Tetrahedron Vol. 34, pp. 3005–3015
© Pergamon Press Ltd., 1978. Printed in Great Britain

0040-4020/78/1001-3005/$02.00/0

SYNTHESIS OF LACHANANTHOCARPONE [9-PHENYL-2,6-DIHYDROXYPHENALEN-1(6)-ONE] BY INTRAMOLECULAR DIELS–ALDER CYCLIZATION OF A 1,7-DIARYLHEPTANOID ORTHOQUINONE[1]; POSSIBLE BIOSYNTHETIC SIGNIFICANCE OF DIELS–ALDER REACTIONS

A. C. BAZAN and J. M. EDWARDS*
School of Pharmacy, University of Connecticut, Storrs, CT 06268, U.S.A.

and

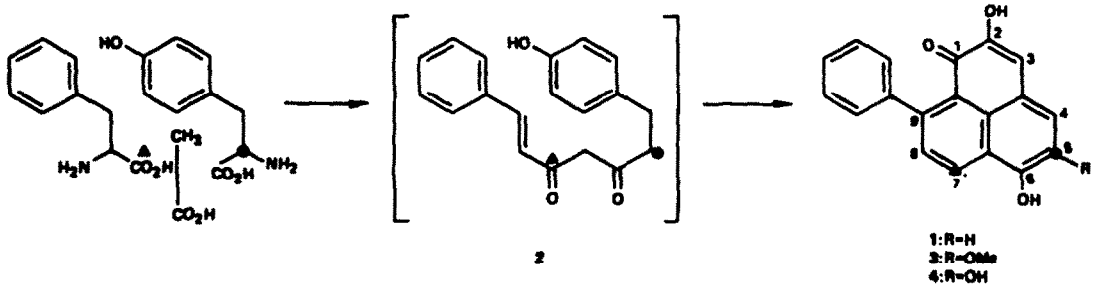
U. WEISS*
Laboratory of Chemical Physics, National Institute of Arthritis, Metabolism, and Digestive Diseases, Bethesda, MD 20014, U.S.A.

(*Received in UK* 10 *April* 1978; *Accepted for publication* 11 *May* 1978)

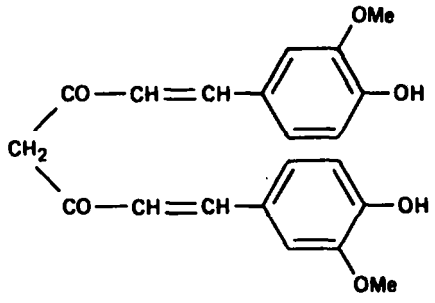
Lachnanthocarpone (1) is the major pigment found in the seed-pods of *Lachnanthes tinctoria* Ell. (Haemodoraceae).[2] The presence of 9-phenylphenalenones with structures very similar to that of 1 has been observed in plants of every genus of this small monocotyledonous family so far investigated: *Haemodorum*,[3] *Lachnanthes*,[4] *Xiphidium*,[5] *Wachendorfia*,[6] *Anigozanthos*.[7] These pigments thus appear characteristic of the family and entirely restricted to it; no 9-phenylphenalenone has ever been observed in any other organism.

The possible biosynthesis of the carbon skeleton of the 9-phenylphenalenones presents a complex problem; it has been studied experimentally, but the interpretation of the findings is by no means straightforward. The pattern of oxygenation observed in these pigments does not suggest a polyketide origin; on the other hand, there is no obvious way in which this C_{19} skeleton can be assembled from shikimate derived units. Thomas[8] has proposed a possible biosynthesis (Scheme 1) involving the condensation of one molecule each of phenylalanine and tyrosine (or their metabolic equivalents) with one molecule of acetic acid, with loss of one of the three carboxyl groups, to yield a diarylheptanoid such as 2. This intermediate could then cyclize to the ring system of the 9-phenylphenalenones. Diarylheptanoids are fairly widely distributed in the plant kingdom (Zingiberaceae, Betulaceae, Leguminosae, Myricaceae, etc.); as yet, however, no compound of this type has been identified in a haemodoraceous plant. In view of the results to be reported here, and of the incomplete state of our knowledge of chemotaxonomy, as well as of the implication of biosynthetic studies carried out in *Haemodorum*[9] and *Lachnanthes*,[10] this need not be regarded as a serious objection to Thomas' hypothesis. The general features of the biosynthetic scheme, i.e. the incorporation of acetate, phenylalanine, and tyrosine into the aromatic system, have been substantiated in both plants; more convincingly, label from 2-^{14}C-tyrosine was found to be incorporated specifically into C-5 of haemocorin aglycone (3),[8] and 1-^{13}C-phenylalanine has been shown to appear only in C-7 of lachnanthoside aglycone (4)[11] (see Scheme 1). None of these findings has directly implicated a diarylheptanoid in the biosynthetic scheme, and the role of acetate remains uncertain, since no specific incorporations have been demonstrated. Furthermore, Roughley and Whiting,[12] after an investigation of the biosynthesis of curcumin (5), the best-known diarylheptanoid, have concluded that this compound is probably formed from one molecule of phenylalanine or tyrosine and five acetate units.

Provided that the actual biosynthesis is related to the

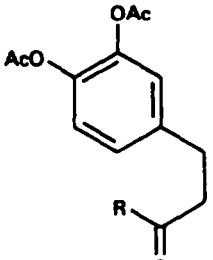


Scheme 1.



5

scheme proposed by Thomas, the cyclization of the intermediate 1,7-diarylheptanoid to a 9-phenylphenalenone could conceivably take place through the biosynthetic equivalent of an intramolecular Diels–Alder[13] reaction of a suitably functionalized orthoquinone such as 6 (Scheme 2). There is ample precedent for the reaction of orthoquinones as dienophiles *in vitro*,[14] and it is of interest that 1, 7-diphenyl-1,3-heptadien-5-one, the hydroxyl-free analog of the *o*-diphenol 7 corresponding to 6, is a natural product isolated from the catkins of *Alnus pendula* (Betulaceae).[15] The assumption of a diarylheptanoid intermediate such as 6 has the additional merit of accounting for the oxygenation patterns found in the naturally-occurring 9-phenylphenalenones so far isolated. These pigments invariably have oxygen functions at carbons 1 and 2; in addition, carbons 6, or 5 and 6 are usually (but not always[7]) oxygenated; on the other hand, an oxygen function has never yet been found at carbon 7, although Scheme 1 implies this possibility. An intermediate similar to 6 would explain this distribution.



8:R = OH
9:R = Cl
10:R = CHN_2
11:R = CH_2Br
12:R = CH_2PPh_3Br
13:R = $CH{=}PPh_3$
14:R = $(CH{=}CH)_2{-}Ph$

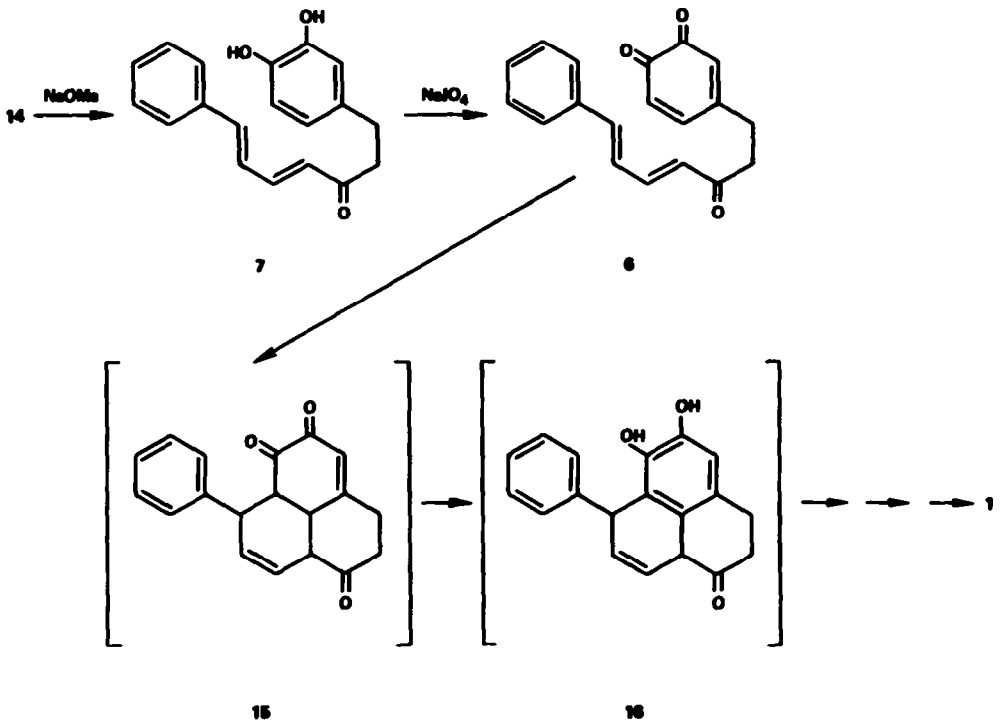
1 - Phenyl - 7 - (3,4 - dihydroxyphenyl) - 1,3 - heptadien - 5 - one (7) was prepared by a synthesis patterned after that of 1, 7-diphenyl-1,3-heptadien-5-one by Sakakibara *et al.*[15] Diacetyldihydrocaffeic acid, 8, was converted to the acid chloride 9. This compound could not readily be purified by vacuum distillation, but was reacted directly with diazomethane to give the diazoketone 10. For generation of 10 without concomitant production of chloromethylketone, three moles of diazomethane in benzene were needed per mole of 9. The diazoketone was not sufficiently stable for purification; it was used directly for conversion to the bromoketone 11 through the addition of an excess of aqueous HBr to its solution in benzene. Compound 11 was purified by column chromatography. The phosphonium bromide 12 was obtained from 11 through reaction with triphenylphosphine in benzene. Generation of the corresponding ylid 13 was accomplished by the addition of aqueous K_2CO_3 to a warm aqueous solution of 12. The precipitated product was used directly in benzene solution for the Wittig reaction with cinnamaldehyde. In order to simplify the chromatographic purification, it was necessary to use the ylid in slight excess for this reaction, because the mobility of the aldehyde was very similar to that of the product in the solvent systems tested. No problems caused by inter- or intramolecular acylation involving the protecting groups were encountered.[16] The major product (m.p. 97–98°) isolated from the Wittig reaction had absorptions in the IR at 1692 (CO), 1618 and 1592 (C=C) and 1000 (*trans-trans* C=C) cm^{-1}, all appropriate to the structure *trans-trans*-1-phenyl-7-(3,4-diacetoxyphenyl)-1, 3-heptadien-5-one (14); the assignement was further supported by the presence of a doublet, δ 6.15 ppm (J = 15 Hz), in the NMR spectrum, which is readily assigned to the olefinic proton alpha to the CO group.

The conversion of 6 into 1 is shown in Scheme 2. Removal of the acetate protecting groups from 14 was accomplished under Zemplén conditions;[17] the product was purified by preparative layer chromatography (PLC). An ethereal solution of the resulting catechol 7 was next treated with aqueous $NaIO_4$[18] (1.1 moles). The products were extracted into chloroform and, after drying with Na_2SO_4, this solution was allowed to stand at room temperature. At the end of 2 hr, the presence of 2-hydroxyphenalenones was indicated by TLC spots which characteristically turned blue upon exposure to ammonia vapor. After the solution had stood overnight, lachnanthocarpone, (1), identical with the natural product according to physical and spectral properties, was isolated by column and preparative layer chromatography in approximately 37% yield.

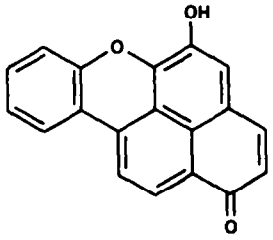
The mechanism by which the diarylheptadienone 7 is thought to have been converted to 1 is shown in Scheme 2. The expected product from $NaIO_4$ oxidation of the catechol 7 is the orthoquinone 6. This compound was never isolated, but is believed to have cyclized through a Diels–Alder reaction to yield 15. Intermediate 15 could then have been converted to the tetrahydrophenalenone 16. Twice-repeated autoxidation of this *o*-diphenol to the orthoquinone, followed both times by intramolecular dehydrogenation, would finally produce 1.

The unusual ease with which this sequence of reactions takes place is readily explained by the fact that the newly-formed cyclohexene ring proceeds further to aromaticity, and by the intramolecular nature of the Diels–Alder cyclization with its resulting entropic assistance;[13] the intermolecular reactions[14] in which orthoquinones function as dienophiles take place much less readily. In our system the sp^3 bond angles in the saturated portion of the biarylheptanoid provide a molecular geometry which allows very favorable relative positioning of the diene and dienophile for a Diels–Alder cyclization.

A surprising result was obtained in several experiments in which the chloroform solution of the products of periodate oxidation was extracted with 0.2 M aqueous NaOH solution, which was then acidified and extracted with chloroform. PLC of the product mixture afforded a small yield of the photoproduct 17 of lachnanthocarpone, previously obtained through strong photolysis of 1.[19] Photolytic conditions were not involved in our synthesis of 17, but the base-acid treatment seems to have played an important, thought not completely understood role in its formation. Treatment of 1 with $NaIO_4$ did not lead to the formation of 17.



Scheme 2.



17

Besides providing a new and presumably general synthetic approach to 2-hydroxyphenalenones, the synthesis of 1 from 6 shows that the 9-phenylphenalenone system present in the pigments from haemodoraceous plants can indeed by constructed from a suitably constituted 1,7-diarylheptane; to this extent, the synthesis may be considered as supporting the hypothesis of Thomas.[8] If precedent for participation of Diels–Alder reactions in biosynthetic sequences could be found, the interpretation of reaction 1→6 as being truly biomimetic[20] would be much strengthened.

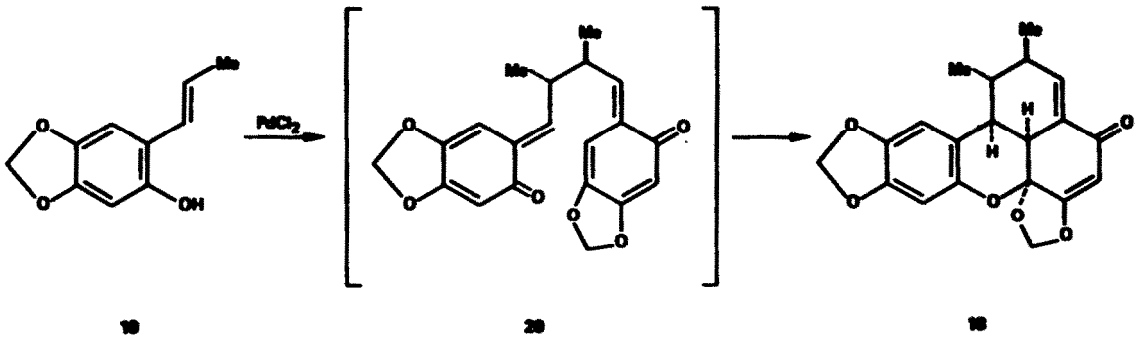
We are not aware of any case in which such a participation has been conclusively proved, e.g. by isotope experiments. However, several compounds isolated from microorganisms or higher plants have structures which strongly suggest such an origin. A discussion of a number of these cases is given below; no exhaustive review of this topic is intended. Some examples of closely related processes, e.g. hetero-diene reactions, are included. In several of the instances to be discussed, it is debatable whether the substances in question are *bona fide* natural products, i.e. whether the Diels–Alder reaction has taken place in the intact organism, or only during isolation. The case for an actual biosynthetic Diels–Alder reaction seems strongest for cyclopiperstachine and cryptoechinuline (aurechinuline) which are discussed below. For a number of the compounds, alternative biosynthetic mechanisms can be written, which do not proceed through Diels–Alder reactions. Again, no reliable evidence for either interpretation appears to be available.

As an example presumably involving an intramolecular [4+2] cyclization of the methide analog of an orthoquinone, the formation of the modified lignan carpanone (18), from a *Cinnamomum* sp. (Lauraceae),[21a] seems closest to our synthesis of 1. The compound has been synthesized[21b] in one operation from phenol 19 by treatment with $PdCl_2$ in a reaction which proceeds undoubtedly through intermediate 20 as shown in Scheme 3. Since natural 18 is racemic and occurs together with carpacin (21), the methyl ether of 19, it appears highly probable that its biosynthesis follows a sequence similar to the one shown in Scheme 3.

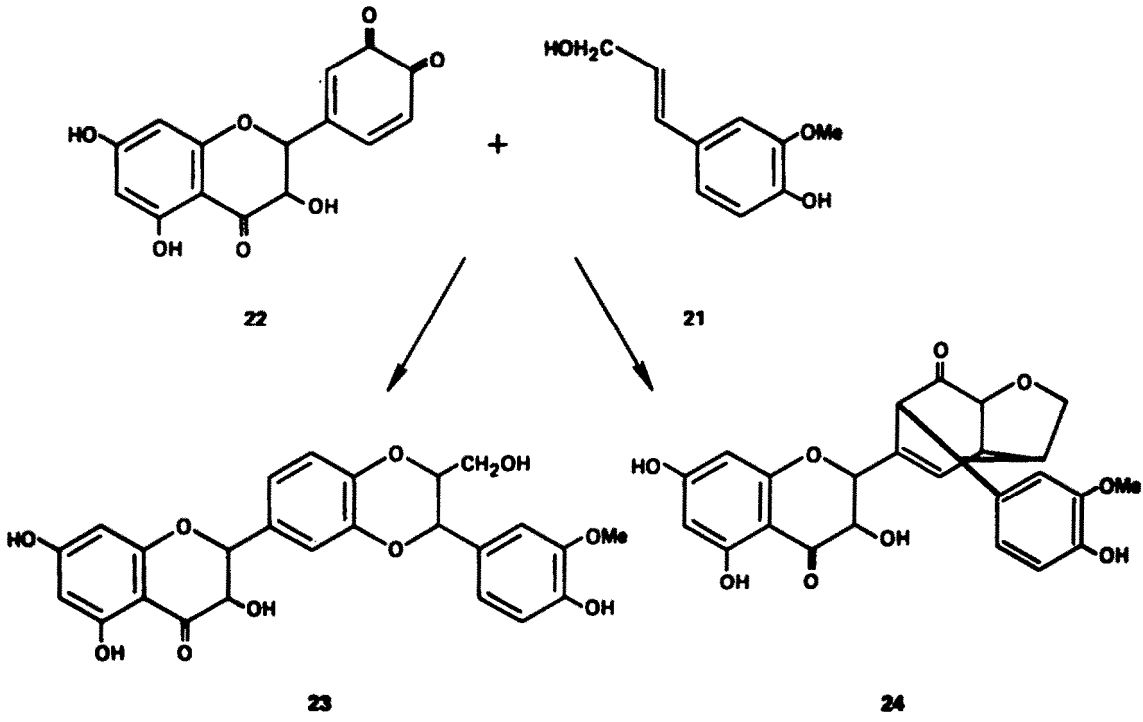
Diels–Alder reactions of coniferyl alcohol (21) with the orthoquinone 22 derived from taxifolin must be assumed to play a role in the biosynthesis of two constituents from *Silybum marianum* (Compositae), silybin[22] (23) and silydianin[23] (24) (Scheme 4). Formation of 24 evidently involves a standard Diels–Alder reaction of the diene of 22, while 23 must arise through a hetero-diene reaction of the ortho-diketone unit of the orthoquinone. In this case, both compounds have been isolated from the plant in optically active form.

No other instances of natural compounds likely to be formed through a diene reaction of an orthoquinonoid precursor have come to our attention.

The remaining examples can be conveniently divided into two groups involving *intra*- or *inter*molecular diene reactions, in the second case with subgroups where two identical or two different units interact. In a strikingly



Scheme 3.



Scheme 4.

large percentage of the compounds to be discussed, mevalonate-derived groupings must take part in the reactions.

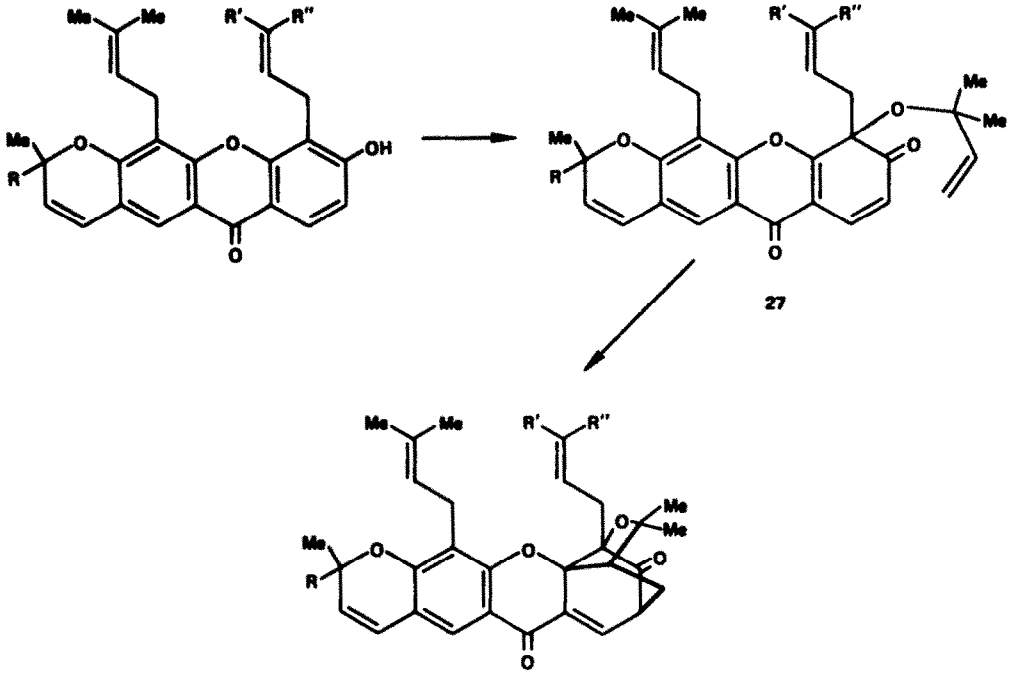
(A) *Intramolecular reactions*

The ring-system present in morellin[24] (25), gambogic acid[24b,25] (26) and a few related compounds[26] from *Garcinia morella* (Guttiferae) could well arise through formation and intramolecular diene cyclization of precursors of type 27 (Scheme 5). A substance with a very similar ring-system has actually been synthesized in this fashion,[27] but the biosynthesis of the natural products can also be formulated differently.[24a]

The mold metabolite proxiphomine[28a] (28) co-occurring with several related compounds in *Phoma* spp. could be formed by the diene cyclization shown. This process would be quite analogous to an intramolecular cyclization *in vitro*[28b] which yielded a very similar tricyclic isoindole system.

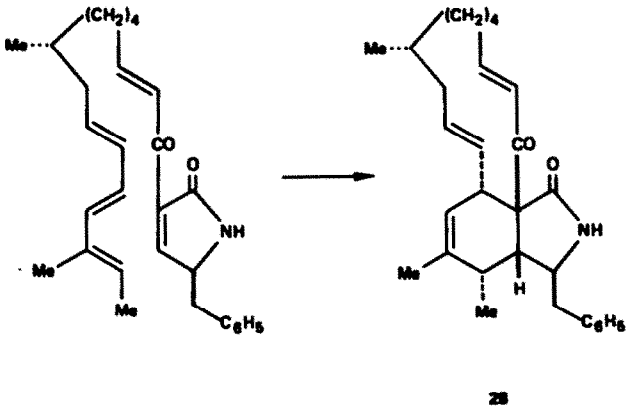
Piper trichostachys (Piperaceae) contains piperstachine[29a] (29) together with three closely related racemic bases.[29b] Of these, cyclopiperstachine (30) could be (and actually *is*) a product of intramolecular Diels–Alder cyclization of 29, while the stereoisomers cyclostachine A (31) and B (32) could form similarly from the N-pyrrolidinyl analog of 29. These cyclization reactions take plane *in vitro*: 29 yields 30, and the methyl ester of the carboxylic acid corresponding to 29 cyclizes to a mixture of two stereoisomeric esters which can be converted to the analogous N-pyrrolidinyl amides identical with 31 and 32, respectively.

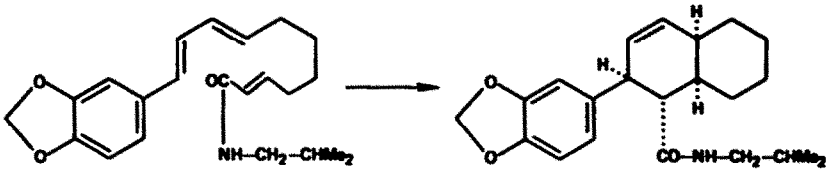
These *in vitro* cyclizations require the temperature of boiling xylene; since the cyclic alkaloids 30, 31 and 32 were isolated by extraction of the plant material with cold hexane, followed directly by chromatographic separation, they could hardly be artefacts formed through thermal cyclization during isolation. It is also noteworthy that 31 and 32 are precisely those stereoisomers which would be expected to form through thermal electrocyclic reactions from trienic precursors of type 29. In the present case, therefore, the status of the cyclic alkaloids as *bona fide* natural products formed by Diels–Alder reactions in the plant seems particularly well established.

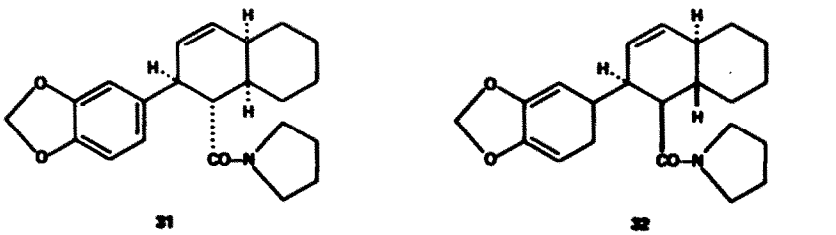


25: R = R'' = Me, R' = CHO
26: R = CH_2–CH_2–CH=CMe_2
R'+R'' = CO_2H + Me

Scheme 5.



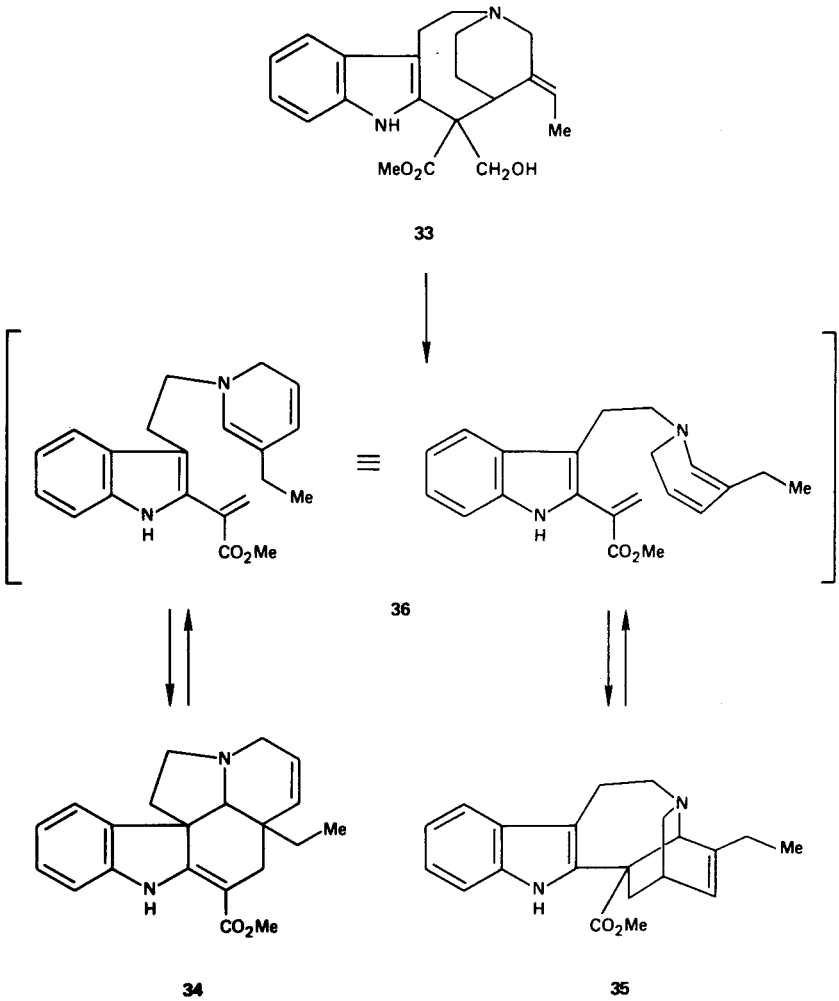




A particularly interesting and important group of processes interpretable as intramolecular Diels–Alder reactions is generally assumed to occur in the biosynthesis and biosynthetic interconversions of certain classes of indole alkaloids. These reactions are often assumed to proceed through Mannich and Michael reactions, but the alternative interpretation as electrocyclic reactions is possible, and has been mentioned and utilized in the literature.[13,30]

The derivation of the vast majority of the innumerable indole alkaloids from tryptamine and the iridoid glucoside secologanin seems securely established, and the way in which these ultimate building blocks yield the various classes of indole alkaloids is now well understood. Several recent reviews of this fascinating field are available.[31–34] During the biosynthesis of some of these classes, the carbon skeleton of the iridoid unit must have been retained without change. Further transformations then lead to types of bases which must have been formed through rearrangements of this part of the molecule. It has become possible to rationalize the processes which must take place during these interconversions by assuming ring-cleavage reactions leading to hypothetical intermediate dienes capable of recyclization to the rearranged structures by either one of the two mechanisms already mentioned.

The reactions which probably take place during the formation of two of the major types with rearranged skeletons are shown in Scheme 6. This scheme demonstrates the probable ways in which stemmadenine (**33**), a base with unrearranged skeleton, can yield tabersonine (**34**) and catharanthine (**35**), representatives of two major rearranged classes, the Aspidosperma and Iboga bases, respectively.[30] These three alkaloids are shown to be interrelated by the hypothetical intermediate dehydrosecodine (**36**). Interconversion of indole alkaloids by way of dihydropyridines closely analogous to **36** had first been postulated by Wenkert.[35] Scheme 6 is supported by the transformation, *in vitro*, of **33** into **34** and **35**[30,36,37] (in very low yield), and of **34** into **35**.[30] Furthermore, intact incorporation of **33** into alkaloids of the Aspidosperma and Iboga classes has been observed.[30,38] Since **33** appears early during alkaloid formation in seedlings of *Catharanthus roseus*, ahead of the alkaloids with rearranged skeleton,[30,39] it qualifies well for the postulated role. Suggestive evidence for the involvement of **36** or closely related structures is provided by the isolation of alkaloids with the same skeleton in a variety of plants,[40] some of which also contain bases which must have formed through Diels–Alder dimerization of precursors related to **36**; they will be discussed later. All the alkaloids which have been isolated are less unsaturated



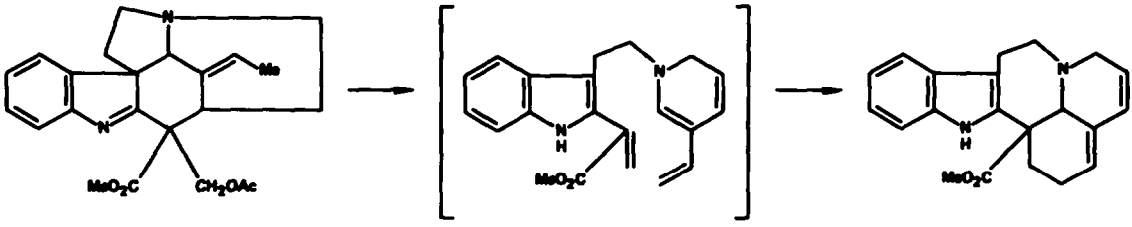
Scheme 6.

than the still hypothetical **36**, and owe their existence to this fact: the known bases which retain the acrylic ester group of **36** show a very strong tendency to dimerize to presecamine-type alkaloids (see below). One of these, secodine (the Δ^3-tetrahydropyridine-analog of **36**) has been synthesized; in spite of its instability, it has been show to be incorporated intact into vindoline, a relative of **34** and, with very low utilization, into **35**.[34]

Scheme 6 is thus made probable by a variety of experimental observations, while direct proof is still lacking, and it suggests Diels–Alder processes as one possible mechanism for the interconversions. A very similar process must be operative in the formation of andranginine (**37**), a racemic natural alkaloid, which is also formed in relatively good yield on thermolysis of the acetate **38** of precondylocarpine, a base closely related to **33**.[41] It seems probable that this conversion, again possibly involving a Diels–Alder reaction, also represents the biosynthesis of **37**.

For maytenone from *Maytenus dispermus* (Celastraceae), the interesting structure **44** has been proposed,[45] which would make it a Diels–Alder dimer of a 6-hydroxycyclohexa-2,4-dienone (**45**) closely related to ferruginol. Unfortunately, structure **44** has never been conclusively proved.

The structure[45] of the alkaloid lobinaline (**46**) from *Lobelia cardinalis* (Campanulaceae) strongly suggests formation from two 2-phenethylpiperidine units; Diels–Alder reaction of two dienic molecules of this type is one possibility, although by no means the only one. Alkaloids with the skeleton of the presumed monomer are widely distributed, and one of them, allosedamine (**47**) occurs in *Lobelia* spp. Furthermore, 2-phenacylpiperidine (**48**), the ketone corresponding to **47**, has been shown[47] to be incorporated into **46** in a way consistent with the assumption that the alkaloid is indeed biosynthesized from two units $C_5H_{10}N$–C–C–C_6H_5 in the manner indicated.



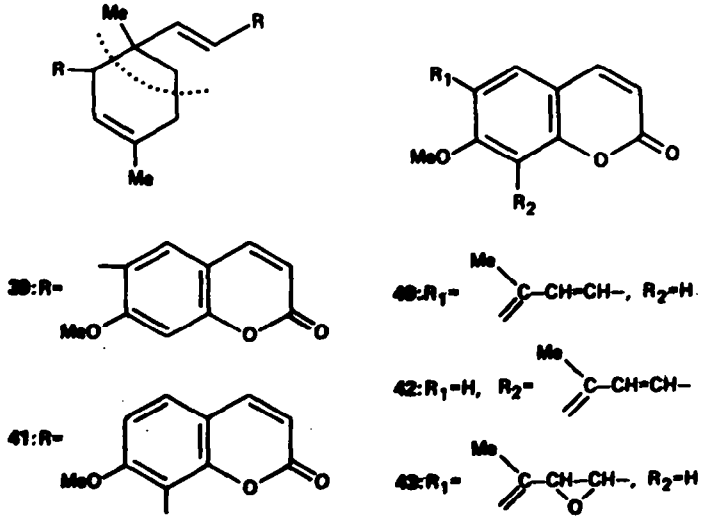
38 **37**

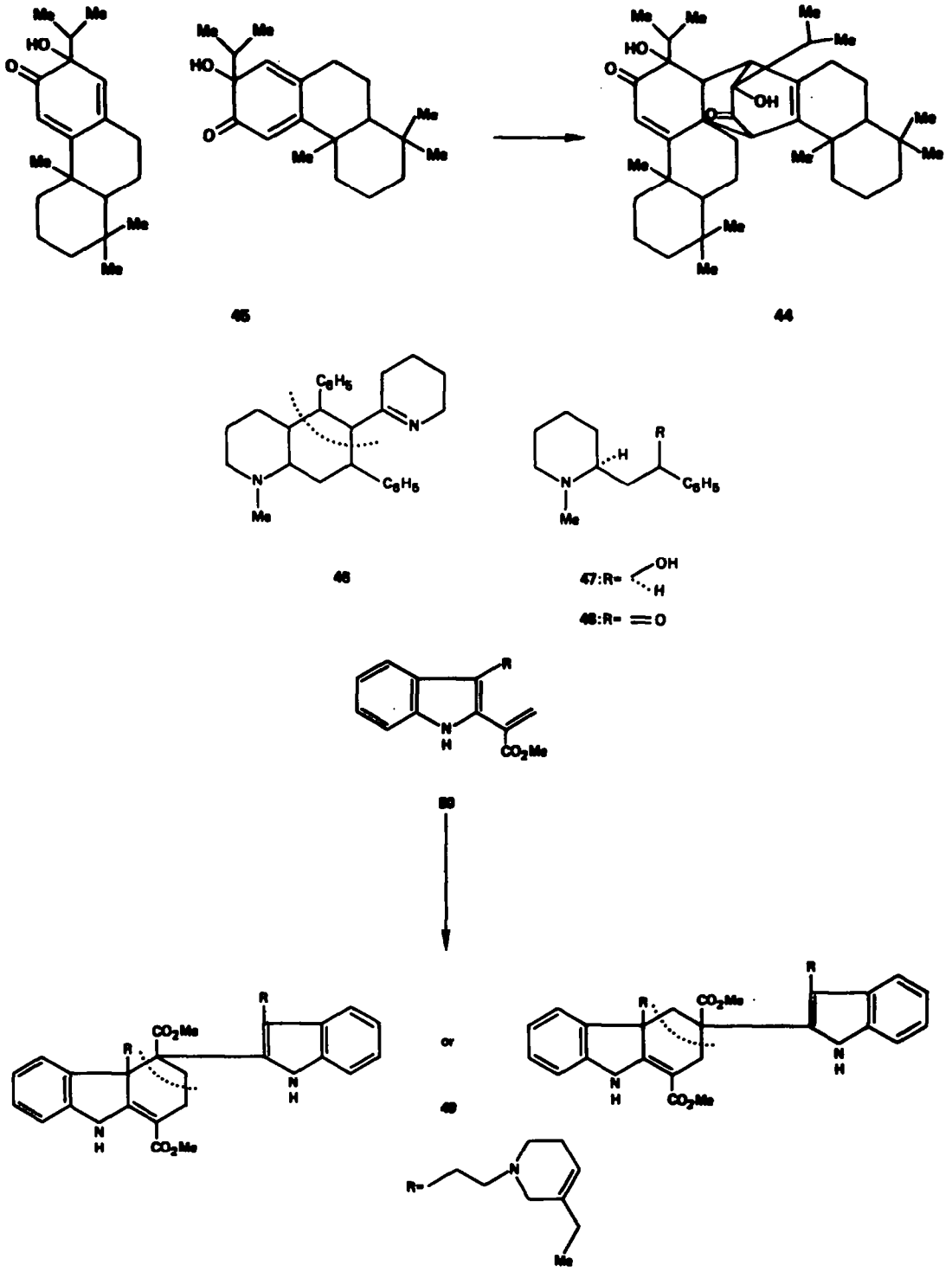
(B) *Intermolecular reactions*

(I) *Compounds formed by interaction of two identical units.* Plants of the family Rutaceae have yielded two closely related substances undoubtedly formed by Diels–Alder dimerization of coumarins with dienic isoprenoid side-chains. From the American *Thamnosma montanum* thamnosin (**39**) has been isolated,[42] which is evidently a dimer of 7-methoxy-6(3-methyl-1,3-butadienyl)coumarin (**40**), while phebalin (**41**)[43] from *Phebalium nudum*, from New Zealand, is the dimer of the analogous coumarin (**42**) with the dienic side-chain at C–6. *Thamnosma* also contains monomeric coumarins,[44] which are closely related to (**40**), e.g. thamnosmin (**43**). Both **39** and **40** are optically inactive.

Several species of *Rhazya* (Apocynaceae) yield[48] presacamine (**49** a or b) and its di- and tetrahydro derivates. These alkaloids, already briefly mentioned before, are Diels–Alder dimers of secodine (**50**) and/or dihydrosecodine: their mode of formation is evident. Vacuum distillation of **49** at 175° gave pure **50**, which reverted to **49** on standing; di- and tetrahydro-(**49**) behaved similarly. It seems possible that the dimeric alkaloids may form non-enzymatically, either in the plant or during isolation.

From *Borreria verticillata* (Rubiaceae) an indole alkaloid borreverine has been isolated very recently[49] which, like **49**, is a Diels–Alder dimer but differs very strongly from **49** in origin and structural type. As formula

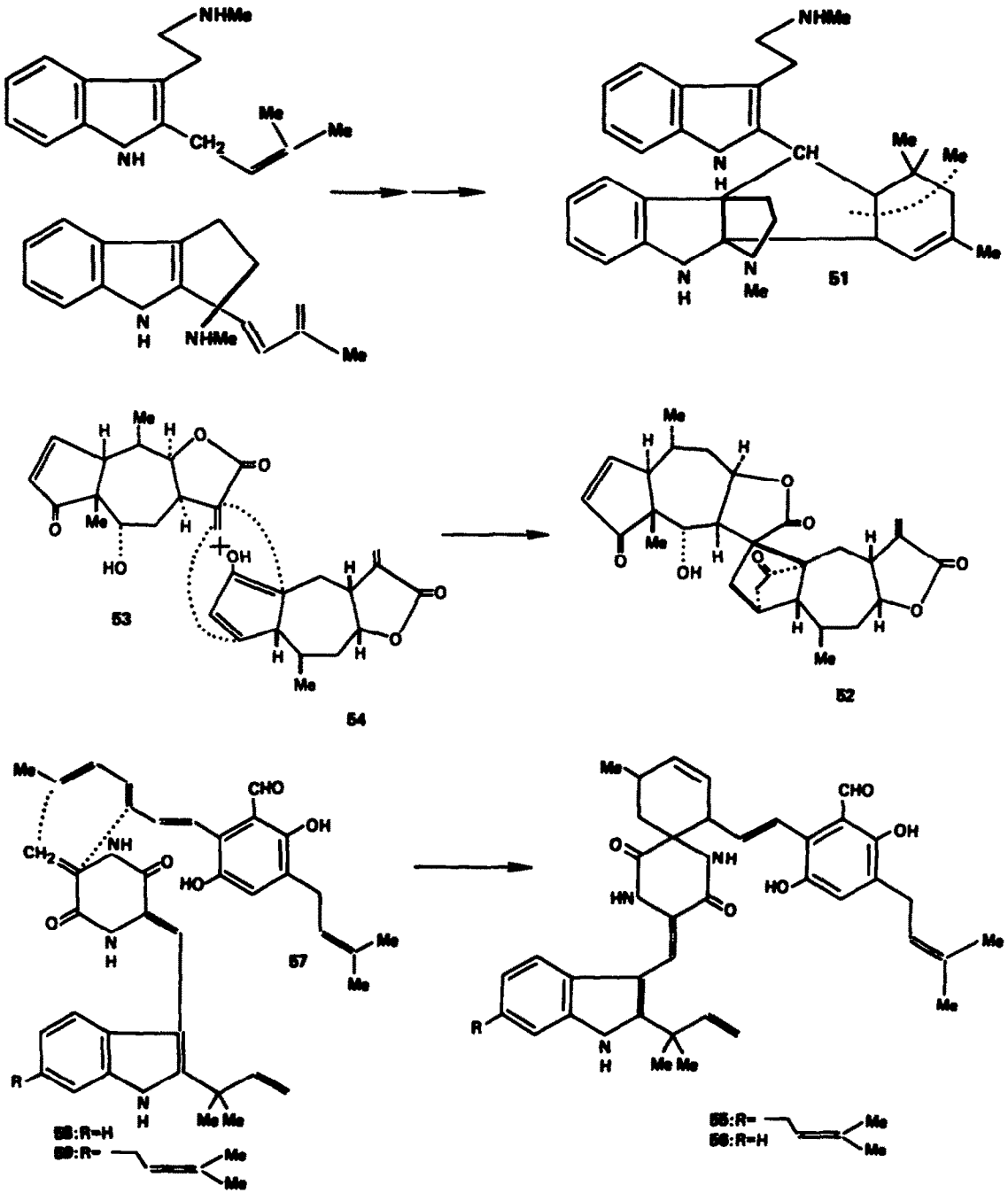




51 shows, borreverine must form by dimerization of an N-methyltryptamine with an unsaturated isoprenoid side-chain by Diels–Alder reaction and subsequent secondary changes. The unprecendented structure of 51 was established by X-ray crystallography.

(II) *Compounds formed by interaction of two different units.* Only a few substances seem to belong to this class. One of them, the terpenoid lactone microlenin[50] (52) from *Helenium microcephalum* (Compositae), represents a borderline case: the two components which must combine in its formation, while not identical, are closely related. One of them is helenalin (53), the other one the enol form of a non-pseudoguaianolide (54).

In contrast, the cryptoechinulins B (55) and D (56), isolated[51] from the mycelium of *Aspergillus amstelodami*, provide examples of Diels–Alder products formed from two widely different components. Compound 53 has also been obtained[52] from the same mold by a group of Japanese workers who name it aurechinulin. From their structures, 55 and 56 are evidently Diels–



Alder products from aurogiaucin (57) and neoechinulin B (58) or C (59) (crytopechinulin A), respectively; compounds 57–59 occur in *A. amstelodami*. Reaction *in vitro* of 57 with 58 or 59 yields 56 and 55, respectively. On this basis, the cryptoechinulins might be artefacts formed during isolation; however, the diene reaction of 57 with 59 was found[52] not to take place under the conditions used for isolation of 55, which should thus be a genuine mold metabolite.

On the basis of the examples given, we believe that participation of Diels–Alder reactions in biosynthetic sequences is a real possibility; it seems to deserve consideration even though conclusive experimental proof is still lacking. Such proof will be difficult to obtain, since it will require the elimination of alternative mechanisms as well as evidence that the reaction actually takes place in the living organism.

EXPERIMENTAL

M.ps were determined on a Kofler hot-stage apparatus and are corrected. NMR spectra were obtained with a Perkin Elmer R24, 60 MHz instrument in $CDCl_3$, unless otherwise noted. IR spectra were determined with a Perkin Elmer IR 21 instrument in KBr discs unless otherwise noted. Mass spectra were determined with a CEC 21-110B spectrometer. MeOH was the solvent for UV spectra. Combustion analyses were performed by Baron Consulting Co., Orange, Connecticut. Si gel means silica gel GF 254. Silica gel (Woelm, Activity Grade V) was used for column chromatography.

3-(3,4-Diacetoxyphenyl)-propionic acid (8). Dihydrocaffeic acid (Aldrich) was treated with pyridine and Ac_2O in the usual way to

yield **8** (87%) as colorless crystals, m.p. 79–80° from hexane, ν_{max} 1779, 1706, and 1200 cm^{-1}, δ 10.20 (s; 1H), 2.75 (m; 4H), 2.25 (s; 6H). (Found: M^+ 266.0789; C, 58.89; H, 5.43%. $C_{13}H_{14}O_6$ required: M^+ 266.0790, C, 58.62; H, 5.30%).

3-(3,4-*Diacetoxyphenyl*)-*propionyl chloride* (**9**). Compound **8** (36.5 g, 0.14 mole) was dissolved in dry benzene (50 ml). Oxalyl chloride (28 ml, 0.33 mole) was added, and after 10 min, the mixture was heated under reflux for 45 min. The excess of reagent was removed by rotary evaporation with repeated addition and removal of solvent. The product was not further purified. ν_{max} (film, crude product mixture): 1793 and 1769 (unresolved) cm^{-1}, δ: 7.10 (s; 3H), 3.00 (m; 4H), 2.25 (s; 6H).

1 - *Diazo* - 4 - (3,4 - *diacetoxyphenyl*) - 2 - *butanone* (**10**). Compound **9** (39 g, 0.14 mole), dissolved in cold, dry benzene, was added dropwise over 30 min to an ice-cold (2–5°), magnetically stirred benzene soln (400 ml) of alcohol-free diazomethane (17.30 g, 0.41 mole).[53] The soln was stored in a refrigerator at 8° overnight, allowed to warm to room temp., and slightly concentrated on a rotary evaporator to remove excess of diazomethane. Tlc analysis (Si gel; chloroform, multiple development) showed the product to be impure, ν_{max} (film, crude product mixture): 2118, 1769, and 1650 cm^{-1}, δ: 7.05 (s; 3H), 2.95 (m; 4H), 2.25 (s; 6H).

1 - *Bromo* - 4 - (3,4 - *diacetoxyphenyl*) - 2 - *butanone* (**11**). 47% HBr (54 ml, 0.5 mole) was added dropwise over 30 min to an ice-cooled, magnetically stirred benzene soln of **10** (0.14 mole). The evolution of gas bubbles was observed only during the addition of the initial portion of the acid. Water was added to the mixture and the benzene layer was separated, washed with 5% $NaHCO_3$aq and water, dried with Na_2SO_4, and evaporated to a golden oil. The crude product was fractionated over a 500 g Si gel column, using benzene/EtOAc with increasing proportions of EtOAc (in 1% increments) to a final ratio of 19:1; the fractions were analyzed by tlc (Si gel: benzene/EtOAc, 19:1). A homogeneous bromoketone (13.8 g, 30% based on dihydrocaffeic acid) was obtained by rotary evaporation of the early fractions. A portion of this material was subjected to PCL, ν_{max}(film): 1771 and 1749 cm^{-1}, δ: 7.05 (s; 3H), 3.80 (m; 2H), 2.80 (s; 4H), 2.25 (s; 6H). (Found M^+ 342.0088. $C_{14}H_{15}BrO_5$ required: 342.0103).

3 - (3,4 - *Diacetoxyphenyl*) - *propionylmethylene triphenylphosphonium bromide* (**12**). Benzene solns (150 ml) of **11** (16.8 g, 0.05 mole) and triphenylphosphine (12.9 g, 0.05 mole) were mixed. The resulting emulsion deposited a small volume of oil. Vigorous magnetic stirring for 48 hr yielded a white solid ppt which was separated by vacuum filtration and gave white needles of **12** (29.7 g, 89% based on **11**), mp 163–165°, upon recrystallization from acetone/hexane, ν_{max}: 1776 and 1715 cm^{-1}, δ: 7.60–7.35 (m; 15H), 7.00 (s; 3H), 5.88 (d, J = 12 Hz; 2H), 3.35 (m; 2H), 2.85 (m; 2H), 2.25 (s; 6H). (Found: M^+ 524.1714. $C_{32}H_{30}BrO_5P$ (M–HBr) required: 524.1752; Found: C, 63.75; H, 5.31; Br, 13.41; P, 5.49%. $C_{32}H_{30}BrO_5P$ required: C, 63.57; H, 5.00; Br, 13.06; P, 5.13%).

1 - *Phenyl* - 7 - (3,4 - *diacetoxyphenyl*) - 1,3 - *heptadien* - 5 - *one* (**14**). The phosphonium bromide **12** (26.33 g, 0.044 mole) was dissolved in hot water (200 ml) and K_2CO_3aq (6.6 g, 0.48 mole) was added with stirring. The white ppt initially formed soon changed to a viscous amber oil. The supernatant water was decanted and discarded, the gummy ylid **13** was dissolved in dry benzene (250 ml), and the resulting pale yellow soln was dried with Na_2SO_4 and filtered. Distilled cinnamaldehyde (5.2 ml, 0.041 mole) was added, and the mixture was heated under reflux for 24 hr to produce a red soln which was evaporated, leaving a red residue. When this was chromatographed over a column of Si gel (500 g, $CHCl_3$), it yielded 5 g (32% based on the cinnamaldehyde) of pure **14**, which gave white needles, m.p. 97–98°, upon recrystallization from MeOH, ν_{max}: 1779, 1692, 1618, 1592, 1262 and 1000 cm^{-1}, δ: 7.50–6.70 (m; 11H, phenyl, H–1,2, and 3), 6.15 (d; J = 15 Hz; H–4), 2.85 (s; 4H at C–6 and C–7), 2.20 (s; 6H, OAc), λ_{max}: 323 nm (log ϵ 4.91). (Found: M^+ 378.1463: C, 72.76; H, 6.26%; $C_{23}H_{22}O_5$ required: M^+ 378.1467; C, 72.99; H, 5.86%).

1 - *Phenyl* - 7 - (3,4 - *dihydroxyphenyl*) - 1,3 - *heptadien* - 5 - *one* (**7**). Compound **14** (0.5 g, 1.3 mmole) was dissolved in abs MeOH (75 ml). NaOMe (20 drops of 1M soln in abs MeOH) was added with swirling, which was continued for 5 min. The soln changed from colorless to pale yellow and finally to a deep red color. Water (100 ml) was added to yield a pale purple suspension of pH 8.5 which was allowed to stand at room temp. for 5 min. The soln was acidified to pH 5.5 by the addition of a few drops of 10% HCl with magnetic stirring. The resulting yellow suspension was allowed to stand for 5 min and was then extracted with $CHCl_3$. The $CHCl_3$ soln was washed with water, dried with Na_2SO_4, evaporated, and subjected to PLC (Si gel PF 254; $CHCl_3$/MeOH, 19:1), yielding 0.31 g (82%) of dark, oily, phenolic material, δ: 8.50–6.50 (m; 11H), 6.15 (d, J = 15 Hz; H–4), 2.80 (s; 4H, at C–6 and C–7) (deuterium oxide added): 8.50–6.60 (m; 9H), 6.15 (d, J = 15 Hz; 1H), 2.80 (s; 4H, at C–6 and C–7). (Found: M^+ 294.1254; $C_{19}H_{18}O_3$ requires: 294.1256).

Lachnanthocarpone (**1**). Compound **7** (212 mg, 0.72 mmole) dissolved in ether (20 ml) was shaken at room temp. for 10 min with an aqueous soln of sodium periodate (0.16 g, 7.3 mmole). The color of the organic phase changed from pale yellow to orange-yellow with the simultaneous formation of a gummy orange-yellow ppt. Additional water (50 ml) was added, and the mixture was extracted with $CHCl_3$. The $CHCl_3$-ether soln was dried with Na_2SO_4 and filtered; analysis by tlc (Si gel; benzene/EtOAc, 1:1 or $CHCl_3$/MeOH, 9:1) showed the presence of several orange spots unchanged in color on exposure to ammonia vapors. After standing overnight at room temp., tlc analysis of the soln revealed a yellow compound of high R_f (0.75), and several compounds near the origin of the chromatogram. Chromatography over a column of dry-packed polyamide, using $CHCl_3$ as the eluant, yielded a fraction of pure **1** (12 mg) as well as impure fractions of the compound (65 mg). Total yield 37%. The synthetic material was recrystallized from benzene/hexane and had a m.p. (218–220°) and IR spectrum identical with those of the natural product.

5 - *Hydroxynaphtho*(8,1,2 - j,k,l) - *xanthenone* (**17**). Compound **7** (34 mg, 0.13 mmole) dissolved in ether (1 ml) was shaken for 10 min with an aqueous soln (5 ml) of sodium periodate (27 mg, 1.3 mmole). The mixture was extracted with $CHCl_3$; tlc analysis (Si gel; $CHCl_3$/MeOH, 9:1) showed a small amount of starting material as well as one faint blue spot above and one below the starting material. Their blue color was intensified upon exposure to ammonia vapor. The $CHCl_3$ soln was extracted with 0.2 M NaOH. The blue-green basic soln was acidified with 10% HCl to give a yellow suspension which was extracted with $CHCl_3$. The $CHCl_3$ soln was washed with water, dried overnight with Na_2SO_4, and subjected to PLC (Si gel; $CHCl_3$/MeOH, 19:1). The pink-coloured band (which appeared red under long-wave UV) yielded a strongly fluorescent red product (less than 1 mg, 3.3%) upon extraction with $CHCl_3$/MeOH. This product was shown to be **17** by two-dimensional co-chromatography (Si gel, EtOAc; $CHCl_3$/MeOH, 8.5:1.5) with authentic material, and by high resolution MS (Found: M^+ 286.0628; $C_{19}H_{10}O_3$ requires: 286.0630).

REFERENCES

[1]For a preliminary account of this work, *Tetrahedron Letters* 147 (1977).

[2]J. M. Edwards and U. Weiss, *Phytochemistry* **9**, 1653 (1970).

[3]R. G. Cooke and W. Segal, *Austral. J. Chem.* **8**, 107, 413 (1955); I. R. C. Bick and A. J. Blackman, *Ibid.* **26**, 1377 (1973).

[4]J. M. Edwards and U. Weiss, *Phytochemistry* **13**, 1597 (1974).

[5]T. Cremona and J. M. Edwards, *Lloydia* **37**, 112 (1974).

[6]J. M. Edwards, *Phytochemistry* **13**, 290 (1974).

[7]R. G. Cooke and R. L. Thomas, *Austral. J. Chem.* **28**, 1053 (1975).

[8]R. Thomas, *Biochem. J.* **78**, 807 (1961).

[9]R. Thomas, *Chem. Commun.* 739 (1971).

[10]J. M. Edwards, R. C. Schmitt and U. Weiss, *Phytochemistry* **11**, 1717 (1972).

[11]A. D. Harmon, J. M. Edwards and R. J. Highet, *Tetrahedron Letters* 4471 (1977).

[12]P. J. Roughley and D. A. Whiting, *J. Chem. Soc.* Perkin I, 2739 (1973).

[13]An excellent recent review of intramolecular [4+2] (and [3+2]) cyclizations is available: W. Oppolzer, *Angew. Chem. Int. Ed.* **16**, 10 (1977). This review brought several pertinent examples to our attention.

[14]Y. Omote and T. Komatsu, *Chem. Commun.* 792 (1974); S. Mazza, S. Danishefsky and P. McCurry, *J. Org. Chem.* 39, 3610 (1974); S. Danishefsky, P. F. Schuda, S. Mazza and K. Kuniki, *Ibid.* 41, 3468 (1976).
[15]M. Sakakibara, K. Mori and M. Matsui, *Agric. Biol. Chem.* 36, 1825 (1972).
[16]H. O. House, *Modern Synthetic Reactions*, (2nd Ed)., p. 692. Benjamin, Menlo Park, California (1972).
[17]I. A. Pearl and S. Parling, *J. Org. Chem.* 22, 1266 (1957).
[18]E. Adler and R. Magnusson, *Acta Chem. Scand.* 13, 505 (1959).
[19]U. Weiss and J. M. Edwards, *Tetrahedron Letters* 4325 (1969).
[20]Preparation of labelled 6 for incorporation studies is planned.
[21a]G. C. Brophy, J. Mohandas, M. Slaytor, S. Sternhell, T. R. Watson and L. A. Wilson, *Tetrahedron Letters* 5159 (1969); [b]O. L. Chapman, M. R. Engel, J. P. Springer and J. C. Clardy, *J. Am. Chem. Soc.* 93, 6696 (1971); [c]J. Mohandas, M. Slaytor and T. R. Watson, *Austral. J. Chem.* 22, 1803 (1969).
[22]A. Pelter and R. Hänsel, *Tetrahedron Letters* 2911 (1968); R. Hänsel, J. Schulz, and A. Pelter, *Chem. Commun.* 195 (1972); *Chem. Ber.* 108, 1482 (1975).
[23]D. J. Abraham, S. Takagi, R. D. Rosenstein, R. Shiono, H. Wagner, L. Hörhammer, O. Seligmann and N. R. Farnsworth, *Tetrahedron Letters* 2675 (1970).
[24a]G. Kartha, G. N. Ramachandran, H. B. Bhat, P. Madhavan Nair, V. K. V. Raghavan and K. Venkataraman, *Ibid.* 459 (1963); [b]P. Yates, S. D. Karmarkar, D. Rosenthal, G. H. Stout and V. F. Stout, *Ibid.* 1623 (1963).
[25]W. D. Ollis, M. V. J. Ramsay, I. O. Sutherland and S. Mongkolsuk, *Tetrahedron* 21, 1453 (1965).
[26]C. G. Karanjgaonkar, P. Madhavan Nair and K. Venkataraman, *Tetrahedron Letters* 687 (1966).
[27]D. J. Bichan and P. Yates, *J. Am. Chem. Soc.* 94, 4773 (1972); *Can. J. Chem.* 53, 2054 (1975).
[28a]M. Binder and C. Tamm, *Helv. Chim. Acta* 56, 2387 (1973); [b]J. Auerbach and S. M. Weinreb, *J. Org. Chem.* 40, 3311 (1975).
[29a]B. S. Joshi, N. Viswanathan, D. H. Gawad and W. v. Philipsborn, *Helv. Chim. Acta* 58, 1551 (1975); [b]B. S. Joshi, N. Viswanathan, D. H. Gawad, V. Balakrishnan and W. v. Philipsborn, *Ibid.* 58, 2295 (1975).
[30]A. A. Qureshi and A. I. Scott, *Chem. Commun.* 945, 947, 948 (1968).
[31]A. I. Scott, *Accounts Chem. Res.* 3, 151 (1970).
[32]A. R. Battersby, *The Chemical Society Specialist Periodical Reports*; *The Alkaloids*, (Edited by J. E. Saxton), Vol. 1, p. 31. The Chemical Society, London (1971).
[33]E. Leete, *The Chemical Society Specialist Periodical Reports*: *Biosynthesis* (Edited by T. A. Geissman), Vol. 1, p. 158; The Chemical Society, London (1972); Vol. 11, p. 106 (1973); Vol. III, p. 113 (1975).
[34]J. P. Kutney, *Heterocycles* 4, 169 (1976).
[35]E. Wenkert, *J. Am. Chem. Soc.* 84, 98 (1962); E. Wenkert and B. Wickberg, *Ibid.* 87, 1580 (1965).
[36]A. I. Scott and P. C. Cherry, *Ibid.* 91, 5872, 5874 (1969).
[37]A. I. Scott and C. C. Wei, *Ibid.* 94, 8263, 8264, 8266 (1972).
[38]J. P. Kutney, C. Ehret, V. R. Nelson and D. Wigfield, *Ibid.* 90, 5929 (1968).
[39]A. I. Scott, P. C. Cherry and A. A. Qureshi, *Ibid.* 91, 4932 (1969).
[40]P. A. Crooks, B. Robinson and G. F. Smith, *Chem. Commun.* 1210 (1968); G. F. Cordell, G. F. Smith and G. N. Smith, *Ibid.* 189 (1970); G. T. Brown, G. F. Smith, K. S. G. Stapleford and D. A. Taylor, *Ibid.* 190 (1970); A. R. Battersby and A. K. Bhatnagar, *Ibid.* 193 (1970).
[41]C. Kan-Fan, G. Massiot, A. Ahond, B. C. Das, H.-P. Husson, P. Potier, A. I. Scott and C.-C. Wei, *Ibid.*, 164 (1974).
[42]J. P. Kutney, T. Inaba and D. L. Dreyer, *J. Am. Chem. Soc.* 90, 814 (1968); *Tetrahedron* 26, 3171 (1970).
[43]K. Brown, R. C. Cambie and D. Hall, *Chem. & Ind.* 1020 (1971); K. L. Brown, A. I. R. Burfitt, R. C. Cambie, D. Hall and K. P. Mathui, *Austral. J. Chem.* 28, 1327 (1975).
[44]J. P. Kutney, R. N. Young and A. K. Verma, *Tetrahedron Letters* 1845 (1969).
[45]A. W. Johnson, T. J. King and R. J. Martin, *J. Chem. Soc.* 4421 (1961).
[46]M. M. Robison, W. G. Pierson, L. Dorfman, B. F. Lambert and R. A. Lucas, *J. Org. Chem.* 31, 3206 (1966).
[47]R. N. Gupta and I. D. Spenser, *Can. J. Chem.* 49, 385 (1971).
[48]G. A. Cordell, G. F. Smith and G. N. Smith, *Chem. Commun.* 191 (1970).
[49]J. L. Pousset, A. Cavé, A. Chiaroni and C. Riche, *Ibid.* 261 (1977).
[50]K.-H. Lee, Y. Imakura, D. Sims, A. T. McPhail and K. D. Onan, *Ibid.* 341 (1976).
[51]G. Gatti, R. Cardillo, C. Fuganti and D. Ghiringhelli, *Ibid.*, 435 (1976).
[52]S. Inoue, N. Takamatsu, K. Hashizume and Y. Kishi, *Yakugaku Zasschi* 97, 582 (1977).
[53]A. I. Vogel, *A. Textbook of Practical Organic Chemistry*, (3rd Edn.,) p. 971. Wiley, New York (1966).