THE CHEMISTRY OF THE PHENALENES

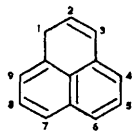
By D. H. REID

(DEPARTMENT OF CHEMISTRY, THE UNIVERSITY, ST. ANDREWS, SCOTLAND)

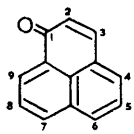
1. Introduction

MOST of the interesting features of the chemistry of the phenalenes have emerged during the past 15 years. Developments have been along two lines. First, the phenalene hydrocarbons have only recently become accessible, and their availability has been followed by experimental and theoretical studies of the phenalene ions and radical, and of novel carbocyclic and heterocyclic aromatic systems based on the phenalene unit. Secondly, several highly oxygenated derivatives have been isolated as plant and fungal pigments. This Review is of these developments and includes all important earlier work.

The nomenclature and numbering adopted are those used in *Chemical Abstracts*. Compounds in this series are named as derivatives of phenalene (1) or phenalenone (2). Earlier names for the hydrocarbon (1) were perinaphthene, perinaphthindene, and benzonaphthene, and the ketone (2) has been variously referred to as "pyrene ketone", phenalone-9, perinaphthindone, 1,8-naphthindenone, 9-ketoperinaphthindene, and perinaphthenone.



(1)



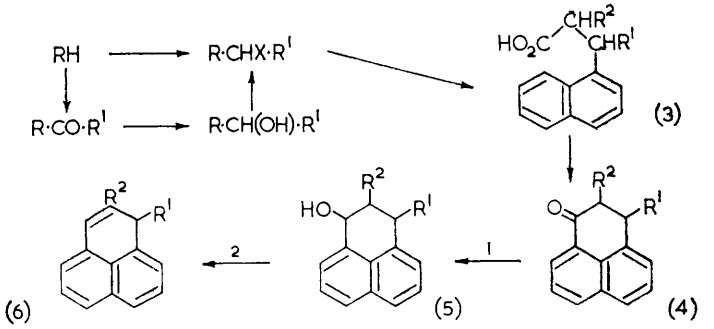
(2)

2. Formation and Synthesis

Oxidation of the hydrocarbon pyrene with chromic acid gave phenalenone-6,7-dicarboxylic acid, the first recorded phenalene derivative,[1] later decarboxylated to phenalenone.[2] All useful syntheses give a phenalenone or 2,3-dihydrophenalenone as an intermediate or final product.

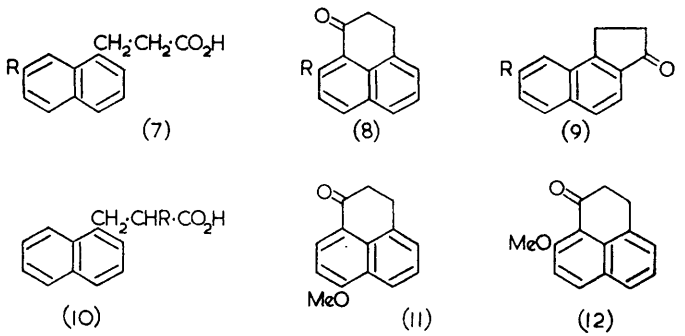
2,1. Phenalenes.—*Synthesis* via *β*-1-*naphthylpropionic acids.* This is the only versatile synthesis of phenalenes, 2,3-dihydrophenalenes, and 2,3-dihydrophenalenones. 1-Halogenomethylnaphthalenes, prepared by chloromethylation[3,4] or, indirectly, by successive formylation (Vilsmeier) or acylation, reduction with lithium aluminium hydride,[5] and treatment

[1] E. Hintz, Dissertation (Strasbourg 1878).
[2] E. Bamberger and M. Philip, *Annalen*, 1887, **240**, 147.
[3] G. Darzens and A. Levy, *Compt. rend.*, 1935, **201**, 902.
[4] L. F. Fieser and M. D. Gates, *J. Amer. Chem. Soc.*, 1940, **62**, 2335.
[5] V. Boekelheide and C. E. Larrabee, *J. Amer. Chem. Soc.*, 1950, **72**, 1240.



Reagents: 1, $LiAlH_4$; 2, HCl–EtOH.

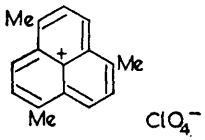
with a phosphorus trihalide, are converted into β-1-naphthylpropionic acids (3) by the malonic ester synthesis.[5–11] Cyclisation, best with hydrogen fluoride,[4,5,7] gives 2,3-dihydrophenalen-1-ones (4). Reduction of the ketone (4) and dehydration of the carbinol (5) gives the phenalene (6).[5–7,12] The scope of this synthesis is subject to steric and electronic effects which affect the direction of cyclisation. Thus, while the acid (7; R = H) gave a small amount of the benzindanone (9; R = H) along with the major product (8; R = H),[4] the 7-alkyl substituted acids (7; R = Me, Et, Pr^i) gave exclusively the six-membered ring ketones.[13] However, the acid (7; R = Bu^t) gave a mixture of ketones (8 and 9; R = Bu^t) in which the latter predominated.[14] Cyclisation of the series of acids (10; R = Me, Et, Pr^n, Bu^t) also gave mixtures of five- and six-membered ring ketones in which the latter predominated, except in the case where R = Bu^t.[15] Again, while the



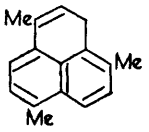
[6] V. Boekelheide and C. E. Larrabee, *J. Amer. Chem. Soc.*, 1950, **72**, 1245.
[7] D. H. Reid and R. G. Sutherland, *J.*, 1963, 3295.
[8] F. Mayer and A. Sieglitz, *Ber.*, 1922, **55B**, 1835.
[9] J. von Braun, G. Manz, and E. Reinsch, *Annalen*, 1929, **468**, 277.
[10] W. Klyne and R. Robinson, *J.*, 1938, 1991.
[11] L. F. Fieser and F. C. Novello, *J. Amer. Chem. Soc.*, 1940, **62**, 1855.
[12] L. F. Fieser and L. W. Newton, *J. Amer. Chem. Soc.*, 1942, **64**, 917.
[13] A. J. M. Wenham and J. S. Whitehurst, *J.*, 1956, 3857.
[14] A. J. M. Wenham and J. S. Whitehurst, *J.*, 1957, 4037.
[15] M. F. Ansell, *J.*, 1954, 575.

cyclisation of 5- and 7-methoxy-β-1-naphthylpropionic acid gave exclusively the dihydrophenalenones (11) and (12), the 6-methoxy-acid gave only the benzindanone.[16]

Phenalenes from phenalenium salts. Reduction of 1,4,7-trimethylphenalenium perchlorate (13) (section 4,3) with lithium aluminium hydride gave 3,6,9-trimethylphenalene (14).[17]



(13)



(14)

Phenalenes from phenalenones. Wolff–Kishner reduction of phenalenone afforded phenalene in modest yield; this was the first preparation of this hydrocarbon.[18] Reduction of phenalenone with lithium aluminium hydride gave phenalene (14%), 2,3-dihydrophenalenone (8; R = H) (65%), and phenolic material.[6] Since phenalenones are abnormally polarised, the yield of phenalenes from phenalenones could doubtlessly be improved by the use of the lithium aluminium hydride–aluminium chloride system.

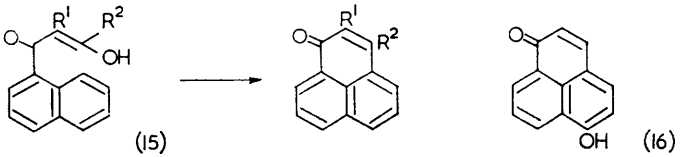
2,2. Phenalenones.—*Dehydrogenation of 2,3-dihydrophenalenones.* 2,3-Dihydrophenalenones are dehydrogenated preparatively to phenalenones by palladium–charcoal,[19] by bromination followed by dehydrobromination,[13] by quinones,[20] and by triphenylmethyl perchlorate.[21] 2,3-Dihydrophenalenones are slowly transformed into phenalenones when exposed to air and light. Metal halides of the type used in the Friedel–Crafts reaction bring about rapid dehydrogenation. It has been concluded[4] that early attempts to prepare 2,3-dihydrophenalenones by the action of aluminium or stannic chloride on β-1-naphthylpropionic acid chlorides invariably gave some of the phenalenone.

Cyclisation of 1-β-hydroxyacryloylnaphthalenes. The Claisen ester condensation of alkyl 1-naphthyl ketones gives compounds (15) which are cyclodehydrated by 80—90% sulphuric acid to phenalenones.[18,22,23]

Condensation of naphthols with acraldehyde. 1- or 2-Naphthol, when heated with glycerol, sulphuric acid, and a mild oxidising agent, give

[16] A. L. Green and D. H. Hey, *J.*, 1954, 4306.
[17] D. H. Reid and R. G. Sutherland, *J.*, 1963, 3295; R. G. Sutherland, Ph.D. Thesis, University of St. Andrews, 1962.
[18] G. Lock and G. Gergely, *Ber.*, 1944, **77B**, 461.
[19] J. D. Loudon and R. K. Razdan, *J.*, 1954, 4299.
[20] D. H. Reid and R. G. Sutherland, unpublished results.
[21] W. Bonthrone and D. H. Reid, *J.*, 1959, 2773.
[22] A. Lüttringhaus and F. Kačer, *Ger.P.*, 489,571 and 490,358.
[23] H. Silberman and S. Silberman, *Austral. J. Chem.*, 1956, **19**, 115.

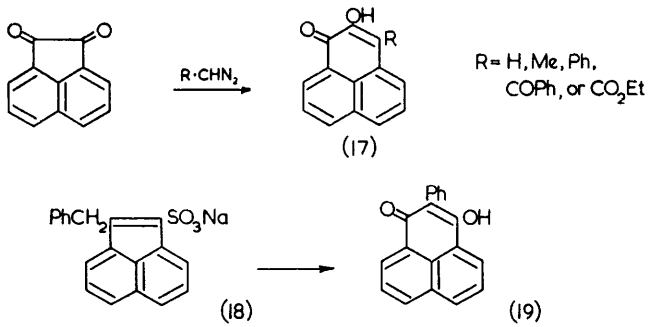
phenalenone (2).[12,24] This procedure, applied to 2,7-dihydroxynaphthalene, gave 6-hydroxyphenalenone (16).[25] The reaction of acraldehyde with 1- or 2- naphthol in the presence of hydrogen fluoride also gives phenalenone, spontaneous dehydrogenation occurring.[26]



(15) (16)

R^1 = H, alkyl, aryl
R^2 = alkyl, aryl, CO_2R

Ring-expansion of acenaphthene derivatives. Aliphatic diazo-compounds bring about ring-expansion of acenaphthenequinone, with *C*-insertion between carbonyl and the aromatic nucleus. 2-Hydroxyphenalenones (17) are formed.[27] Successive ozonolysis and treatment with aqueous alkali of the sulphonate (18) gave 3-hydroxy-2-phenylphenalenone (19).[28]



(17) (18) (19)

Rearrangement of oxygen heterocycles. The dihydrocoumarin (20) with dimethyl sulphate and alkali gave the acid (21) whose chloride was cyclised with aluminium chloride to the dihydrophenalenone (22).[29] Treatment of the dihydrocoumarin (23) with aluminium chloride at an elevated temperature gave 4-hydroxyphenalenone (24), dehydrogenation accompanying the rearrangement.[19] Under similar conditions the chro-

[24] M. A. Kunz and G. Kochendorfer, *Ger.P.*, 614,940; G. B. Silberman and S. M. Barkov, *J. Gen. Chem. U.S.S.R.*, 1937, **12**, 1733; L. F. Fieser and E. B. Herschberg, *J. Amer. Chem. Soc.*, 1938, **60**, 1658.

[25] R. G. Cooke, B. L. Johnstone, and W. Segal, *Austral. J. Chem.*, 1958, **11**, 230.

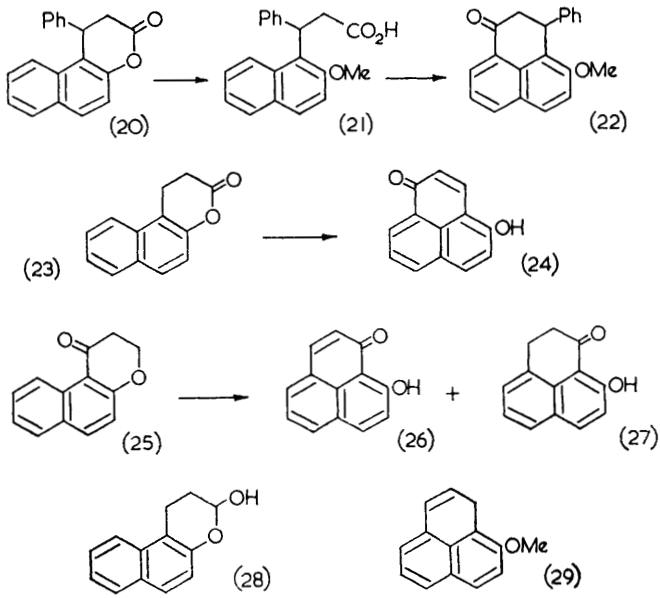
[26] W. Calcott, J. M. Tinker, and V. Weinmayr, *J. Amer. Chem. Soc.*, 1939, **61**, 949.

[27] B. Eistert and A. Schönberg, *Chem. Ber.*, 1962, **95**, 2416; B. Eistert and H. Selzer, *Chem. Ber.*, 1963, **96**, 314.

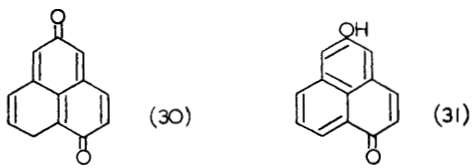
[28] E. Henmo, P. de Mayo, A. M. B. Abdus Sattar, and A. Stoessl, *Proc. Chem. Soc.*, 1961, 238.

[29] C. F. Koelsch, *J. Amer. Chem. Soc.*, 1936, **58**, 1326.

manone (25) gave a mixture of 9-hydroxyphenalenone (26) and its dihydroderivative (27).[19] The recent report[30] that treatment of the tetrahydrocoumarin (28) with methanolic hydrogen chloride gives 9-methoxyphenalene (29) requires further investigation since previous attempts[4,7,31] to prepare methoxyphenalenes have given 2,3-dihydrophenalenones (see following section).



Miscellaneous. A large number of 3-hydroxyphenalenones have been prepared (*a*) by the condensation of naphthalene or its alkyl or alkoxyderivatives with malonic acid or a substituted malonic acid and hydrogen fluoride,[32] or with malonyl chloride and aluminium chloride,[33] (*b*) by the reaction of naphthalic anhydride in the presence of zinc chloride with compounds containing a reactive methyl(ene) group, for example, with diethyl

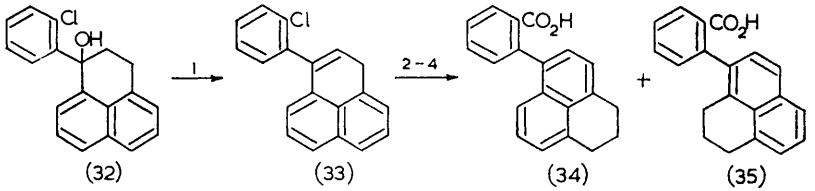


[30] J. Cologne, G. Descotes, and R. Puthet, *Bull. Soc. chim. France*, 1963, 553.
[31] G. M. Badger, W. Carruthers, and J. W. Cook, *J.*, 1949, 1768.
[32] H. Greune and G. Langbein, *Ger. P.*, 753,210.
[33] K. Fleischer and E. Retze, *Ber.*, 1922, **55B**, 3280.

malonate,[34] phenylacetic acid,[35] and 2-methylpyridine.[36] 5-Hydroxytetralone reacts in the presence of sulphuric acid with glucose and other hexoses, also with glyceraldehyde to give a compound formulated as (30), but more likely to possess the tautomeric structure (31) (see section 6,1.).[37]

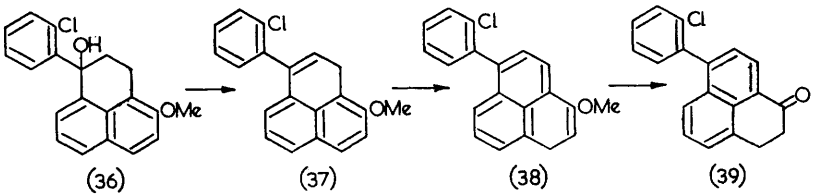
3. Tautomerism of Phenalenes

Klyne and Robinson suggested, by analogy with indene, that phenalenes might exhibit six-fold tautomerism, each of the three rings assuming the aromatic and the unsaturated character in turn.[38] In the case of phenalene the six tautomers are identical, but they become chemically distinguishable in a 1-substituted phenalene. Consequently, oxidation of 1-methylphenalene might yield a mixture of three dicarboxylic acids, *i.e.*, naphthalic acid and its 2- and 4- methyl derivatives. Unfortunately this hypothesis could not be tested since the required 1-methylphenalene could not be synthesised. Fieser and Gates subsequently showed that the carbinol (32), obtained by the reaction of *o*-chlorophenylmagnesium bromide with 2,3-dihydrophenalenone (8; R = H), gives rise to a mixture of two acids (34) and (35), both of which are rearrangement products, and interpreted



Reagents: 1, $MeCO_2H$; 2, H_2–Pt; 3, $Cu_2(CN)_2$; 4, KOH.

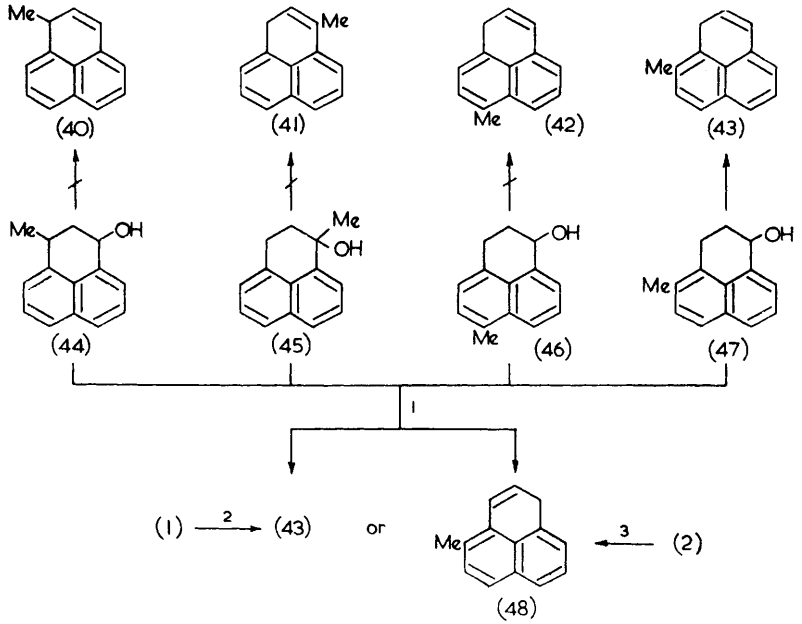
this as resulting from tautomerisation of the phenalene (33) which, however, was not isolated.[4] In a related reaction sequence the carbinol (36) upon dehydration gave the ketone (39) by tautomerisation of the primary dehydration product (37) to the isomeric phenalene (38) which, as an enol ether, hydrolyses and rearranges to the product (39)[31] (see also section 4,3.).



Reagents: 1, HCl–MeOH–C_6H_6; 2, Tautomerisation.

[34] G. Errera, *Gazzetta*, 1911, **41**, 190.
[35] M. Cesaris, *Gazzetta*, 1912, **42**, 453.
[36] A. Taurins, *J. prakt. Chem.*, 1939, **153**, 177.
[37] T. Momose and Y. Ohkura, *Chem. Pharm. Bull. (Tokyo)*, 1958, **6**, 412.
[38] W. Klyne and R. Robinson, *J.*, 1938, 1991.

In an elegant series of experiments Boekelheide and his co-workers attempted to prepare four different methylphenalenes (40)—(43) by the acid-catalysed dehydration of the alcohols (44)—(47), respectively, in order to determine whether interconversion would occur.[5] The same hydrocarbon, shown to be (43) or (48), was obtained from all four alcohols.

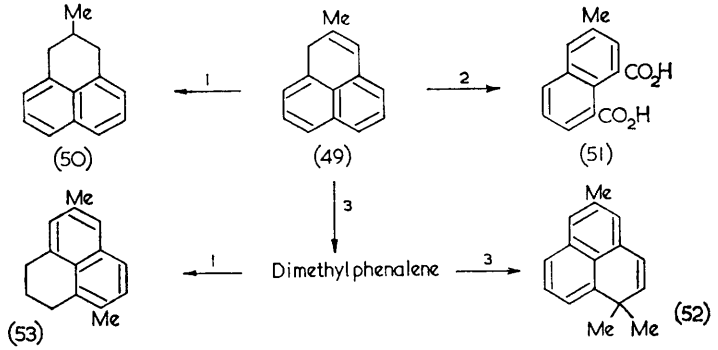


Reagents: 1, HCl–EtOH; 2, PhLi, MeI; 3, MeMgI.

This hydrocarbon was also obtained by methylation of phenalene with phenyl-lithium followed by methyl iodide, and from the reaction of phenalenone with methylmagnesium iodide, showing that isomerisation is not accounted for by acid or base catalysis alone. Further, the hydrocarbon was not isomerised by treatment with phenyl-lithium followed by hydrolysis.

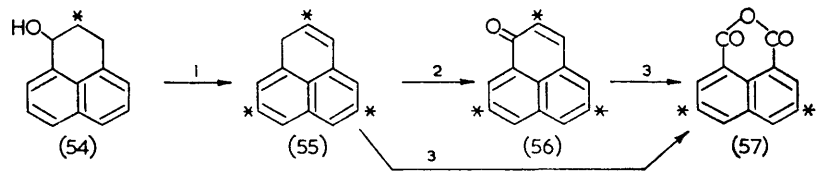
These results illustrate the tendency of the phenalene nucleus to behave as a unit, making it difficult to determine which ring should be designated the *peri* (incompletely conjugated) ring. Different rings may be involved in different reactions.[39] For example, catalytic hydrogenation of 2-methylphenalene (49) gives the hydrocarbon (50), while oxidation gives the acid (51). Methylation of 2-methylphenalene (49) gives a dimethylphenalene as a tautomeric mixture. This on further methylation gives the hydrocarbon (52) but on catalytic hydrogenation affords the hydrocarbon (53).[39]

[39] V. Boekelheide and M. Goldman, *J. Org. Chem.*, 1954, **19**, 575.



Reagents: 1, H_2–Pt; 2, $KMnO_4$; 3, PhLi, MeI.

In a further study the preparation and degradation of a ^{14}C-labelled phenalene was carried out.[40] The alcohol (54) was synthesised from 1-chloromethylnaphthalene and diethyl [2-^{14}C]malonate (section 2,1.) and dehydrated to the labelled phenalene (55). Permanganate oxidation of the latter in acetone gave naphthalic anhydride (57) having two-thirds of the specific activity of compounds (54) and (55). Oxidation was also carried out stepwise, first with sodium dichromate in acetic acid to give labelled phenalenone (56) in order to avoid possible formation of the phenalene anion (section 4,2.), when positions 2,5, and 8 would become equivalent, and the ketone (56) was further oxidised with permanganate to naphthalic anhydride. The specific activity of the anhydride in both degradations was the same. It was concluded that the even distribution of ^{14}C between positions 2, 5, and 8 had occurred at the dehydration step.



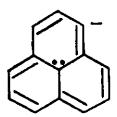
Reagents: 1, HCl–EtOH; 2, $Na_2Cr_2O_7$–$CH_3 \cdot CO_2H$; 3, $KMnO_4$–acetone.

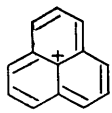
It is clear from the foregoing that although ready isomerisation of phenalenes occurs under the conditions employed in their preparation, the nature of the isomerisation has not yet been fully defined.

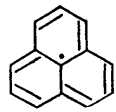
4. Ions and Radicals

4,1. Theoretical Considerations.—Phenalene is remarkable in that it gives rise to a relatively stable anion (58), cation (59), and radical (60). These result both in practice and in theory by the loss of a proton, hydride ion, or hydrogen atom, respectively.

[40] M. Nakazaki, *U.S. Atomic Energy Commission Reports*, UCRL-3700 (1957).

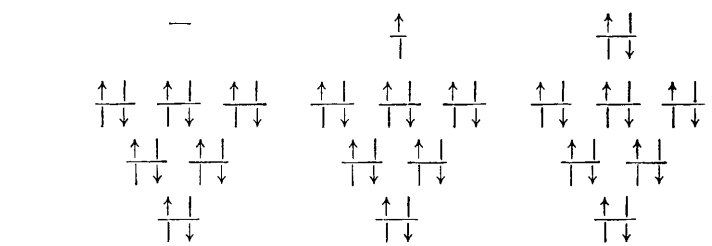

(58)


(59)


(60)

All three entities possess three-fold rotational symmetry about an axis which passes through the internal carbon atom perpendicular to the molecular plane, also three identical two-fold axes in the molecular plane. It was first pointed out[6] that this symmetry might make possible considerable resonance stabilisation of these entities. Quantum chemical studies later provided a satisfactory explanation of their stability. Hückel molecular orbital (HMO) calculations[41–43] predict that the phenalene anion, cation, and radical should all possess the same π-electron delocalisation energy, namely $5{\cdot}83\beta$. Fig. 1 shows the energy levels for the

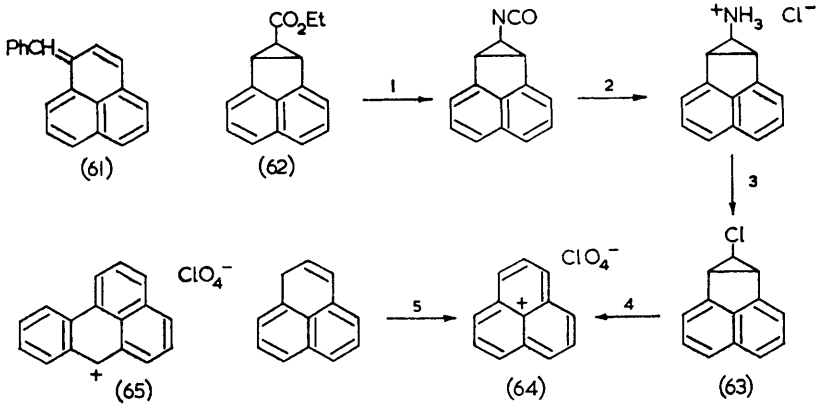
FIG. 1 HMO energy levels for phenalenyl systems[41–43]



phenalenyl system which, in addition to possessing six bonding molecular orbitals, has one of zero energy relative to the energy of an electron in a p_z orbital of an isolated sp^2 hybridised carbon atom. The phenalenium cation possesses 12 π-electrons which exactly fill pairwise the six bonding molecular orbitals. The extra one and two electrons of the phenalene radical and anion occupy the zero-energy orbital. Since the phenalenyl radical is an odd-alternant radical the electron density is unity at each position. The electron density distribution in the phenalenium cation and in the anion, however, is non-uniform. The charge densities (= 1–electron density) in the phenalenium cation are + 0·167 at positions 1, 3, 4, 6, 7, and 9, and zero at the remaining positions. The charge distribution in the phenalene anion is the same but with negative sign.

[41] R. Pettit, *Chem. and Ind.*, 1956, 1306; *J. Amer. Chem. Soc.*, 1960, **82**, 1972.
[42] M. E. Dyatkina and E. M. Shustorovitch, *Doklady Akad. Nauk S.S.S.R.*, 1957, **117**, 1021.
[43] R. Zahradník, J. Michl, and J. Koutecký, *Coll. Czech. Chem. Comm.*, 1964, **29**, 1932.

4,2. Phenalene Anion.—Treatment of phenalene with phenyl-lithium[6] or potassium methoxide[44,45] gives solutions containing the red anion (58) which reacts with methyl iodide to give 4(9)-methylphenalene (section 3) and condenses with benzaldehyde to give presumably compound (61).[6] Comparative studies showed that phenalene is more acidic than triphenylmethane (pK 25) and less so than cyclopentadiene (pK 16).[6] Using HMO theory Streitwieser calculated the change in π-bond energy in going from phenalene to its anion, and, on the assumption that this quantity is a direct measure of the acidity, calculated the pK of phenalene.[46] The value found (pK 22) agrees only moderately satisfactorily with experimental data. The true value must, in fact, be nearer to that of cyclopentadiene since the anion (58) is liberated by methoxide ion (pK of methanol, 17). Aerial oxidation of the anion gives the phenalenyl radical (see section 4,4.).[44]

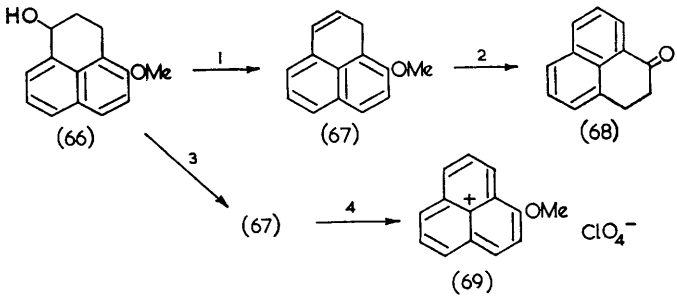


Reagents: 1, NaOH, $SOCl_2$, NaN_3; 2, HCl; 3, HONO; 4, $AgClO_4$; 5, *o*- Chloranil–70% $HClO_4$.

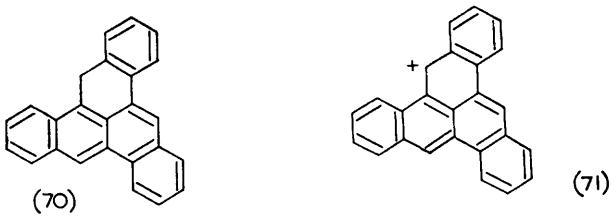
4.3. Phenalenium Cation.—The phenalenium cation was first prepared as its perchlorate (64) by the sequence (62)—(64).[41] Compound (62) was obtained by the addition of ethyl diazoacetate to acenaphthylene. Attempts to prepare the alcohol (63; OH in place of Cl) were unsuccessful. Formation of the covalent chloride (63) appears to result from the collapse of a diazonium chloride ion pair, with internal nucleophilic attack, without the intervention of a free carbonium ion. A more general synthesis of phenalenium salts involves hydride abstraction from phenalenes by high potential quinones in the presence of perchloric acid[7] or by triphenylmethyl perchlorate.[21] Several alkyl- and methoxy-phenalenium perchlorates have been prepared by this method, for example, the salt (13), as well as benzo[*a*]phenalenium perchlorate (65).

[44] D. H. Reid, *Chem. and Ind.*, 1956, 1504.
[45] D. H. Reid, *Tetrahedron*, 1958, **3**, 339.
[46] A. Streitwieser, *Tetrahedron Letters*, 1960, No. 6, 23.

Methoxyphenalenium perchlorates result directly from treatment of 1-hydroxy-2,3-dihydrophenalenes with these reagents. For example, dehydration of the alcohol (66) gives 2,3-dihydrophenalenone (68) by isomerisation and demethylation of the primary dehydration product (67) (section 3), but in the presence of a quinone or the triphenylmethyl cation rapid hydride abstraction diverts the intermediate (67) to the salt (69) before isomerisation can occur.[7] The tribenzo-derivative (71) results from the oxygenation of the hydrocarbon (70) in acetic acid containing perchloric acid.[47]



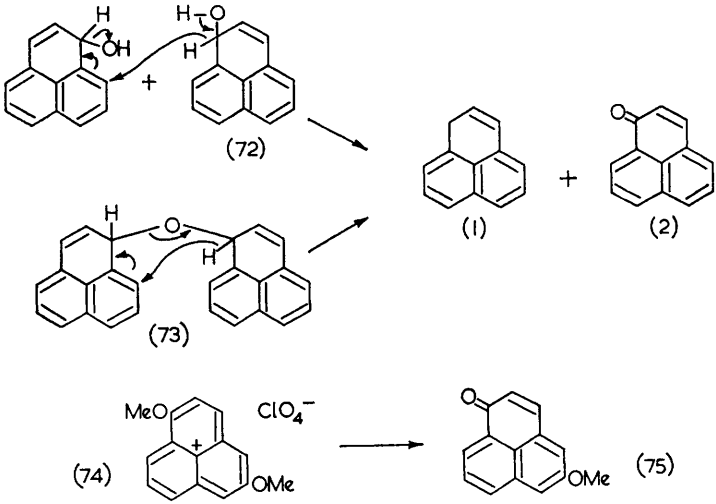
Reagents and reactions: 1, HCl–EtOH; 2, Isomerisation–demethylation; 3, $HClO_4$–$CH_3 \cdot CO_2H$; 4, Abstraction of H^- by *o*-chloranil.



Phenalenium perchlorate is rapidly attacked by moist air.[7,21,41] Alkyl- and alkoxy-phenalenium perchlorates are more stable.[7] All these salts are hydrolysed irreversibly in water. Phenalenium and alkylphenalenium perchlorates give an equimolecular mixture of the corresponding phenalene (or its tautomeric mixture) and phenalenone. The process doubtless proceeds by hydride abstraction, possibly as shown or by a related route, involving the carbinol (72) or the derived ether (73).

Alkoxyphenalenium perchlorates give phenalenones as the only hydrolysis product. 1-Methoxyphenalenium perchlorate (69) gave phenalenone (2), while 1,5-dimethoxyphenalenium perchlorate (74) afforded a methoxyphenalenone, believed to be (75).[20]

[47] E. Clar and D. G. Stewart, *J.*, 1958, 23.



Using the correlation between the constant for the equilibrium

$$ROH + H^+ \rightleftharpoons R^+ + H_2O$$

and the difference in π-bond energies of ROH and R^+ calculated by HMO theory, pK_{R^+} for the pair phenalenium–1-hydroxyphenalene was estimated to be around 0—2.[48] Unfortunately this could not be checked owing to the irreversible disproportionation of 1-hydroxyphenalene (72).

Good agreement was obtained between the predicted and experimentally determined ultraviolet and visible transitions [$\lambda_{max.}$ 400, 378 (shoulder), and 226] when the effect of interaction between ground and excited states on the spectrum of the phenalenium cation was taken into account.[49]

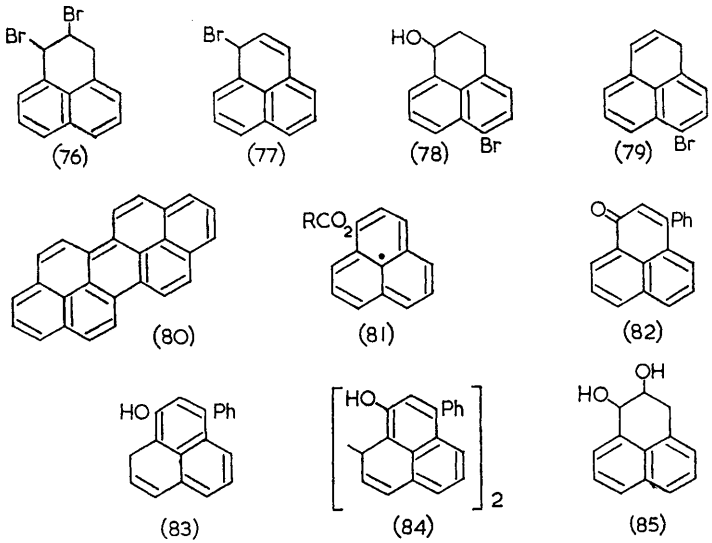
Chemical shifts due to ring current effects have been calculated for the phenalenium cation by both the Hückel and the Self Consistent Field (SCF) procedures.[50] The predicted shifts for H-1 and H-2, expressed as ratios to the corresponding effect in benzene, are, respectively, 0·85 (HMO), 1·02 (SCF) and 0·77 (HMO), 0·92 (SCF). The larger shifts shown by the SCF method arise because the central carbon atom, which has a negative charge of 0·024 in the SCF treatment and is neutral in the HMO version, increases the ring current by making the periphery more nearly of the $(4n + 2)$ type. Unfortunately it has not yet been possible to obtain the proton magnetic resonance spectrum of phenalenium perchlorate owing to its great tendency to form radical-containing material, and consequent line-broadening in the spectrum. The spectrum of the derivative (13) in trifluoroacetic acid shows a methyl singlet (9H) at δ 3·36 and an

[48] D. Meuche, H. Strauss, and E. Heilbronner, *Helv. Chim. Acta*, 1958, **41**, 57.
[49] N. S. Ham, *J. Chem. Phys.*, 1960, **32**, 1445.
[50] G. G. Hall, A. Hardisson, and L. M. Jackman, *Discuss. Faraday Soc.*, 1962, **34**, 15.

AB system (6H) with components centred at δ 8·18 (H-2) and 9·30 (H-3) p.p.m. (J = 8·3 c./sec.), consistent with its symmetry.[51] There is thus no evidence of abnormally large ring current effects.

4,4. Phenalenyl Radical.—Early attempts to prepare the phenalenyl radical involved the bromination of phenalene with *N*-bromosuccinimide and dehydrobromination of the dibromide (76).[6] It was hoped that 1-bromophenalene (77) or phenalenium bromide might result and that these might be transformed into the radical. Green-blue solutions were obtained. In a further attempt, the alcohol (78) was dehydrated with the expectation that tautomerisation of the primary dehydration product (79) would give the bromo-compound (77).[52] A yellow solid was obtained which rapidly changed into a high-melting substance, doubtlessly peropyrene (80).

The formation and preparation of several derivatives of the phenalenyl radical has been reported. Treatment of phenalenone with magnesium in ethereal acetyl or benzoyl chloride is reported to give blue solutions of the 1-acetoxy- and 1-benzoyloxy-phenalenyl radicals (81; R = MeCO or

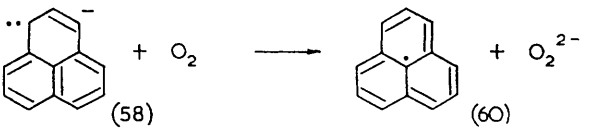


PhCO).[53] Reduction of 3-phenylphenalenone (82) with zinc in acetic acid gave a colourless compound, formulated as (83), which on partial re-oxidation with air gave a red substance to which structure (84) was assigned. This substance was also formed upon mixing solutions of equimolecular amounts of compounds (82) and (83), and was claimed to disproportionate

[51] W. Bonthrone and D. H. Reid, unpublished results.
[52] V. Boekelheide and M. Goldman, *J. Amer. Chem. Soc.*, 1954, **76**, 604.
[53] E. Clar, "Aromatische Kohlenwasserstoffe", Springer Verlag, Berlin, 1952, 2nd edn., p. 431.

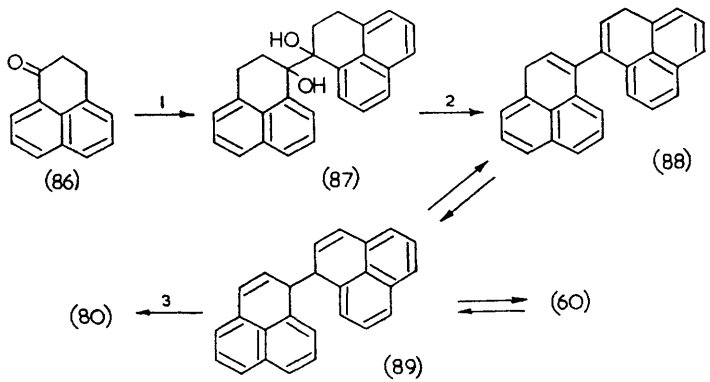
into these compounds in solution.[54] The properties of compound (83) are not in accord with those of simple phenalenes, and further studies of these reactions seem desirable.

Preparation of the phenalenyl radical (60) was first carried out by shaking a solution of the anion (58) in an atmosphere of oxygen. Continued uptake



(58) (60)

of oxygen gives a green "peroxide" of unknown constitution which breaks down thermally to a mixture of phenalenone (2) and peropyrene (80).[44,45] The phenalenyl radical has not been isolated but exists in solution ($\lambda_{max.}$ 613 mμ). Formation of the phenalenyl radical has also been observed in the oxidation of phenalene with quinones or osmium tetroxide.[20] In the latter case the diol (85) was also produced. In a different approach the diol (87), obtained by bimolecular reduction of the ketone (86), gave solutions of the radical when treated with acid.[45] The sequence (87) → (88) → (89) → (60)



(86) (87) (88) (80) (89) (60)

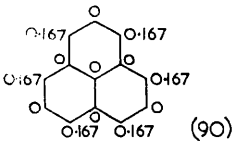
Reagents: 1, Al–EtOH–C_6H_6;
2, HCl–$CH_3{\cdot}CO_2H$; 3, Heat.

was suggested to account for this transformation. Solutions of the phenalenyl radical when boiled give peropyrene (80). Treatment of phenalenium perchlorate with zinc dust also gives peropyrene[41] as does a boiling solution of the diol (87) in acetic acid containing a catalytic amount of mineral acid.[45] The course of these reactions is rationalised by postulating the equilibrium (60) ⇌ (89) which is disturbed by the irreversible transformation of the dimer (89) into peropyrene. In the foregoing experiments no attempt was made to exclude oxygen. In the absence of oxidising agents the

[54] C. F. Koelsch and J. A. Anthes, *J. Org. Chem*,. 1941, **6**, 558.

phenalenyl radical is stable for indefinitely long periods.[55,56] Phenalenyl has been reported to be present in the pyrolysis products of petroleum fractions of widely varying boiling range and "aromatics" content.[55,56]

Although the electron density at each position of an odd-alternant hydrocarbon radical is unity,[57] the density distribution of the electron in the non-bonding molecular orbital is non-uniform. Calculation within the framework of the HMO procedure predicts that the unpaired electron density in the phenalenyl radical should be zero on seven carbon atoms and have positive values at the remaining six. This is shown in structure (90), from which a seven-line pattern is predicted in the electron spin



(90)

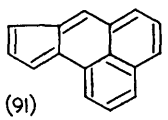
resonance (e.s.r.) spectrum with a total spread of about 28 gauss. In fact, however, seven principal lines are present, each is further split into a quartet, and the total spacing is 49 gauss.[58]* The relative intensities of the principal lines were 1:6:15:20:15:6:1, those of the components of the quartets 1:3:3:1. The hyperfine splittings were 7·3 and 2·2 gauss, later revised[55] to 6·30 and 1·82 gauss. The structure of the e.s.r. spectra of phenalenyl and other odd-alternant hydrocarbon radicals are accounted for by refined molecular orbital theory which introduces the concept of negative spin density.[59] This takes into account the disturbing effect of the unpaired electron on the orbitals of the paired electrons. Partial unpairing occurs which induces at the adjacent carbon atom odd-electron density of opposite sign to that of the electron responsible. The spin densities at positions 2, 5, and 8 of the phenalenyl radical therefore are negative, those at positions 1, 3, 4, 6, 7, and 9 positive and correspondingly greater.[60] The negative spin density accounts for the fine structure of the e.s.r. spectrum of phenalenyl. Since the total width of the e.s.r. spectrum of a conjugated radical or ion is a measure of the sum of the absolute values of the spin densities, the large spread (49 gauss) in the case of phenalenyl is accounted for. It is interesting that simple valence bond theory gives directly positive and negative spin densities in good agreement with experiment.[61]

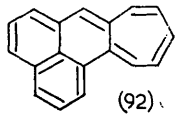
* In these studies a solution of the phenalenyl radical was produced[58] by allowing a solution of phenalene in carbon tetrachloride, sealed in air, to stand for several months.

[55] J. E. Bennett, *Proc. Chem. Soc.*, 1961, 144.
[56] K. W. Bartz and F. C. Stehling, *J. Chem. Phys.*, 1961, **34**, 1076.
[57] C. A. Coulson and C. A. Rushbrooke, *Proc. Cambridge Phil. Soc.*, 1940, **36**, 193.
[58] P. B. Sogo, M. Nakazaki, and M. Calvin, *J. Chem. Phys.*, 1958, **28**, 107.
[59] H. M. McConnell and D. B. Chesnut, *J. Chem. Phys.*, 1958, **28**, 107.
[60] R. Lefebvre, H. H. Dearman, and H. M. McConnell, *J. Chem. Phys.*, 1960, **32**, 176.
[61] H. M. McConnell and H. H. Dearman, *J. Chem. Phys.*, 1958, **28**, 51.

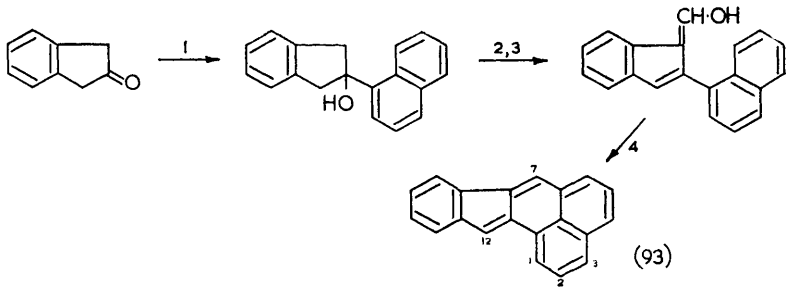
5. Aromatic Systems Based on the Phenalene Nucleus

Consideration of the fact that phenalene forms both a stable cation and anion (preceding section) led to the suggestion that stable non-alternant aromatic systems (91) and (92) might result by fusion of these units to the


(91)


(92)

cyclopentadienide and tropylium ions, respectively,[45,62] that is, by *ortho*-fusion of two stable, oppositely-charged, cyclic π-electron systems. Indeno-[2,1-*a*]phenalene (93), a derivative of the hydrocarbon (91), has been synthesised by the route shown, and a study of its properties has substantiated the expectation of its aromatic properties.[62] The results of a theoretical treatment[63] of the hydrocarbons (91)—(93) and their heterocyclic

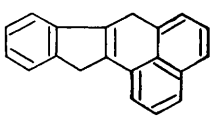


Reagents: 1, 1-$C_{10}H_7MgBr$, H_2O; 2, HCO_2H;
3, HCO_2Et–KOMe; 4, 93% H_2SO_4.

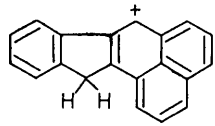
analogues are in excellent agreement with those of chemical studies. The hydrocarbon (93) is readily formed by dehydrogenation of a dihydro-derivative (94 or isomer) with palladium–charcoal at room temperature or triphenylmethyl perchlorate,[45] in agreement with its considerable delocalisation energy (0·402 β/π-electron). The relatively low level of the frontier bonding orbital (0·374β) explains its general chemical stability. The hydrocarbon (93) reacts under mild conditions with electrophiles, for example, with trifluoroacetic anhydride, triphenylmethyl perchlorate, and tetranitromethane, to give monosubstitution products.[20,21,62] These results are consistent with the reactivity indices (charge densities, superdelocalisabilities, and localisation energies), all of which predict position 12 to be the most reactive in electrophilic substitution reactions. Half-protonation of the hydrocarbon (93) occurs in 64% sulphuric acid (H_0 = −4·80), placing it alongside the azulenes and heptalene as one of the most basic

[62] I. M. Aitken and D. H. Reid, *J.*, 1956, 3487.
[63] R. Zahradník and J. Michl, *Coll. Czech. Chem. Comm.*, 1965, **30**, 520.

hydrocarbons. The nuclear magnetic resonance (n.m.r.) spectrum in trifluoroacetic–sulphuric acid (4:1 v/v) shows a methylene signal at δ 4·51 and aromatic signals in the range δ 7·4—9·5 p.p.m. (intensity ratio 2:11) supporting the σ-protonated structure (95) for the cation.[64] The high basicity of the hydrocarbon is consistent with the low electrophilic localisation energy (1·827β) for position 12.



(94)



(95)

Addition reactions occur easily. Reduction with zinc and acetic acid gives a dihydro-derivative.[45] The hydrocarbon (93) is a reactive diene, affording with maleic anhydride the compound (96),[62] and reacting with benzyne with concomitant dehydrogenation to give the hydrocarbon (97).[65] Bicentric localisation energies are lowest for the pairs of positions 7, 12 (3·45β) and 1, 12 (3·52β), both of which are low enough to explain the ease of Diels–Alder addition reactions.[63] The dihydro-derivative is thus predicted to be (94) if formed under thermodynamically controlled reaction conditions.

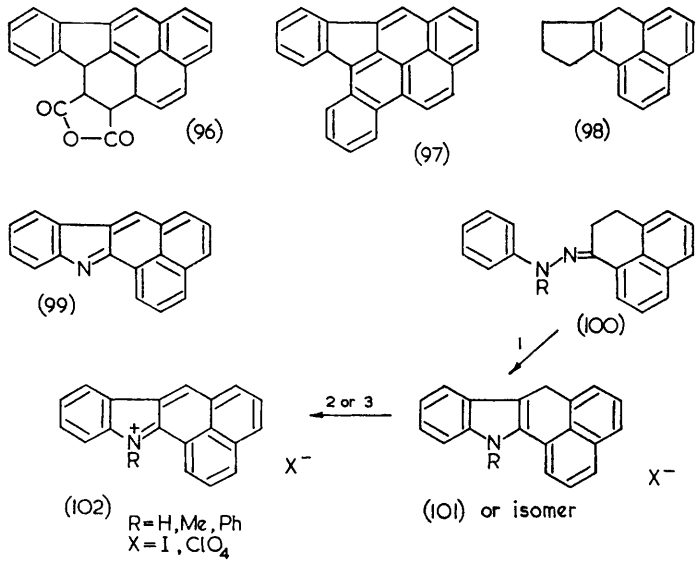
Neither of the hydrocarbons (91) and (92) has yet been synthesised. Attempts to dehydrogenate the tetrahydro-derivative (98) were unsuccessful. However, the conditions employed were severe.[45] Energy characteristics and reactivity indices of (91) and (92) augur favourably for their synthesis and stability.[62]

Several derivatives (102) of a heterocyclic analogue (99) of the hydrocarbon (93) are known. These have been prepared by the Fischer indolization of the phenylhydrazones (100) of 2,3-dihydrophenalenone, followed by dehydrogenation of the resulting phenalenes (101). The stability of the cation in the salts (102) is reflected in their ready formation from the phenalenes (101) by disproportionation in boiling acetic acid containing perchloric acid. The heterocycle (99) is a strong base. It is reactive and attempts to isolate it have given insoluble high-melting products of unknown structure.

6. Phenalenones

Phenalenones constitute the largest group of phenalene derivatives. They are stable and readily formed by mild oxidation of the phenalene hydrocarbons. Samples of phenalenes become yellow in air within a few hours owing to aerial oxidation to phenalenones.[6,7,18] Most methods of formation of the phenalene nucleus give phenalenones directly. All the

[64] D. H. Reid, unpublished results.
[65] I. M. Aitken and D. H. Reid, *J.*, 1960, 663.



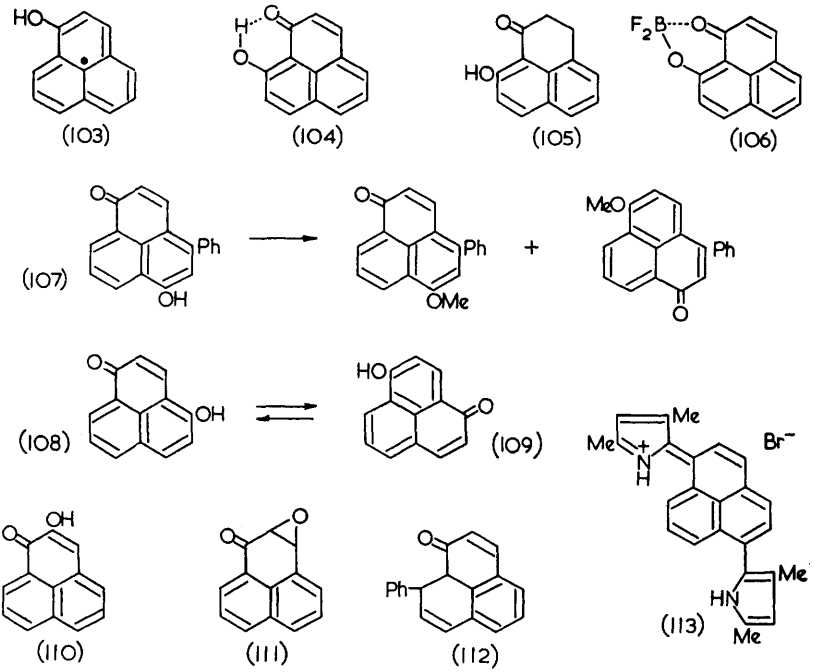
Reagents: 1, HCl–CH_3COOH; 2, I_2–MeOH; 3, $HClO_4$ in $CH_3{\cdot}CO_2H$, boil.

known naturally occurring compounds in this class are polyhydroxyphenalenones.

6,1. Physical Properties.—Phenalenone is an abnormally highly polarised ketone, resembling in many of its properties tropone, cyclopropenones, and some heterocyclic ketones. The polarisation is attested to by the high dipole moment (3·89D)[66] and the low infrared carbonyl frequency (1637 cm.$^{-1}$).[67] Infrared data demonstrating the effect of substitution on the carbonyl frequency are available for a large number of phenalenones.[68] Phenalenone is abnormally highly basic (pK_b = 0·4).[69] It dissolves reversibly in concentrated hydrochloric acid and forms stable salts with strong acids (see section 6,4.). This property is useful in the purification of phenalenones.[20,21] A polarographic investigation showed that the reduction of phenalenone proceeds in two steps, each involving the uptake of one electron.[70] The first and more positive step is reversible; it gives rise to the 1-hydroxyphenalenyl radical (103). The second stage is irreversible, and its exact nature is not entirely clear. Values of $E_{\frac{1}{2}}$ for the

[66] V. A. Kogan, O. A. Osipov, O. E. Shelepin, and Y. A. Zhdanov, *Doklady Akad. Nauk S.S.S.R.*, 1959, **128**, 719.
[67] N. H. Cromwell and G. V. Hudson, *J. Amer. Chem. Soc.*, 1953, **75**, 872.
[68] H. L. Josien, N. Fuson, J. M. Jacobs, and T. M. Gregory, *J. Chem. Phys.*, 1953, **21**, 331; N. Fuson and M. L. Josien, *Bull. Soc. chim. France*, 1952, 389; R. D. Campbell and N. H. Cromwell, *J. Amer. Chem. Soc.*, 1957, **79**, 3456; W. I. Awad and O. M. Aly, *J. Org. Chem.*, 1960, **25**, 1872; B. Eistert and A. Schönberg, *Chem. Ber.*, 1962, **95**, 2416; B. Eistert and H. Selzer, *Chem. Ber.*, 1963, **96**, 314.
[69] T. Handa, *Bull. Chem. Soc. Japan*, 1955, **28**, 483.
[70] P. Beckmann, *Austral. J. Chem.*, 1961, **14**, 229.

reversible step in the polarography of a series of phenalenones and the pK_a values of their conjugate acids show a parallel dependence on the nature of the substituents.[71] Irradiation of phenalenone in certain polar solvents, notably isopropyl alcohol, produces the radical (103), detected by its e.s.r. spectrum, and ultimately the ketone (68).[72]

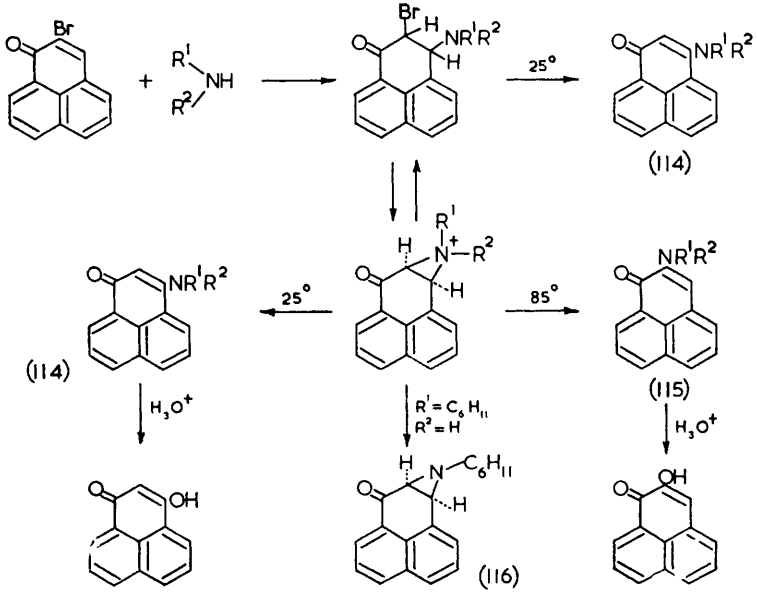


6,2. Tautomerism of Hydroxyphenalenones.—Tautomerism is possible among the hydroxyphenalenones, involving prototropic shifts from hydroxy to carbonyl oxygen. Three cases are distinguishable. (*a*) 3-,[34,73] 6-[25], and 9-Hydroxyphenalenone[19] can tautomerise but the tautomers are identical. The first two give rise accordingly to only one methyl ether.[25,34,73] 9-Hydroxyphenalenone (104) has the properties of a strongly intramolecular hydrogen bonded hydroxy-ketone.[19,54,74] It shows striking resistance to hydroxyl and carbonyl reagents. Hydrogenation proceeds cleanly to give the dihydro-derivative (105).[19] With the boron trifluoride–ether complex it forms the stable complex (106).[75] Unsymmetrical substitution of 3-, 6-, and 9-hydroxyphenalenone gives rise to pairs of non-identical tauto-

[71] P. Beckmann, *Chem. and Ind.*, 1955, 1635.
[72] H. Köller, G. P. Rabold, K. Weiss, and T. K. Mukherjee, *Proc. Chem. Soc.*, 1964, 332.
[73] M. Goldman, *J. Amer. Chem. Soc.*, 1954, **76**, 4032.
[74] R. G. Cooke and W. Segal, *Austral. J. Chem.*, 1955, **8**, 413.
[75] I. C. Paul and G. A. Sim, *Proc. Chem. Soc.*, 1962, 352.

mers. Accordingly, 4-phenyl-6-hydroxyphenalenone (107) affords two methyl ethers.[74] (*b*) 4- (108) and 7-Hydroxyphenalenone (109) are tautomers of one another.[19,74] Methylation gives a mixture of 4- and 7-methoxyphenalenone.[74] The first of these ethers has been synthesised unambiguously by alternative routes.[20,31] (*c*) 2-, 5-, and 8-Hydroxyphenalenone cannot tautomerise. Only the first (110) is known. It is formed by the base-catalysed condensation of the ketone (68) with *p*-nitrosodimethylaniline followed by acid hydrolysis,[76] and by rearrangement of 2,3-epoxyphenalenone (111) with acid.[12]

6,3. Reactions of Phenalenones.—The abnormal polarisation of phenalenones modifies the ketonic properties. Phenalenone forms a hydrazone in boiling glycol,[18] but not a 2,4-dinitrophenylhydrazone. Hydrogen peroxide with sodium carbonate in ethanol gives the epoxide (111).[12] The 2,3-double bond of phenalenone is unreactive as a dienophilic centre, unless further activated, for example, as in the 3-carboxy-derivative.[12] Phenalenones undergo 1,4-addition with organometallic reagents.[54,77] Position 9 is involved. Aromatisation frequently follows addition. Thus, phenalenone with phenylmagnesium bromide gives the intermediate (112) which, when distilled, dehydrogenates to 9-phenylphenalenone.[54] 9-Substituted phenalenones also result from the reactions of 3-hydroxy- and 3-ethoxy-phenalenone with organometallic reagents.[77–79]



[76] N. P. Buu-Hoï and P. Cagniant, *Revue Sci.*, 1942, **80**, 271.
[77] C. F. Koelsch and R. H. Rosenwald, *J. Amer. Chem. Soc.*, 1938, **59**, 2166.
[78] C. F. Koelsch and R. H. Rosenwald, *J. Org. Chem.*, 1938, **3**, 462.
[79] E. Calderera, *Gazzetta*, 1913, **43**, 632.

Phenalenone condenses with two molecules of 2,4-dimethylpyrrole in ethanolic hydrogen bromide to give a blue salt, formulated as (113).[80]

The bromine atom in 2-bromophenalenone is inert to silver acetate,[12] but is replaceable by primary or secondary amino-groups, in some cases with rearrangement.[81] Treatment with piperidine at 85° gives 2-piperidinophenalenone (115) as the major product, but at 25° the 3-piperidino-derivative (114) is obtained. Parallel behaviour is shown with morpholine. With cyclohexylamine, however, the azirine (116) was isolated; this with acid gave 2-cyclohexylaminophenalenone. The annexed mechanism has been suggested. Detailed stereochemical information is lacking.

6,4. Hydroxyphenalenium Salts and Related Compounds.—The long known[2] basicity of phenalenone depends on the stability of the conjugate acid (117), a derivative of the phenalenium cation, which is formed when phenalenone dissolves in strong acids. The ultraviolet spectrum of phenalenone in 60% sulphuric acid is similar to that of phenalenium perchlorate.[41] Phenalenone with triethyloxonium fluoroborate gives 1-ethoxyphenalenium fluoroborate (118)[64,82] whose ultraviolet and nuclear magnetic resonance spectra correlate well with those of 1-methoxyphenalenium perchlorate.[7,64] The salt (118) reacts with secondary amines to form 1-dialkylaminophenalenium salts (119),[64] and with the sodium salt of malononitrile or cyanoacetic ester to yield compounds of the type (120).[82]

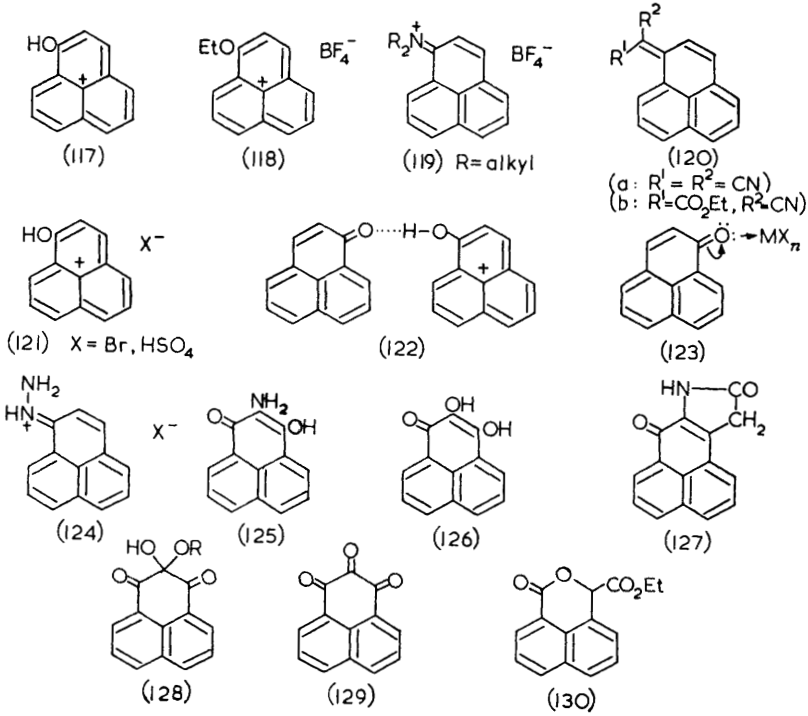
While solutions of phenalenone in acids contain the cation (117) the molecular ratio of ketone to acid in the solid salts varies. Hydrogen bromide and sulphuric acid give 1-hydroxyphenalenium salts (121),[83] but perchloric and tetrachloroferric acid give 2:1 compounds,[84] possibly containing the hydrogen-bridged cation (122).

Phenalenone reacts with inorganic halides ($AlCl_3$, $SbCl_5$, $SbCl_3$, $HgCl_2$, $SnCl_4$, PCl_5) to form 1:1 co-ordination compounds (123).[84,85] The phenalenone moiety in these substances is substantially polarised, as shown by the high dipole moment of the complex with $SbCl_5$ (8·49D). The acceptance of an electron pair of the oxygen atom by the metal atom disperses the negative charge and promotes the ground-state polarisation of the phenalenone. Similar compounds are formed with dinitrogen tetroxide[86,87] and sulphur trioxide.[88] Phenalenone is recovered from all these compounds by

[80] E. Herrmann, A. Treibs, and E. Meissner, *Annalen*, 1958, **612**, 229.
[81] D. B. Capps, N. H. Cromwell, and S. E. Palmer, *J. Amer. Chem. Soc.*, 1951, **73**, 1226; N. H. Cromwell, *J. Amer. Chem. Soc.*, 1959, **81**, 4706.
[82] H. Prinzbach and V. Freudenberger, *Angew. Chem. Internat. Edn.*, 1965, **4**, 243.
[83] A. M. Lukin, *Bull. Acad. Sci. U.R.S.S.*, 1941, **29**, 411.
[84] G. B. Silberman and S. M. Barkov, *Zhur. obshchei Khim.*, 1937, **7**, 1733.
[85] O. E. Shelepin and Y. A. Zhdanov, *Izvest. Vysshikh Ucheb.*, 1960, **3**, 1036.
[86] A. M. Lukin and L. D. Dachevskaya, *Compt. rend. Acad. Sci.*, 1947, **55**, 825.
[87] A. M. Lukin and L. D. Dachevskaya, *Zhur. obschei Khim.*, 1948, **18**, 1703.
[88] A. M. Lukin and G. B. Zavarikhina, *Compt. rend. Acad. Sci.*, 1947, **55**, 617.

hydrolysis. Phenalenone hydrazone forms salts (124) with acids, and co-ordination compounds with metal halides.[89]

With bromine in benzene or acetic acid at room temperature, phenalenone forms an orange-yellow complex, $C_{13}H_{10}O,Br_2$,[90] from which it is recovered by treatment with thiosulphate or upon attempted recrystallisation.[91,92] In boiling benzene, however, a colourless compound is obtained, formulated as (76), which when treated with ethanolic ammonia or simply on being boiled in acetic acid gives 2-bromophenalenone.[91,92] Similar behaviour is shown when phenalenone is treated with chlorine.[93] The nature of the intermediates in these reactions is by no means certain.



6,5. Miscellaneous.—The reaction of 3-hydroxyphenalenone with phenylhydrazine does not produce a phenylhydrazone; instead, the amino-ketone (125) and aniline are formed.[94] Acid hydrolysis of the amino-ketone (125) gives 2,3-di-hydroxyphenalenone (126) whose *N*-acetyl derivative is reported to cyclise to the heterocycle (127).[94] Oxidation of the diol (126)

[89] O. E. Shelepin and Y. A. Zhdanov, *Izvest. Vysshikh Ucheb. Zavedenii*, 1959, **2**, 200.
[90] K. Brass and E. Clar, *Ber.*, 1939, **72**, 1882.
[91] A. M. Lukin, *Compt. rend. Acad. Sci. U.R.S.S.*, 1940, **28**, 60.
[92] A. M. Lukin, *Bull. Acad. Sci. U.R.S.S.*, 1941, **29**, 695.
[93] A. M. Lukin, *Bull. Acad. Sci. U.R.S.S.*, 1941, **29**, 565.
[94] G. Errera, *Gazzetta*, 1914, **44**, 18; G. Errera, *ibid.*, 1913, **43**, 583.

with hypobromous acid gives the yellow trione hydrate (128; R = H) which when heated loses water reversibly to give the red trione (129).[94] The hydrate or hemiketal (128; R = H or Et), heated with ethanolic sodium carbonate, ring-contracts to a mixture of acenaphthenequinone and the lactone (130).[95] The trione (129), when heated with selenium in air, also gives acenaphthenequinone.[96]

The trione (129) behaves normally with *o*-phenylenediamine, forming a quinoxaline, but is reduced to the diol (126) with hydroxylamine or phenylhydrazine. It may be used as an alternative to ninhydrin in the detection and quantitative estimation of α-amino acids.[97] Carbon dioxide, ammonia, and an aldehyde or ketone are produced. Primary amines are also degraded to aldehydes.[98] The trione (129) has also been employed in the quantitative determination of ascorbic acid and other reductones in biological samples.[99]

7. Naturally Occurring Phenalenones

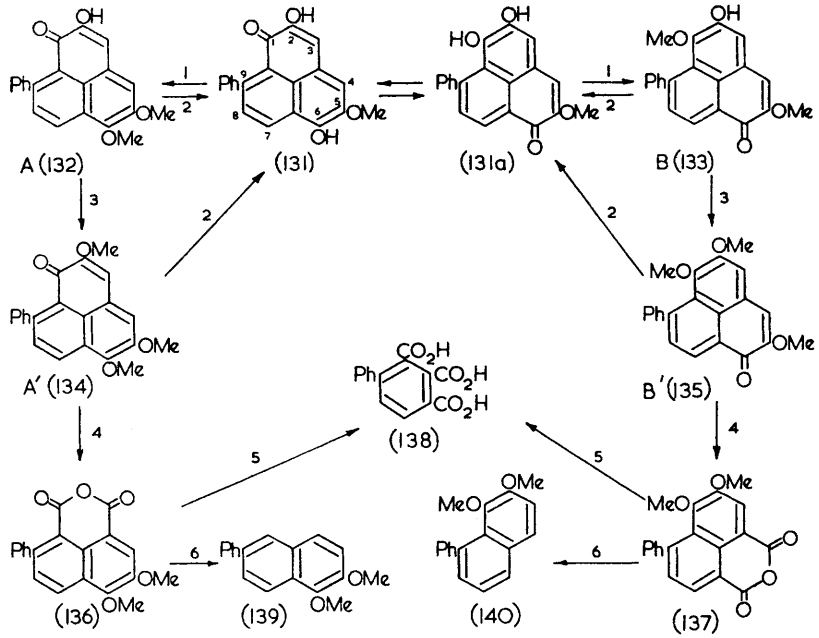
The presence of the phenalenone nucleus in a naturally occurring compound, the plant pigment hæmocorin, was first recognised in 1955. Shortly afterwards the constitution of several fungal pigments was found to be based on the phenalenone structure. None of these compounds has yet been synthesised.

7,1. Plant Pigments.—*Hæmocorin.*[25,74,100] This, the only plant pigment known to contain the phenalenone nucleus, is the red colouring matter of the roots of *Hæmodorum corymbosum* Vahl., one of about seventeen species of the genus *Hæmodorum* which is found in Australia. The plant is reputed to be toxic to livestock. The roots when roasted have been used as food by the aborigines, and the plants medicinally.

Hæmocorin is a glycoside which crystallises as the hydrate $C_{32}H_{34}O_4$, H_2O. Acid hydrolysis gives a purple-red aglycone $C_{20}H_{14}O_4$ and cellobiose.[100] The aglycone (131) contains one methoxyl group, forms a diacetate, and is a weak acid giving a blue colour with alkali. Methylation gave a mixture of monomethyl ethers *A* (132) and *B* (133), $C_{21}H_{16}O_4$. Each ether on further methylation gave a dimethyl ether *A'* (134) and *B'* (135) $C_{22}H_{18}O_4$, respectively. The aglycone did not form carbonyl derivatives. Monomethyl ether *B* showed infrared absorption in Nujol at 1620 cm.$^{-1}$, indicating the presence of a carbonyl group, and broad absorption at

[95] G. Errera and G. Ajon, *Gazzetta*, 1914, **44**, 92.
[96] A. Mostafa, R. Moubasher, and A. Schönberg, *J.*, 1946, 966.
[97] W. I. Awad and R. Moubasher, *J. Biol. Chem.*, 1949, **179**, 915; W. I. Awad and R. Moubasher, *J.*, 1949, 1137; A. Mostafa, R. Moubasher, and A. Schönberg, *J.*, 1948, 476.
[98] R. Moubasher and A. M. Othman, *J. Amer. Chem. Soc.*, 1950, **72**, 2666.
[99] R. Moubasher, *J. Biol. Chem.*, 1948, **176**, 529; Z. F. Hassan, R. Moubasher, and M. S. El-Ridi, *Biochem. J.*, 1951, **49**, 246.
[100] R. G. Cooke and W. Segal, *Austral. J. Chem.*, 1955, **8**, 107.

3200 cm.$^{-1}$ due to intermolecular hydrogen-bonded hydroxyl. In chloroform, however, the hydroxyl absorption at 3519 cm.$^{-1}$ was sharp. Monomethyl ether *A* showed evidence of internal hydrogen bonding, since the hydroxyl absorption in chloroform (3387 cm.$^{-1}$) was broad and little different from that in Nujol. These and other physical properties suggested that the aglycone was an extended tautomeric system containing a 1,2-dicarbonyl structure.



Oxidation of the dimethyl ether *A′* gave a neutral compound $C_{20}H_{14}O_5$ containing two methoxyl groups, indicated to be a derivative (136) of naphthalic anhydride by its characteristic infrared absorption at 1764 and 1727 cm.$^{-1}$, and by its chemical behaviour. Thus it dissolved in alkali, and acidification gave a colourless acid which lost water giving back the anhydride upon attempted recrystallisation, but which formed a dimethyl ester with diazomethane. Parallel behaviour was shown by the dimethyl ether *B′* which gave an isomeric anhydride (137). Both anhydrides and the aglycone showed infrared absorption characteristic of the unsubstituted phenyl group (700 and 750 cm.$^{-1}$). The foregoing data, taken with the composition, indicated that these compounds are phenyldimethoxynaphthalic anhydrides. Comparison of the ultraviolet spectra of the anhydrides and the derived dimethyl ethers with those of model compounds

supported those conclusions, as did further oxidation of the anhydrides (136) and (137), both of which gave the acid (138).

The accumulated evidence at this stage suggested that the aglycone is a dihydroxymethoxyphenylphenalenone. Ultraviolet spectral studies of model hydroxyphenalenones showed that different arrangements of hydroxyl (methoxyl) substituents in the phenalenone nucleus can be clearly distinguished, and it was concluded that the aglycone is a derivative of 2,5,6-trihydroxyphenalenone. It remained to determine the position of the phenyl and methoxy-substituents. This was obtained as follows. The anhydrides (136) and (137) gave upon decarboxylation the dimethoxyphenylnaphthalenes (139) and (140), respectively, whose structures followed from independent syntheses. Thus the phenyl group must occupy position 9 of structure (131). Monomethyl ether *A* and the dimethyl ether *A'* were oxidised to the same anhydride (136) which must therefore contain the methoxyl group of the original pigment. It follows that the methoxyl group in the aglycone occupies position 5. The structure of the aglycone is thus (131). The tautomeric structure (131a) is also possible, but structure (131) is favoured because it would be stabilised by internal hydrogen bonding (see section 6,2).

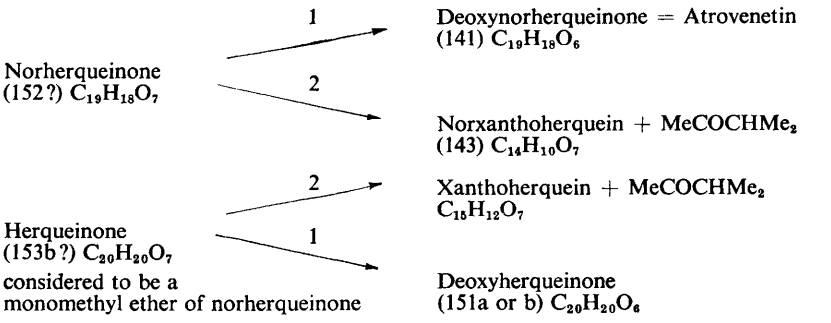
The position and stereochemistry of the glycoside link in hæmocorin have not been established. It seems, however, that the sugar is not attached to the hydroxyl group at position 6 (structure 131), since the ultraviolet spectrum of the glycoside resembles that of the aglycone monomethyl ether (133) rather than (132).

7,2. Fungal Pigments.—Several phenalenone pigments have been isolated from two series of the section Biverticillata Symmetrica of the genus *Penicillium*. Two of these compounds, herqueinone[101–103] and norherqueinone,[102] account in large measure for the colour of the mycelium of stationary cultures of *Penicillium herquei* Bainier and Sartory, while a third, atrovenetin,[104,105] is produced by *Penicillium atrovenetum* G. Smith. These pigments are chemically related,[106,107] but only the structure of atrovenetin has been fully elucidated.[107,108]

Information derived from the chemistry of herqueinone and norherqueinone was used in determining the structure of atrovenetin, the most important being summarised in Fig. 2. Atrovenetin is stable to acid but

[101] F. H. Stodola, K. B. Raper, and D. I. Fennel, *Nature*, 1951, **167**, 773.
[102] J. A. Galarraga, K. G. Neill, and H. Raistrick, *Biochem. J.*, 1955, **61**, 456.
[103] R. E. Harman, J. Cason, F. H. Stodola, and A. L. Adkins, *J. Org. Chem.*, 1955, **20**, 1260.
[104] K. G. Neill and H. Raistrick, *Chem. and Ind.*, 1956, 551.
[105] K. G. Neill and H. Raistrick, *Biochem. J.*, 1957, **65**, 166.
[106] D. H. R. Barton, P. de Mayo, G. A. Morrison, W. H. Schaeppi, and H. Raistrick, *Chem. and Ind.*, 1956, 552.
[107] D. H. R. Barton, P. de Mayo, G. A. Morrison, and H. Raistrick, *Tetrahedron*, 1959, **6**, 48.
[108] G. A. Morrison, I. C. Paul, and G. A. Sim, *Proc. Chem. Soc.*, 1962, 352; I. C. Paul and G. A. Sim, *J.*, 1965, 1097.

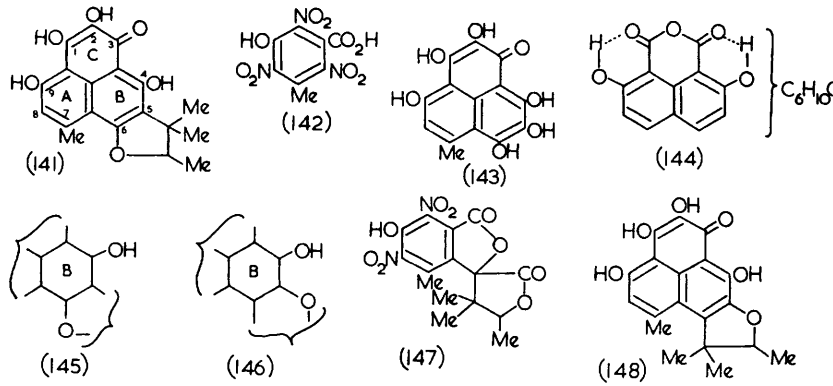
FIG. 2. Chemical relationship between atrovenetin, herqueinone, and norherqueinone



Reagents: 1, $Zn\text{–}CH_3{\cdot}CO_2H$; 2, H_3O^+.

herqueinone and norherqueinone break up into two fragments which together account for the total carbon content of the pigments.

Atrovenetin. Atrovenetin (141), $C_{19}H_{18}O_6$, is optically active, forms two tetramethyl ethers, thus showing the presence of potentially four hydroxyl groups, and contains an inert hydrogen-bonded conjugated carbonyl groups ($\nu_{C=O}$ 1620 cm.$^{-1}$). It also contains (Kühn–Roth) three *C*-methyl groups. The tetramethyl ethers are insoluble in alkali, indicating the remaining oxygen function to be ethereal.[104,105]



Acid hydrolysis of herqueinone and norherqueinone, both of which are optically active, gave xanthoherquein ($C_{15}H_{12}O_7$) and norxanthoherquein ($C_{14}H_{10}O_7$), both of which are optically inactive, together with isopropyl methyl ketone.[102,103] This information suggested[107] that norxanthoherquein represents the atrovenetin nucleus, and that the five-carbon hydrolysis product contains both the ethereal oxygen atom and the asymmetric centre responsible for the optical activity of atrovenetin. These conclusions were supported by comparative ultraviolet spectral studies which also suggested that these pigments are derivatives of 9-hydroxyphenalenone.

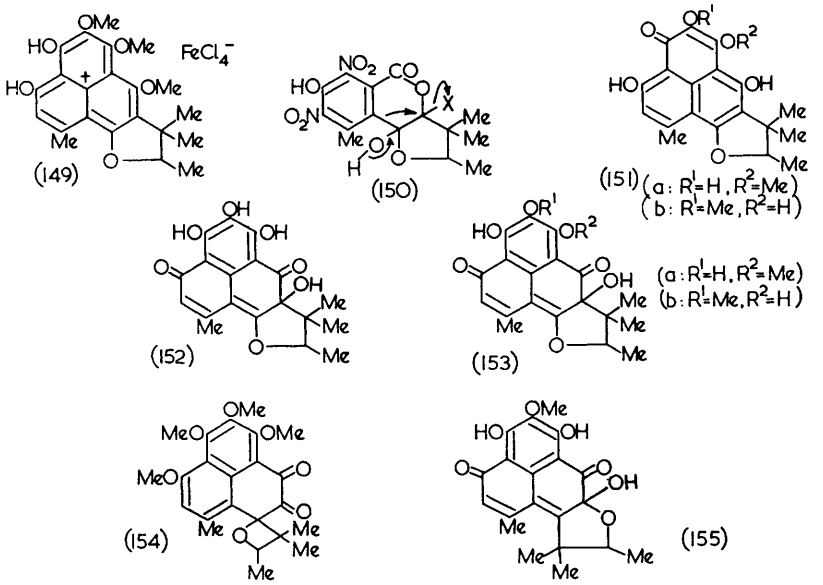
In order to establish the presence of the phenalenone nucleus, norxanthoherquein, xanthoherquein, and atrovenetin were degraded with concentrated nitric acid. All three gave nitrococussic acid (142). If norxanthoherquein is a phenalenone then the acid (142) must represent the ring which carries the methyl group and bears only one hydroxyl group. Since norxanthoherquein has seven oxygen atoms attached to the nucleus, every pheripheral carbon atom must be linked to oxygen except the angular ones, that one carrying the methyl group, and the C–H carbon which is nitrated during the oxidation. Norxanthoherquein must, therefore, be (143), and this taken with the already established inter-relationship of the pigments indicates that atrovenetin also contains the phenalenone nucleus.

Degradative studies of atrovenetin showed that the ether bridge is attached to ring B. Brief oxidation with alkaline hydrogen peroxide gave a compound $C_{18}H_{16}O_6$ which was optically active, formed a diacetate, and was assigned the part structure (144) with hydrogen bonding between hydroxyl and carbonyl on both sides of the anhydride ring. This assignment rested on the correspondence in position of the carbonyl bands of the anhydride (144) (1703 and 1660 cm.$^{-1}$) and 2,7-dihydroxynaphthalic anhydride (1720 and 1685 cm.$^{-1}$), and of the bands of the diacetate of the anhydride (144) (1750 and 1720 cm.$^{-1}$) and 2,7-diacetoxynaphthalic anhydride (1760 and 1720 cm.$^{-1}$).

The foregoing evidence restricts the mode of fusion of the ether ring of atrovenetin to the two possibilities (145) and (146). The latter was favoured because oxidation of atrovenetin with nitric acid had given,[104,105] together with the acid (142), a phenolic product to which structure (147) was assigned on the basis of chemical and spectral studies. Atrovenetin was therefore assigned structure (148). However, subsequent *X*-ray crystallographic studies[108] showed that the ferrichloride of a trimethyl ether of atrovenetin possesses the phenalenium structure (149), thus establishing conclusively structure (141) for atrovenetin. It is apparent that a skeletal rearrangement must have occurred during the nitric acid degradation of atrovenetin, through, it is suggested,[108] the intermediate (150) as shown. Deoxyherqueinone has been shown to possess structure (151a or b).[107,108]

Herqueinone and Norherqueinone. These compounds possess the same skeleton as atrovenetin[106,107] but contain an extra atom of oxygen. They are also unstable to acid, as already noted, in contrast to atrovenetin which is stable. It has been suggested that the extra oxygen atom in herqueinone and norherqueinone is situated at a tertiary position such that it blocks the aromatic conjugation of the system present in atrovenetin.[106,107] Reduction of norherqueinone to atrovenetin (Fig. 2) removes this conjugation barrier. Structure (152) has been suggested for norherqueinone; this would account for the reduction to atrovenetin and the acid-catalysed cleavage to norxanthoherquein (143) and isopropyl methyl ketone. Since deoxyherqueinone has structure (151a or b), herqueinone would then be

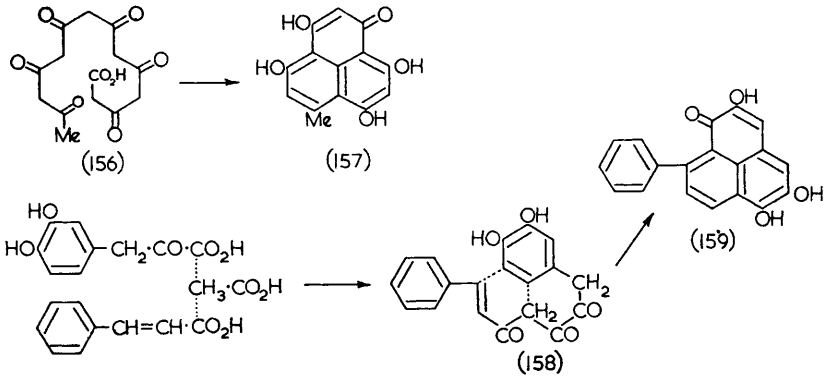
(153a or b). Cason and his co-workers arrived at structure (154) for a trimethyl ether of herqueinone on the basis of degradation and nuclear magnetic resonance studies, thence deducing structure (155) for herqueinone.[109] Since the arguments leading to this structure were based on formula (148) for atrovenetin, Cason's structure for herqueinone becomes identical to the alternative (153b) suggested by Paul and Sim.[108]



8. Biosynthesis of Naturally Occurring Phenalenones

Since the structurally similar atrovenetin, herqueinone, and norherqueinone have their origin in closely related fungal species, it seems reasonable to expect their carbon skeletons to arise by the same biosynthetic mechanism. Barton suggested that the origin of the phenalenone nucleus is a poly-β-diketone system, possibly (156), and the ether ring in atrovenetin is derived from a mevalonic acid precursor.[107] Alternatively, one or more of the three rings might arise from shikimic acid.[110] Barton's scheme was shown to be correct by the results of degradative experiments on ^{14}C-labelled norherqueinone, produced by feeding *Penicillium herquei* with sodium [1-^{14}C]acetate and DL-[2-^{14}C]mevalonic acid lactone in parallel experiments.[110] The norherqueinone was hydrolysed by acid to norxanthoherquein and isopropyl methyl ketone for radioassay. The norxanthoherquein from both experiments was degraded (Kühn–Roth) to acetic acid and carbon dioxide. The sodium [1-^{14}C]acetate-derived

[109] J. Cason, J. S. Correia, R. B. Hutchison, and R. F. Porter, *Tetrahedron*, 1962, 839.
[110] R. Thomas, *Biochem. J.*, 1961, **78**, 807.



norherqueinone contained two-ninths of the total activity in the side chain and one ninth in the methyl-substituted carbon atom of the norxanthoherquein nucleus; the methyl group itself was inactive. The carbon dioxide accounted for the remaining activity. The DL-[2-^{14}C]mevalonic acid lactone-derived norherqueinone on the other hand contained all its activity in the side-chain. Hypohalite degradation of isopropyl methyl ketone from both experiments showed that one-half of the activity resided in the non-*gem*-methyl group. These results demonstrate the isoprenoid nature of the side-chain, the mevalonate precursor arising from acetate, probably by way of β-hydroxy-β-methylglutarylcoenzyme A. Acetate is incorporated into the aromatic nucleus and the isoprenoid ether ring to the same extent.

Although the foregoing results are consistent with the derivation of the phenalenone nucleus (157) from the suitably coiled linear structure (156), formation from a branched structure is not ruled out. It is interesting that the presumption of normal head-to-tail linking of acetate units predicted the recently revised structure (141), which moreover contains more β-orientated oxygen substituents. The biosynthetic mechanism whereby the C-2 hydroxyl group is introduced into these pigments remains to be elucidated. The anhydride (144) has been isolated from cultures of *Penicillium herquei* along with atrovenetin, herqueinone, and norherqueinone.[111]

A different biosynthetic mechanism has been suggested for the formation of hæmocorin, since this pigment contains two sets of *ortho*-oxygen substituents, which is unusual among acetate-derived phenols.[110] An intermediate (158) is envisaged as arising from two shikimic acid-derived C_6–C_3 units, namely, cinnamic and 3,4-dihydroxyphenylpyruvic acid. These substitute into the methyl group of an acetate unit before decarboxylation and ring-closure to the nucleus (159) of the hæmocorin aglycone.

[111] N. Narasimhachari and L. C. Vining, *Canad. J. Chem.*, 1963, **41**, 641.