDCl_3$ with TMS as the internal standard. Mass spectra were run in an AE1 MS9 instrument equipped with a direct inlet system and operating at 70 eV. All analytical samples were routinely dried over P_2O_5 at 80° for 24 hr *in vacuo*. Anhydrous Na_2SO_4 was used for drying organic solvents, and the petrol used had bp 60–80°.