556. *Polynuclear Heterocyclic Systems. Part VII.* Syntheses using the Elbs Reaction.*

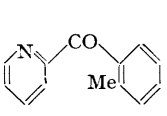
By G. M. Badger and R. Pettit.

Three aryl pyridyl ketones and two aryl quinolyl ketones have been prepared and pyrolysed according to Elbs's method. In three cases extensive decomposition took place and no pure product could be isolated; but 3-*o*-toluoylquinoline (II) gave 5 : 10-dihydro-2 : 3-benzacridine (V), and 2-(2-methyl-1-naphthoyl)pyridine (VI) gave 9-hydroxy-8-aza-1 : 2-benzanthracene (VII).

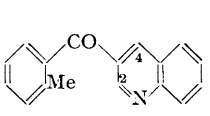
The mechanism of the Elbs reaction is discussed and a free-radical mechanism is proposed.

The Elbs reaction has been extensively used for the preparation of polycyclic aromatic hydrocarbons. It involves the elimination of water from an *o*-methyldiaryl ketone by pyrolysis; although the yields are often poor, this is usually offset by the ready availability of the intermediate ketones. Little use has so far been made of this reaction for the preparation of polynuclear heterocyclic compounds, although Fieser and Hershberg (*J. Amer. Chem. Soc.*, 1940, **62**, 1640) have prepared 4'-aza-1 : 2-benzanthracene from 7-methyl-4-indanyl 5-quinolyl ketone. The reaction has, however, been made to provide a number of polycyclic derivatives of thiophen (Buu-Hoï and Hoán, *Rec. Trav. chim.*, 1948, **67**, 309). Two carbazole derivatives have also been prepared by pyrolysis of 3-aroyl-2-methylindoles, but several ketones of this type underwent extensive decomposition and gave tars (Buu-Hoï, Hoán, and Khôi, *J. Org. Chem.*, 1950, **15**, 131). These few examples all involved cyclisation into a carbocyclic ring, and there seems to have been no attempt to investigate the possibility of cyclisation into a ring containing a hetero-atom. The work now reported was undertaken in order to examine the possibilities of the method in this field and, at the same time, the mechanism of the reaction.

Three aryl pyridyl ketones and two aryl quinolyl ketones have been prepared, and it was hoped that these would undergo cyclisation into the heterocyclic ring to give aza-anthracenes or aza-benzanthracenes. Success was, however, limited. Water certainly was evolved on pyrolysis of 2-*o*-toluoylpyridine (I), but owing to extensive decomposition no pure product could be isolated. Similarly, no pure product could be isolated after pyrolysis of 3-(2-methyl-1-naphthoyl)pyridine and of 4-*o*-toluoylquinoline.



(I)



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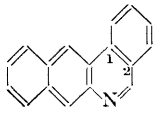

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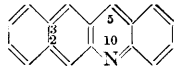

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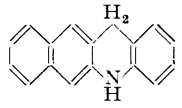


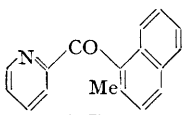
(V)

3-*o*-Toluoylquinoline (II) might undergo cyclisation at the 2- or the 4-position and yield 4-aza-1 : 2-benzanthracene (III) or 2 : 3-benzacridine (IV) respectively. In fact, the former took place and 5 : 10-dihydro-2 : 3-benzacridine (V) was isolated in 10% yield. It was identified by oxidation to 2 : 3-benzacridone.

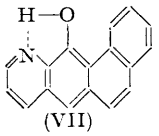
Pyrolysis of 2-(2-methyl-1-naphthoyl)pyridine (VI) gave a complex mixture from which a yellow crystalline compound was isolated. Although this contained one oxygen atom, it was insoluble in sodium hydroxide solution, was unaffected by zinc dust and boiling acetic anhydride, and could not be acetylated or benzoylated. It is suggested that it is 9-hydroxy-8-aza-1 : 2-benzanthracene (VII, or the tautomer, VII*a*), and that it was formed from the ketone (VI) by dehydrogenation rather than by dehydration. Such a compound would exhibit strong hydrogen-bonding between the hydroxyl group and the hetero-atom. Indeed, the pronounced conjugation between the hydroxyl group and the

* Part VI, *J.*, 1952, 1877.

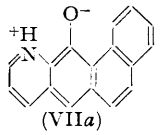
meso-position which would occur in such a structure would tend to make the hydrogen bond a very strong one, and hence depress all the hydroxyl group reactions (such as alkali solubility). As is well known, *o*-hydroxyazobenzenes are insoluble in alkali and can be acylated only with great difficulty.



(VI)



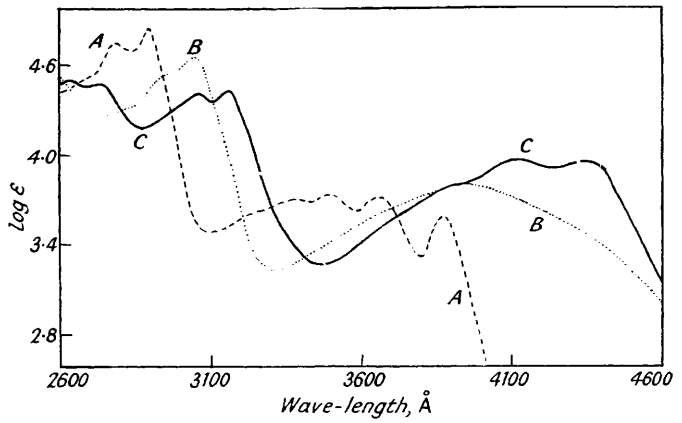
(VII)



(VII*a*)

The absorption spectrum of 9-hydroxy-8-aza-1 : 2-benzanthracene was unexpectedly different from that of 5-aza-1 : 2-benzanthracene (Badger, Pearce, and Pettit, *J.*, 1951, 3199) (see Figure), probably because the hydroxy-compound exists largely in the tauto-

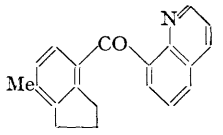
Absorption spectra of aza-benzanthracenes.

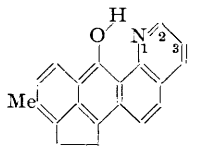


A, 5-*Aza*-1 : 2-*benzanthracene in ethanol* (Badger, Pearce, and Pettit, *loc. cit.*).
B, 5-*Aza*-1 : 2-*benzanthracene in alcoholic hydrochloric acid* (*prepared by diluting concentrated hydrochloric acid with alcohol to give a solution containing* 7·5% *of hydrogen chloride*).
C, 9-*Hydroxy*-8-*aza*-1 : 2-*benzanthracene in ethanol.*

meric form (VII*a*) in ethanol. This conclusion is strongly supported by the fact that its absorption spectrum *in ethanol* very closely resembles that of 5-aza-1 : 2-benzanthracene in *alcoholic hydrochloric acid*. The latter solution must contain the 5-aza-1 : 2-benzanthracene cation, and this structure very closely resembles the ionic form (VII*a*).

Fieser and Hershberg (*loc. cit.*) obtained an oxygenated compound having rather similar properties by pyrolysis of 7-methyl-4-indanyl 8-quinolyl ketone (VIII), and a similar hydrogen-bonded structure (IX) was proposed for it. They pointed out that the absorption spectrum of this substance (not reproduced by them) did not resemble that of the analogous substance, 20-methyl-4-azacholanthrene; the present work suggests that it may resemble that of the 20-methyl-4-azacholanthrene cation.

(VIII)




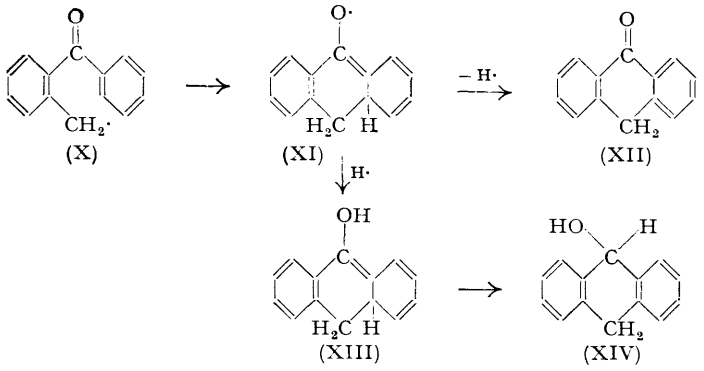
(IX)

The various heterocyclic ketones used in this investigation were prepared by condensing *o*-tolylmagnesium bromide or 2-methyl-1-naphthylmagnesium bromide with a cyanopyridine or cyanoquinoline. The resulting complexes were generally decomposed by boiling hydrochloric acid, and the required ketones obtained directly and in good yield. In a few cases

in which decomposition with ammonium chloride was attempted, the intermediate ketimines were isolated; these were hydrolysed to the ketones by boiling acid.

Mechanism of the Elbs Reaction.—Very little is known about the mechanism of the Elbs reaction (see, however, Fieser, "The Chemistry of Natural Products related to Phenanthrene," Reinhold Publ. Corp., New York, 2nd edn., p. 107; "Organic Reactions," 1942, Vol. I, p. 129), and none of the suggested mechanisms is completely satisfactory. Anthrones have often been obtained as by-products and have sometimes been the chief products (Morgan and Coulson, *J.*, 1931, 2323). It is difficult to explain their formation unless the intermediate dihydroanthranols undergo oxidation rather than dehydration, and this seems extremely unlikely. Moreover, Campbell, Marks, and Reid (*J.*, 1950, 3466) found that the pyrolysis of 4-*o*-toluoylfluoranthene gives some 4 : 5-*o*-xylylenefluoranthene as well as some of the expected product and it is difficult to see how the xylylene compound could arise by any mechanism involving addition to a diene system.

No catalyst has been found for the Elbs reaction, and the high temperature necessary suggests that it may be of free-radical nature. For these and other reasons, the following modification of the Fieser–Dietz mechanism is proposed. It is suggested that the first step is loss of a hydrogen atom from the activated methyl group to give a radical such as (X). Intramolecular substitution would give the intermediate (XI, and resonance structures) which could either lose a hydrogen atom to yield anthrone (XII) or undergo reduction to (XIII) and rearrangement to dihydroanthranol (XIV).



The nature of the ketone evidently determines which route is favoured, although both probably occur to some extent in most cases. Some of the anthrone formed might undergo reduction with two atoms of hydrogen to give dihydroanthranol, but the work of Hurd and Azorlosa (*J. Amer. Chem. Soc.*, 1951, **73**, 37) indicates that this route cannot be of great importance. Incidentally, the above mechanism satisfactorily accounts for the formation of hydroxy-aza-compounds (such as VII and IX), the intermediate being stabilised by hydrogen-bonding.

Although the evidence is still inconclusive there are several facts which support a free-radical mechanism. The presence of free hydrogen atoms during the reaction is supported by the fact that dihydro-aromatic compounds are often formed: pyrolysis of 4 : 6-dibenzoyl-1 : 3-xylene, for example, gives dihydropentacene as the major product (Clar and John, *Ber.*, 1929, **62**, 3021; 1931, **64**, 981); and in the present work 5 : 10-dihydro-2 : 3-benzacridine (V) was obtained by pyrolysis of (II). Finally, various by-products have been obtained in certain Elbs reactions which can only have been formed by decomposition of the ketones into free radicals and reduction with hydrogen atoms. Phenanthrene has been obtained from an aryl phenanthryl ketone (Fieser and Dietz, *loc. cit.*), anthracene from an anthryl aryl ketone (Clar, John, and Hawran, *Ber.*, 1929, **62**, 940), and 2-methylnaphthalene from 1-benzoyl-2-methylnaphthalene (present work). Pyrolysis of the last compound also gave some benzaldehyde; and benzoic acid and benzaldehyde have been detected on pyrolysis of 1 : 5-dibenzoyl-2 : 6-dimethylnaphthalene (Clar, Wallenstein, and Avenarius,

Ber., 1929, **62**, 950). The formation of all these products is consistent with the view that the ketone undergoes homolytic fission to some extent and that the fragments are reduced by hydrogen atoms.

Experimental

2-o-*Toluoylpyridine* (I).—To a Grignard solution from *o*-bromotoluene (37·5 g.), magnesium (5·3 g.), and anhydrous ether (150 c.c.), benzene (50 c.c.) was added, and the mixture distilled until the temperature rose to 55°. To the cooled mixture, a solution of 2-cyanopyridine (15 g.) [prepared from 2-aminopyridine (*Org. Synth.*, 1946, **26**, 16) by Craig's method (*J. Amer. Chem. Soc.*, 1934, **56**, 231)] in anhydrous benzene (50 c.c.) was slowly added with constant stirring. The mixture was then refluxed for 8 hr. (cf. Fieser and Bowen, *J. Amer. Chem. Soc.*, 1940, **62**, 2103), then poured on ice (200 g.) and ammonium chloride (160 g.), and the whole was refluxed for 2 hr. During this time the ether was removed. The aqueous solution was then discarded, the crude product taken up in benzene, and the benzene solution dried and evaporated. After distillation under reduced pressure (b. p. 180—200°/12 mm.) and crystallisation from light petroleum, 2-o-*toluoylpyridine* (12·0 g.) was obtained as colourless prisms, m. p. 69—70° (Found : C, 79·4; H, 5·7; N, 7·2. $C_{13}H_{11}ON$ requires C, 79·2; H, 5·6; N, 7·1%). The *picrate* formed yellow needles, m. p. 122—124°, from ethanol (Found : C, 53·45; H, 3·3. $C_{19}H_{14}O_8N_4$ requires C, 53·5; H, 3·3%).

2-(2-*Methyl*-1-*naphthoyl*)*pyridine*.—A Grignard solution from 1-bromo-2-methylnaphthalene (106·3 g.) (Adams and Binder, *J. Amer. Chem. Soc.*, 1941, **63**, 2773), magnesium (11 g.), anhydrous ether (300 c.c.), and anhydrous benzene (200 c.c.) was treated as above with 2-cyanopyridine (25 g.) in anhydrous benzene (200 c.c.) at 5°. Next morning the mixture was refluxed for 1 hr., cooled, and poured on ice (300 g.). Concentrated hydrochloric acid (100 c.c.) was added, and the mixture steam-distilled for 5 hr. The aqueous phase was discarded, and aqueous ammonia added to the residue. The product was taken up in chloroform (300 c.c.), and the solution washed and evaporated. After recrystallisation of the residue from light petroleum, 2-(2-*methyl*-1-*naphthoyl*)*pyridine* (39·5 g.) was obtained as colourless prisms, m. p. 126—128° (Found : C, 82·9; H, 5·4; N, 5·9. $C_{17}H_{13}ON$ requires C, 82·6; H, 5·3; N, 5·7%). The *picrate* formed yellow needles, m. p. 143—146°, from benzene (Found : C, 57·6; H, 3·65. $C_{17}H_{13}ON,C_6H_3O_7N_3$ requires C, 58·0; H, 3·4%).

In a preliminary run, the hydrolysis of the complex was attempted with ammonium chloride instead of hydrochloric acid. Hydrolysis was incomplete and the product was 2-*methyl*-1-*naphthyl* 2-*pyridyl ketimine*. It crystallised from light petroleum in colourless prisms, m. p. 84—86° (Found : C, 83·1; H, 5·8; N, 10·85. $C_{17}H_{14}N_2$ requires C, 82·9; H, 5·7; N, 11·4%). The *picrate* crystallised from ethanol in yellow prisms, m. p. 191—193° (Found : C, 58·2; H, 3·6. $C_{23}H_{17}O_7N_5$ requires C, 58·1; H, 3·6%). Hydrolysis with boiling alcoholic hydrochloric acid for 5 hr. gave 2-(2-methyl-1-naphthoyl)pyridine.

3-(2-*Methyl*-1-*naphthoyl*)*pyridine* (VI).—As in the previous experiment a Grignard solution from 1-bromo-2-methylnaphthalene (106·3 g.) was treated with 3-cyanopyridine (25 g.) (Adkins, Wolff, Pavlic, and Hutchinson, *J. Amer. Chem. Soc.*, 1944, **66**, 1293) in benzene (250 c.c.), at 5°, the mixture refluxed for 3 hr., and the yellow precipitate collected and added to crushed ice (200 g.). Concentrated hydrochloric acid (100 c.c.) was then added and the mixture steam-distilled for 4 hr., additional concentrated hydrochloric acid (100 c.c.) being added at half-hourly intervals. The aqueous solution was then discarded and the dark viscous material taken up in ether, washed with aqueous ammonia, and filtered. After drying, the ether was evaporated and the 3-(2-*methyl*-1-*naphthoyl*)*pyridine* distilled (b. p. 200—210°/14 mm.). It then crystallised during several weeks, and was recrystallised from light petroleum as prisms (22·5 g.), m. p. 97—98° (Found: C, 82·9; H, 5·5; N, 5·8. $C_{17}H_{13}ON$ requires C, 82·6; H, 5·3; N, 5·7%). The *picrate* crystallised from ethanol in yellow prisms, m. p. 183—184° (Found : C, 58·2; H, 3·2. $C_{23}H_{16}O_8N_4$ requires C, 58·0; H, 3·4%).

Use of ammonium chloride as above gave 2-*methyl*-1-*naphthyl* 3-*pyridyl ketimine*, prisms (from light petroleum), m. p. 97—98° (Found : C, 83·1; H, 5·6; N, 10·85. $C_{17}H_{14}N_2$ requires C, 82·9; H, 5·7; N, 11·4%).

3-*Cyanoquinoline*.—3-Bromoquinoline was prepared essentially as described by Claus and Collischonn (*Ber.*, 1886, **19**, 2763), except that 48% hydrobromic acid was used as solvent instead of ether, and gave 3-cyanoquinoline on treatment with cuprous cyanide by Gilman and Spatz's method (*J. Amer. Chem. Soc.*, 1941, **63**, 1553).

3-o-*Toluoylquinoline* (II).—A Grignard solution prepared from *o*-bromotoluene (66·6 g.), magnesium (9·4 g.) and anhydrous ether (300 c.c.) was added to a solution of 3-cyanoquinoline

(30 g.) in anhydrous benzene (250 c.c.), at 0°. The mixture was then stirred at 0° for an hr., refluxed for a further hr., and poured on crushed ice (200 g.). Concentrated hydrochloric acid (100 c.c.) was added, and the mixture steam-distilled for 4 hr. After cooling, the viscous residue was made alkaline with aqueous ammonia, dissolved in ether, and extracted with concentrated hydrochloric acid (3 × 100 c.c.). The acid extracts were made alkaline with ammonia, the liberated product taken up in ether, the ether evaporated and the residue distilled (b. p. 215—230°/14 mm.). The resulting pale yellow viscous oil (20 g.) solidified during several weeks and was recrystallised from light petroleum. 3-o-*Toluoylquinoline* formed plates, m. p. 80·5—81·4° (Found: C, 82·85; H, 5·3; N, 5·7. $C_{17}H_{13}ON$ requires C, 82·6; H, 5·3; N, 5·8%). The *picrate* crystallised from ethyl acetate in yellow plates, m. p. 209—210° (Found: C, 58·2; H, 3·4; N, 11·6. $C_{23}H_{16}O_8N_4$ requires C, 58·0; H, 3·4; N, 11·8%).

4-o-*Toluoylquinoline*.—A solution of *o*-tolylmagnesium bromide (76 g.) in anhydrous ether (250 c.c.) was added with constant stirring to a solution of 4-cyanoquinoline (30 g.) (Hamer, *J.*, 1939, 1008), in benzene (200 c.c.), at 5°, stirred for 1 hr., and gently refluxed for a further hr. It was then poured on crushed ice (200 g.), concentrated hydrochloric acid (100 c.c.) added, and the mixture steam-distilled for 4 hr. The residual tarry material was dissolved in ether, and washed several times with dilute aqueous ammonia, the ether evaporated off, and the product distilled (b. p. 195—215°/0·5 mm.). The resulting viscous 4-o-*toluoylquinoline* (30 g.) slowly crystallised and recrystallised from light petroleum as prisms, m. p. 63—64·5° (Found: C, 82·9; H, 5·5; N, 5·8%). The *picrate* crystallised from ethanol in bright yellow plates, m. p. 191—192° (Found: C, 58·4; H, 3·8; N, 11·2%).

Pyrolysis of the Ketones.—(i) Preliminary experiments were carried out on the pyrolysis of 1-benzoyl-2-methylnaphthalene under a variety of conditions. The fore-run obtained on pyrolysis at 360° for 7 hr. contained benzaldehyde (identified as the 2 : 4-dinitrophenylhydrazone) and 2-methylnaphthalene (identified as the picrate). Extraction of the residue with benzene and chromatography on alumina gave 0·75 g. of 1 : 2-benzanthracene.

(ii) 2-(2-Methyl-1-naphthoyl)pyridine (5 g.) was heated in a small distillation flask in a metal-bath at 280°. After 2 hr. evolution of water had ceased, and the residue was distilled at 1 mm. Alcohol (2 c.c.) was added to the dark red viscous distillate, and the solid which separated (0·5 g.) was collected. After recrystallisation from benzene 9-*hydroxy*-8-*aza*-1 : 2-*benzanthracene* formed yellow needles, m. p. 184·5—185·5° (Found: C, 83·4; H, 4·4; N, 5·8. $C_{17}H_{11}ON$ requires C, 83·25; H, 4·5; N, 5·7%). It dissolved in alcohol, benzene, and chloroform to give yellow solutions with a yellow-green fluorescence.

(iii) 3-*o*-Toluoylquinoline (5 g.) was heated at 380—400° for 4 hr. The residue was distilled at 1 mm., and the dark red, viscous distillate triturated with alcohol. The resulting solid was collected (0·5 g.), and after recrystallisation from chloroform 5 : 10-dihydro-2 : 3-benzacridine formed colourless needles, m. p. 285° (rapid heating) (Found: C, 88·4; H, 5·7; N, 6·2. Calc. for $C_{17}H_{13}N$: C, 88·3; H, 5·7; N, 6·1%). It also crystallised from benzene in pale orange plates, m. p. 285° (rapid heating).

Oxidation with potassium dichromate in boiling glacial acetic acid followed by sublimation of the product and recrystallisation from glacial acetic acid gave 2 : 3-benzacridone as orange-yellow, m. p. 304° in agreement with the literature (Schöpff, *Ber.*, 1893, **26**, 2589).

(iv) The remaining ketones were pyrolysed under a variety of different conditions of time and temperature. Water was invariably evolved, and a small yield of a dark viscous oil was obtained on distillation. No pure product could, however, be isolated.

Absorption Spectra.—These were determined with a Hilger Uvispek spectrophotometer.

Microanalyses were carried out by the C.S.I.R.O. Microanalytical Laboratory, Melbourne.

UNIVERSITY OF ADELAIDE. [*Received, January 23rd*, 1953.]