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SYNTHESIS OF LACHNANTHOCARPONE [9-PHENYL-2,6-DIHYDROXYPHENALEN-1(6)-ONE] BY INTRAMOLECULAR DIELS-ALDER CYCLIZATION OF A 1,7-DIARYLHEPTADIENOID ORTHOQUINONE.

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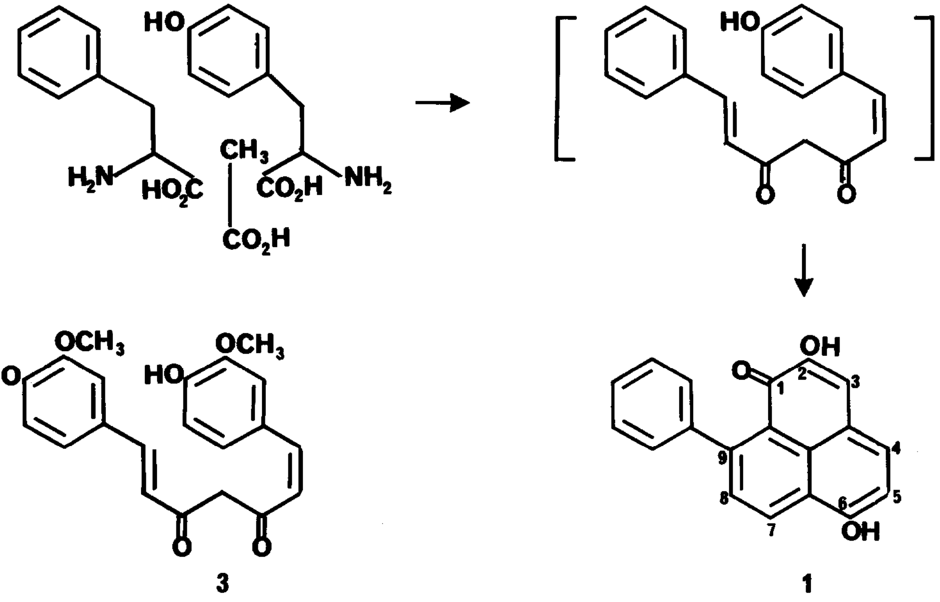
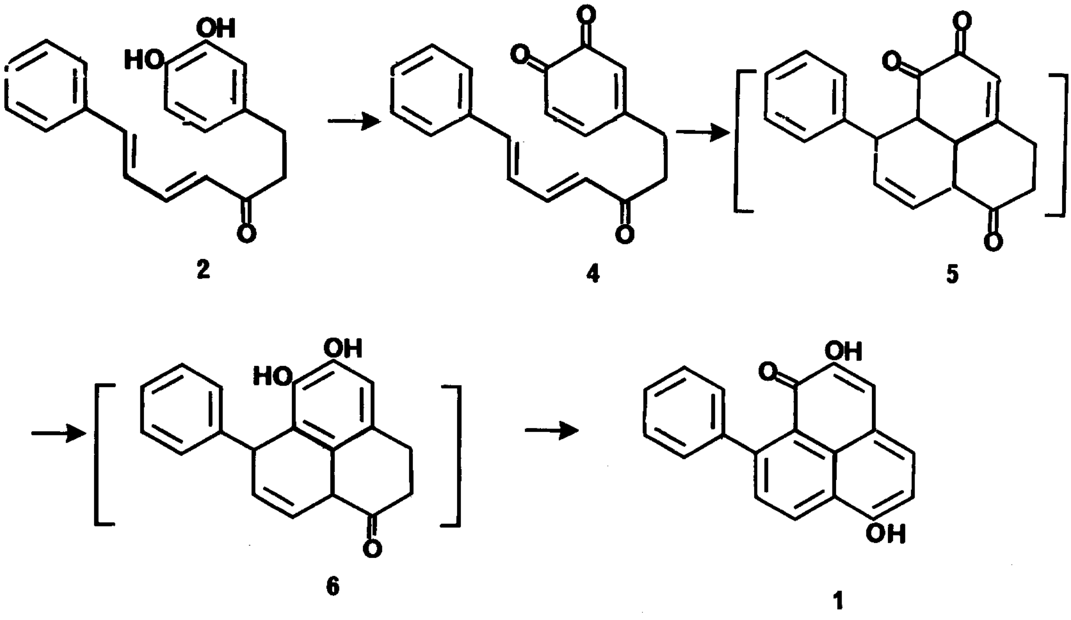
We wish to report on a synthesis of the 9-phenylphenalenone lachnanthocarpone[1] (**1**), the main pigment of the pericarp of Lachnanthes tinctoria Ell., from the 1,7-diarylheptanoid **2** through a sequence suggested by the presumed biosynthesis.

9-Phenylphenalenones appear to be characteristic of the family Haemodoraceae. They have been encountered in every species examined so far [Haemodorum spp. [2a,b]; L. tinctoria[1,3]; Xiphidium caeruleum[4]; Wachendorfia spp.[5]; Anigozanthos spp.[6]], but never in any other plant. The biosynthesis of their C_{19} skeleton presents an unusual problem in the pattern of oxygenated substituents: carbons 1 and 2 always carry oxygen, and carbons 5 and 6 are often but not always oxygenated[6]. This arrangement is inconsistent with a polyketide origin, while the ring system is not readily constructed from shikimate-derived units. In 1961, Thomas[7] suggested that the 9-phenylphenalenones might be formed biosynthetically by the cyclization of a 1,7-diarylheptanoid, itself derived by a unique combination of one mole each of phenylalanine, tyrosine, and acetic acid. The diarylheptanoids, of which curcumin (**3**) is the best-known example, are widely distributed[8] in the plant kingdom (Zingiberaceae, Betulaceae, Leguminosae, etc.), but no compound of this type has ever yet been found in a haemodoraceous plant.

The basic implications of Scheme I (i.e. the incorporation of acetic acid, phenylalanine, and tyrosine into the plant phenalenones) have received experimental support in both Haemodorum[9] and Lachnanthes[8]; however, a conflicting interpretation of the biosynthesis of **3** has appeared[10], and the actual involvement of a 1,7-diarylheptanoid intermediate has not been experimentally established.



Scheme I



Scheme II

Provided the actual biosynthesis is related to the one proposed by Thomas, the cyclization of the 1,7-diarylheptanoid skeleton to that of the 9-phenylphenalenones could conceivably take place through the biosynthetic equivalent of an intramolecular Diels-Alder reaction of an appropriately functionalized orthoquinone, such as **4** (Scheme 2). Ample precedent for the function of orthoquinones, as dienophiles is available[11], and it is suggestive that 1,7-diphenyl-1,3-heptadiene-5-one, the hydroxyl-free analog of **2**, is a natural compound, found in the catkins of <u>Alnus pendula</u> (Betulaceae)[12]. We have now shown that formation of a 9-phenylphenalenone by this route is indeed feasible.

The bis-acetyl derivative[13] of **2**, m.p. 97.5°, was prepared from 3-[3,4-diacetoxyphenyl]-propionylmethylene phosphorane[13] and cinnamaldehyde in a synthesis patterned after that of 1,7-diphenyl-1,3-heptadiene-5-one by Sakakibara and co-workers[14]. Removal of the protecting acetyl groups was achieved using Zemplén conditions[15]. After purification by PLC, an ethereal solution of the catechol **2** was oxidized with aqueous $NaIO_4$[16] (1.1 mol). The resulting orthoquinone **4** was extracted into chloroform. This solution gave **1** on standing at room-temperature for 5 hours; the overall yield from **2** was 37%. Synthetic and natural **1** were identical in every respect (m.p., mixture m.p., IR spectrum).

This direct formation of **1** was unexpected, but the compound can hardly have formed otherwise than by dehydrogenation of the anticipated Diels-Alder product **5**. We assume that **5** isomerized to the <u>ortho</u>-diphenol **6**, which, through two cycles of autoxidation to the corresponding orthoquinones, followed by dehydrogenation, would yield **1**.

This facile synthesis of the 9-phenylphenalenone **1** from the 1,7-diarylheptanoid **2** lends support to the hypothesis of Thomas[7], and in particular it explains the observed oxygenation patterns (see above). On the other hand, an oxygen function has never been found at C-7, although Scheme I implies the possibility. A dienic intermediate of type **2** would however explain this. No experimentally proven case of a biosynthetic Diels-Alder reaction has come to our attention; however, several compounds isolated from plants have structures strongly suggestive of such an origin. The closely related coumarins thamnosin[17] and phebalin[18], are particularly convincing cases; other pertinent examples are provided by the sesquiterpene lactone microlenin[19] and the dimeric indole alkaloid presecamine[20].

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