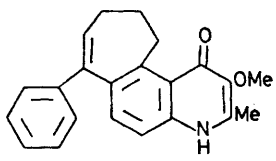
Phenylpentylisatins: a Novel Class of Alkaloids from *Melochia tomentosa*

By GOVIND J. KAPADIA,* YOGENDRA N. SHUKLA, BEJOY K. CHOWDHURY, and SAKTI P. BASAK
(*Department of Biomedicinal Chemistry, College of Pharmacy and Pharmacal Sciences, Howard University, Washington D.C.* 20059)
and HENRY M. FALES and EDWARD A. SOKOLOSKI
(*Laboratory of Chemistry, National Heart, Lung, and Blood Institute, Bethesda, Maryland* 20014)

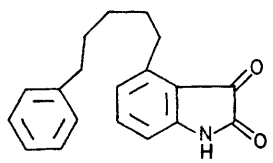
Summary The novel alkaloids, melosatin A and B, isolated from the tumourigenic plant, *Melochia tomentosa* have been characterized by physical and chemical methods as 6,7-dimethoxy-4-(5-phenylpentyl)isatin (**3**) and 4-(5-phenylpentyl)isatin (**2**), respectively; the structure of (**3**) has been corroborated by synthesis.

RECENTLY we reported the isolation and structures of several of the constituents of the tumourigenic plant, *Melochia tomentosa*. These included 6-methoxy-7,8-methylenedioxycoumarin,[1] two new cyclopeptide alkaloids (melonovines A and B),[2] and the known scutianine B,[3] as well as an unusual quinolinone alkaloid, melochinone[4] (**1**). We indicated that several other alkaloids were present in trace quantities and now report the structures of two of them, melosatin B (**2**) and melosatin A (**3**), and the synthesis of the latter.

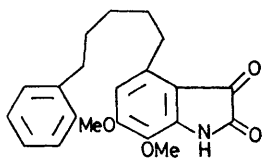
The alkaloids (**2**) and (**3**), isolated by silica gel chromatography are neutral, yellow compounds having empirical formulae $C_{19}H_{19}NO_2$ ($M^{+\cdot}$ 293, amorphous) and $C_{21}H_{23}NO_4$ [$M^{+\cdot}$ 353·162, chemical ionisation, methane, 354; m.p. 119—121 °C; λ_{max} 202, 225, 250, and 345 nm; ν_{max} 3200 (NH), 1750, 1725 (CO), 1645 (CONH), 1250, and 1135 (OMe) cm^{-1}], respectively. Comparison of their n.m.r. spectra confirmed that the latter was an aromatic dimethoxy [δ ($CDCl_3$) 3·88 (3H) and 3·98 (3H)] analogue of the former. The presence of a 1,2-dicarbonyl system in (**3**) was shown by formation of an *o*-phenylenediamine adduct ($M^{+\cdot}$ 425) and one carbonyl group was reduced by sodium borohydride resulting in a colourless alcohol ($M^{+\cdot}$ 355, m.p. 110—112 °C). These facts suggested the presence of an isatin nucleus in both (**2**) and (**3**). Reaction of (**3**) with diazomethane resulted in ring expansion typical of isatins,[5] forming two isomeric quinolinone methyl ethers which were separated by g.l.c.-mass spectrometry ($M^{+\cdot}$ 395). Mass spectra of (**2**) and (**3**) showed that both molecules were cleaved at the benzyl linkage, and both benzyl ions and the corresponding isatin ions at *m/e* 202 and 262 were observed for (**2**) and (**3**), respectively.



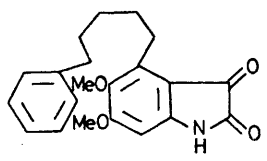
(1)



(2)



(3)



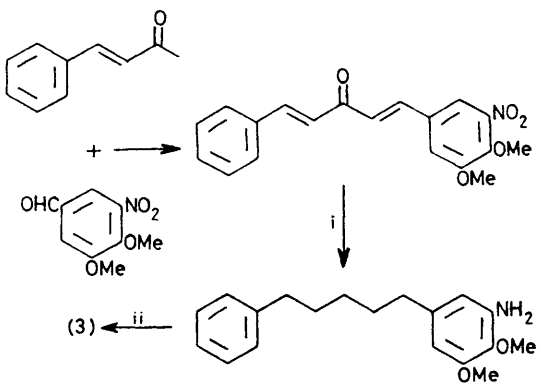
(4)

The n.m.r. spectra of (**2**) [δ 7·26 (5H)] and (**3**) [δ 7·24 (5H)] confirmed the presence of free phenyl groups and further showed three aliphatic methylene groups [(**2**): δ 1·64 (m br, 6H); (**3**): δ 1·60 (m br, 6H)] located between two benzyl methylenes [(**2**): δ 2·62 and 2·94 (t, 2H); (**3**): δ 2·62 and 2·90 (t, 2H)] indicating the presence of a 5-carbon chain between two aromatic systems. Three vicinal protons were observed on the isatin nucleus of (**2**) [δ 6·70 (d, *J* 7 Hz), 7·42 (t, *J* 7 Hz), and 6·88 (d, *J* 7 Hz)]. The triplet nature and the chemical shift of the proton at δ 7·42 require it to be at position 6 by comparison with *N*-methylisatin.[6]

In melosatin A (**3**) the orientation of the substituents on the isatin nucleus was not immediately apparent but the chemical shift of its single aromatic proton (δ 6·37) argued against positions 4 and 6, *ortho* and *para* to the isatin carbonyl group. Assuming that the phenylpentyl group of (**3**) is in the same location as it is in (**2**), two structures, (**3**) and (**4**), are possible. Compound (**3**) was synthesised by the route shown in the Scheme.

The synthetic product was found identical in all respects (m.p., mixed m.p., u.v., m.s., n.m.r., i.r.) with the natural product.

Indole alkaloids are widely distributed in nature but we are not aware of any cases where they have reached the oxidation state of isatin. However, we feel they are unlikely to be artifacts in this case since their presence in simple lipid extracts could be demonstrated by t.l.c. prior to extensive work-up.



SCHEME. i: (1) $NaBH_4$, (2) H_2, Pd–C, (3) P_2O_5, (4) H_2, Pd–C; ii: $(COCl)_2$.

Melosatins A and B are uncyclized analogues of melochinone (**1**) in which the hypothetical anthranilate–pyruvate construction of the quinolinone ring perhaps has been replaced by *o*-aminophenylpyruvate or some equivalent structure arising from the degradation of kynurenine.

Research at Howard University was supported by a grant from the National Cancer Institute.

(*Received*, 26*th April* 1977; *Com.* 399.)

[1] Y. N. Shukla, E. A. Sokoloski, H. M. Fales, and G. J. Kapadia, *Phytochemistry*, 1976, **15**, 1788.
[2] G. J. Kapadia, Y. N. Shukla, J. F. Morton, and H. A. Lloyd, *Phytochemistry*, in the press.
[3] R. Tschesche, E. Ammermann, and H. W. Fehlhaber, *Tetrahedron Letters*, 1971, 4405.
[4] G. J. Kapadia, B. D. Paul, J. V. Silverton, H. M. Fales, and E. A. Sokoloski, *J. Amer. Chem. Soc.*, 1975, **97**, 6814.
[5] R. Gompper in 'Advances in Heterocyclic Chemistry,' eds. A. R. Katritzky, A. J. Boulton, and J. M. Lagowski, Academic Press, New York, 1963, Vol. 2, p. 245.
[6] V. Galasso, G. Pellizer, A. Lisino, and A. Bigotto, *Org. Magnetic Resonance*, 1975, **7**, 591.