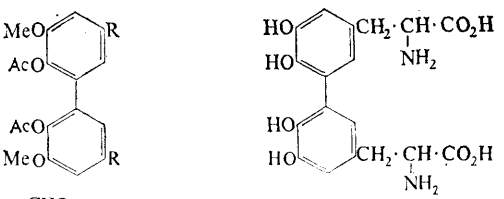
DOPA Dimer

By YOSHIMORI OMOTE, YOSHIMORI FUJINUMA, and NOBORU SUGIYAMA*
(*Department of Chemistry, Tokyo Kyoiku University, Otsuka, Tokyo, Japan*)

IT is generally accepted that the action of oxygen in the presence of tyrosinase on 3,4-dihydroxyphenylalanine (DOPA) yields melanin.[1] Recently the presence of uncyclised units in DOPA melanin has been suggested by several groups of investigators.[2-4] Molecular orbital calculation[5,6] suggests that 5,6-dihydroxyindole will polymerise oxidatively at positions 4 and 7, which correspond to positions 2 and 5 of DOPA. It is of interest to show that DOPA dimer can be an intermediate of melanogenesis. One of the DOPA dimers, the biphenyl (V) has been synthesized.



(I) R = CHO

(II) R = 

(III) R = CH=C(NH·COPh)·CO$_2$Me

(IV) R = CH$_2$·CH(NH·COPh)·CO$_2$Me

(V)

Heating 2,2′-diacetoxy-5,5′-diformyl-3,3′-dimethoxybiphenyl[7] (I) and hippuric acid under reflux with fused sodium acetate in acetic anhydride gave the oxazolone (II), m.p. 287°, λ_{max} ($CHCl_3$) 380, 402 mμ (ε 75,000, 76,000), ν(KBr) 1790, 1766, 1653, 1593 cm.$^{-1}$.

By heating the oxazolone (II) under reflux with fused sodium acetate in methanol, the unsaturated ester (III) was obtained as an amorphous powder (from benzene), m.p. 141—145°, λ_{max} (EtOH) 225, 295 mμ (ε 46,600, 31,000), ν(KBr) 3320, 1766, 1720, 1655, 1585 cm.$^{-1}$.

The catalytic reduction of (III) with platinum oxide in acetic acid at atmospheric pressure and room temperature gave the diester (IV), m.p. 65—75°, λ_{max} (EtOH) 281 mμ (ε 4,500), ν (KBr) 3400, 1770, 1753, 1653, 1600 cm.$^{-1}$. When this was hydrolysed with hydrobromic acid and neutralized with ammonium hydroxide, DOPA dimer (V) was obtained as a colourless powder from water containing sulphur dioxide, m.p. >300°, λ_{max} (H_2O) 287 mμ (ε 4,700), ν(KBr) 3200 br, 1628, 1598 cm.$^{-1}$. Analytical results conformed with structure (V).

Preliminary experiments on the oxidation of (V), as well as DOPA itself, have shown that both polymerise in the presence of atmospheric oxygen and tyrosinase at about the same rate. This result is consistent with the possibility of (V) as an intermediate in the melanogenesis of DOPA.

(*Received, December 8th*, 1967; *Com.* 1316.)

[1] H. S. Raper, *Biochem. J.*, 1927, **21**, 89.
[2] S. N. Mishra and G. A. Swan, *J. Chem. Soc.* (*C*), 1967, 1424.
[3] M. Piattelli, E. Fattorusso, S. Magno, and R. A. Nicolaus, *Tetrahedron*, 1962, **28**, 941.
[4] G. W. Kirby and L. Ogunkoya, *Chem. Comm.*, 1965, **546**.
[5] B. Pullman, *Biochim. Biophys. Acta*, 1963, **66**, 164.
[6] H. Chang, *Acta Phys. Sinica*, 1964, **20**, 1289.
[7] H. Booth and B. C. Saunders, *J. Chem. Soc.*, 1956, 940.