Tetrahedron Letters No.33, pp. 2863-2866, 1969. Pergamon Press. Printed in Great Britain.

BIOGENETIC-TYPE SYNTHESES OF OBTUSASTYRENE AND 4-METHOXYDALBERGIONE

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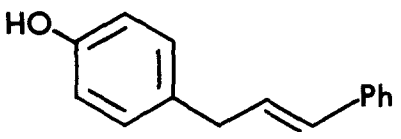
(Received in USA 19 May 1969; received in UK for publication 16 June 1969)

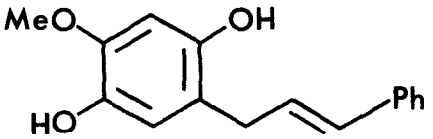
Some years ago Ollis and his associates noted that cinnamylphenols co-occur with dalbergiones and other neoflavanoids in Dalbergia and Machaerium species, and suggested that the biogenesis of both of these new types of natural products may involve C-cinnamylation of phenols, e.g. by cinnamyl pyrophosphate (1, 2, 3). Mechanistic support for this theory was recently provided (4, 5) by the observation that cinnamyl alcohol condensed readily with pyrogallol or resorcinol in aqueous acetic acids to yield cinnamylphenols and isomeric neoflavanoids. Cardillo, Cricchio and Merlini (6) have since prepared a number of model cinnamylphenols by this method and have shown, furthermore, that these compounds are readily oxidized by quinones to flav-3-enes, which then disproportionate to flavans and flavylium salts. This reaction sequence is in complete accord with, and mechanistically supports, a scheme proposed (4) for the biogenesis of these types of flavanoids.

The recent publication of structural details of nine natural cinnamylphenols (7) prompts this report of the applicability of the acid condensation method to the synthesis of obtusastyrene I, the cinnamylquinol II, which occurs as its monomethyl derivative, isoviolastyrene, and is isomeric with 4-methoxydalbergioquinol, and of (±)-4-methoxydalbergione. In these syntheses the model reaction conditions, which employed aqueous acetic acid, were modified by use of aqueous citric acid containing ascorbic acid. Ascorbic acid is not necessary for the successful synthesis of cinnamylphenols such as obtusastyrene

which are reasonably stable to aerial oxidation, but it is particularly useful in minimizing undesirable oxidation to quinones of methoxyquinol and its quinol condensation products, e.g., II, during the reaction with cinnamyl alcohol.



I



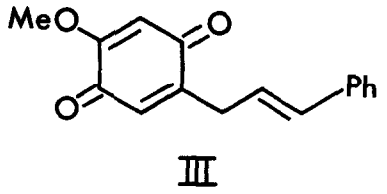
II

Obtusastyrene was synthesized in quantity by warming phenol (60 g) and cinnamyl alcohol (40 g) in 5% aq. citric acid (1 liter) containing ascorbic acid (5 g) for 12 hours. The alkali soluble portion of the oily product was distilled to give a colorless fraction (19.0 g; b.p.$_{0.4\ mm}$ 169-170°) which rapidly crystallized. Recrystallized from low boiling petroleum ether obtusastyrene I was obtained as long, colorless needles, m.p. 64°, identical in all respects (m.m.p., IR, NMR, kindly compared by Professor Ollis) with the natural product. (Found: C, 85.6; H, 6.68. Calcd. for $C_{15}H_{14}O$: C, 85.7; H, 6.71.) I gave a crystalline monoacetate, m.p. 29°, and monobenzoate, m.p. 91-92°.

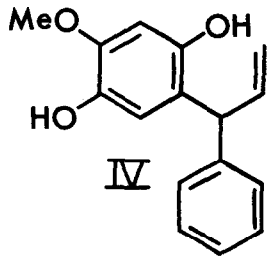
II was synthesized by warming a mixture of methoxyquinol (20 g), cinnamyl alcohol (20 g) and ascorbic acid (5 g) in 5% aq. citric acid (500 ml) for 20 hours. A solution of the oily product in benzene-petroleum ether deposited the crystalline cinnamylquinol II as cream-colored needles, m.p. 108° (14.5 g). (Found: C, 74.9; H, 6.27; MeO-, 12.4. Calcd. for $C_{16}H_{16}O_3$: C, 75.0; H, 6.29; 1 MeO-, 12.1.) II formed a crystalline diacetate, m.p. 103-104°, and dibenzoate, m.p. 147-148°. Aerial oxidation of a solution of II (1.6 g) in ether (100 ml) and sat. aq. Na_2CO_3 (40 ml) gave the cinnamylquinone, III, isomeric with natural 4-methoxydalbergiones. III was also obtained by aerial oxidation of II in aqueous acetic acid solution. It crystallized from methanol as golden-yellow, flat needles, m.p. 131° (0.61 g), λ_{max}^{EtOH} 257, ∿368 mμ (Log ε 4.45, 3.24).

Evaporation of the benzene-petroleum ether filtrate from II gave an oil, the acetate of which crystallized readily from methanol to give 4-methoxydalbergioquinol IV as its diacetate, m.p. 101° (8.0 g). The diacetate (2.0 g) was deacetylated in aq. alcoholic NaOH in the presence of sodium borohydride and a solution of the crude quinol in ether

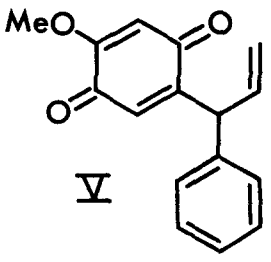
was allowed to stand over aq. K_2CO_3. (±)-4-Methoxydalbergione V (8) was thereby obtained as yellow needles (from methanol), m.p. 125° (0.55 g).



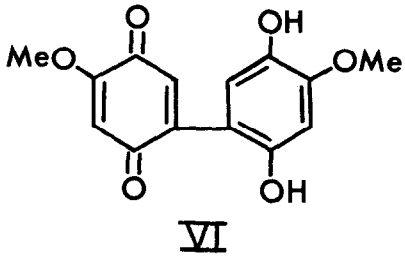
III



IV



V



VI

As mentioned above, previous attempts to synthesize II by condensation in aqueous acetic acid without ascorbic acid were not successful, due to extensive oxidation of the quinols to mixtures of quinones (5). From these reactions small quantities of the cinnamylquinone III and a deep red methoxyquinone-methoxyquinol condensation product VI have been isolated. The formation of VI by the reaction of aqueous acids on methoxyquinone has been described previously (9).

Acknowledgment--Satisfactory analytical data and NMR spectra were obtained on all products described in this communication. For these determinations the author is indebted to Mrs. N. Bennett, L. M. White and Miss G. Secor.

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