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N-BENZOYL-L-PHENYLALANINOL FROM CATHARANTHUS PUSILLUS (Murr.) G. Don (= VINCA PUSILLA Murr.)

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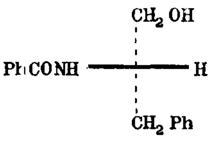
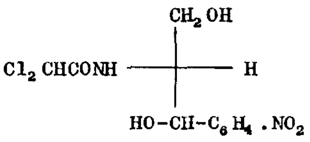
Catharanthus pusillus, a plant of the Apocynaceae, has been little investigated[1] despite the intense research effort on several related Catharanthus species which was generated by the discovery of alkaloids having therapeutic value.[2] Our work on the alkaloids of this plant has afforded (a) several crystalline bases, the structural study of which will be reported elsewhere and (b) a neutral substance from the "weakly basic" fraction. The neutral product was isolated in $1 \times 10^{-4}\%$ yield from dry whole plant material and had m.p. 171-173°, $[\alpha]_D^{24}$ -78° (c, 0.24 in pyridine).

Mass spectrometry established the molecular formula $C_{16}H_{17}NO_2$ (M^+, 255.1247; calc. 255.1259) and the base peak at m/e 105 is assigned to $Ph\overset{+}{C}O$. Abundant ions at m/e 91 and 77 correspond to $Ph\overset{+}{C}H_2$ and $C_6H_5^+$ whilst those at m/e 237, 224, 164 arise by loss of H_2O, CH_2OH and $PhCH_2$, respectively, from the parent $\overset{\bullet}{i}$on. It follows that the neutral product contains a benzyl, a benzoyl and a primary alcoholic group. The infrared spectrum (mull) showed $\nu_{max.}$ 3360 cm.$^{-1}$ (bonded OH), 3310 cm.$^{-1}$ and 1640 cm.$^{-1}$ (-CO.NH-) and this information when combined with the previous data leads to the working structure (I) for the neutral product. In keeping with this, the ultraviolet spectrum showed a maximum at 229 mμ (ε, 9,200) and the n.m.r. spectrum (in CF_3CO_2H) showed a doublet centred at τ 6.8 (2H; *J* 7 c./s.), a singlet at τ 5.3 (2H) and two singlets corresponding each to 5H in the region τ 2.0 - 3.0; one of the latter signals was broad.



(I)



(II)

<u>L</u>-Phenylalaninol[3] was benzoylated with benzoyl chloride in an excess of alkali to afford <u>N</u>-benzoyl-<u>L</u>-phenylalaninol, m.p. (and mixed m.p. with the natural product) 171-173°, $[\alpha]_D^{24}$ -79° (c, 1.0 in pyridine). This had been prepared previously,[4] m.p. 169°. (Found: C, 75.1; H, 6.5; N, 5.6. Calc. for $C_{16}H_{17}NO_2$ C, 75.3; H, 6.7; N, 5.5%). Further evidence for the identity of the synthetic and natural products was obtained by comparison of infrared and ultraviolet spectra, by mass spectrometry and by thin-layer chromatography on alumina in 1:1 (vol.) ethyl acetate - chloroform.

With the structure of the amide established, one further aspect of its mass spectrum deserves comment. An interesting peak appears strongly at m/e 122 and the accurate mass (found: 122.0606) establishes the composition as C_7H_8NO (calculated: 122.0606). This corresponds to protonated benzamide but experiments with deuterium labelled materials will be required to determine the origin of this fragment.

Other amides have been found in higher plants[5] and the occurrence of N-benzoyltyramine in Casimiroa edulis[6] is a closely related example. However, the present isolation of N-benzoyl-L-phenylalaninol appears to be the first occurrence of a phenylalaninol derivative in plant material. Chloramphenicol (II) from Streptomyces[7] can be regarded as a modified phenylalaninol derivative.

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REFERENCES

1. W. Dymock, C.J.H. Warden, and D. Hooper, Pharmacographia Indica, London, Bombay and Calcutta, Appendix p. 173; D.N. Majumdar, and B. Paul, Ind. J. Pharm., 21, 255 (1959)

2. I.S. Johnson, H.F. Wright, G.H. Svoboda, and J. Vlantis, Cancer Research, 20, 1016 (1960); N. Neuss, M. Gorman, H.E. Boaz, and N.J. Cone, J. Amer. Chem. Soc., 84, 1509 (1962) and refs. therein

3. P. Karrer, P. Portmann, and M. Suter, Helv. chim. Acta, 31, 1617 (1948)

4. J.H. Hunt, and D. McHale, J. Chem. Soc., 2073 (1957)

5. W. Karrer, "Konstitution und Vorkommen der organishen Pflanzenstoffe", Birkhäuser, Basel, 1958; H.-G. Boit, "Ergebnisse der Alkaloid Chemie bis 1960", Akademie-Verlag, Berlin, 1961

6. F.A. Kincl, J. Romo, G. Rosenkranz, and F. Sondheimer, J. Chem. Soc., 4163 (1956).

7. J. Ehrlich, Q.R. Bartz, R.M. Smith, A.A. Joslyn, and P.R. Burkholder, Science, 106, 417 (1947); H.E. Carter, D. Gottlieb, and H.W. Anderson, Science, 107, 113 (1948); M.C. Rebstock, H.M. Crooks, J. Controulis, and Q.R. Bartz, J. Amer. Chem. Soc., 71, 2458 (1949).