# 706. *Polynuclear Heterocyclic Systems. Part III.* The 3 : 4-Benzacridine–5 : 10-Dihydro-3 : 4-benzacridine Complex.*

By G. M. Badger, J. H. Seidler, and B. Thomson.

The reduction of 3 : 4-benzacridone with lithium aluminium hydride has been shown to give an orange molecular complex of 3 : 4-benzacridine and its 5 : 10-dihydro-derivative. The same reagent reduced phenanthridone and 9-chlorophenanthridine to 9 : 10-dihydrophenanthridine, which was dehydrogenated over palladium to phenanthridine in good yield. 3 : 4-Benzocinnoline has been obtained by reduction of its *N*-oxide with lithium aluminium hydride, and also, in one step, by reduction of 2 : 2′-dinitrodiphenyl.

One of the most interesting properties of phenazine is that it forms a deep blue crystalline complex with dihydrophenazine. Certain derivatives of phenazine also form such complexes, which have been known as " phenazhydrins," and it is significant that the complex formed from phenazine and 9 : 10-dihydro-1-methylphenazine is identical with that formed from 9 : 10-dihydrophenazine and 1-methylphenazine (Clemo and McIlwain, *J.*, 1934, 1991). Relatively few complexes of this nature have been reported, however, although " Morgan's base " has recently been shown to be a molecular complex of 3 : 4-6 : 7-dibenzacridine and 5 : 10-dihydro-3 : 4-6 : 7-dibenzacridine (Blout and Corley, *J. Amer. Chem. Soc.*, 1947, **69**, 763). The present paper records the ready preparation of an orange complex between 3 : 4-benzacridine (I) and its 5 : 10-dihydro-derivative.

The 3 : 4-benzacridine–5 : 10-dihydro-3 : 4-benzacridine complex was obtained by two different methods : (i) in quantitative yield by reduction of 3 : 4-benzacridone with lithium aluminium hydride, and (ii) by dehalogenation of 5-chloro-3 : 4-benzacridine with hydrogen and Raney nickel. In (ii) it was accompanied by the colourless 5 : 10-dihydro-3 : 4-benzacridine, from which it was separated by chromatography on alumina.

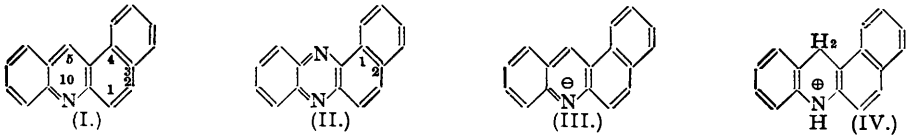
The nature of the complex follows from the following facts. When treated with hydrochloric acid, part of the material dissolved. The acid-insoluble part was identified as the (non-basic) 5 : 10-dihydro-3 : 4-benzacridine by comparison with an authentic specimen, and the acid-soluble part, after precipitation with alkali and recrystallisation from alcohol, was similarly identified as 3 : 4-benzacridine (I). Moreover, the orange complex was obtained without difficulty by mixing equimolecular quantities of 3 : 4-benzacridine and 5 : 10-dihydro-3 : 4-benzacridine, in alcoholic solution. Finally, the absorption spectrum of the complex (Fig. 1) shows that, like " phenazhydrin," it is dissociated into its components in alcoholic solution.

Clemo and McIlwain (*loc. cit.*) stated that acridine does not form a complex with acridan, and this observation has now been confirmed. Furthermore, a complex could not be obtained between phenanthridine and 9 : 10-dihydrophenanthridine. Attempts to prepare a complex between 1 : 2-benzophenazine (II) and 9 : 10-dihydro-1 : 2-benzophenazine were frustrated by

* Part II, preceding paper.

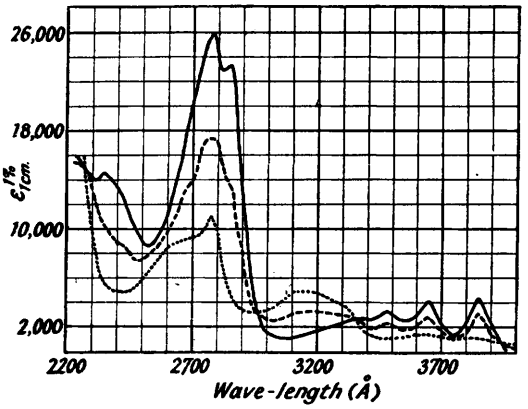
the fact that the latter appears to be unstable, all attempts at reduction of 1 : 2-benzophenazine yielding either unchanged material or a more highly reduced compound.

The available evidence indicates that complexes are formed only when the dihydro-compound has an optimum degree of stability, and the aromatic component an optimum degree of electro-




negativity. The complexes seem to be very closely related to the quinhydrones, and to be formed by electron transfer from the dihydro-compound to the aromatic compound (Weiss, *J.*, 1942, 245; 1943, 462; 1944, 464). The application of this concept to the 3 : 4-benzacridine–5 : 10-dihydro-3 : 4-benzacridine complex gives the two ions (III and IV). Each ion would be stabilised by resonance, and the complex can be pictured as being built up of successive layers of planar molecules having positive or negative charges " smeared out " over the whole of the conjugated systems, the molecules being held together by electrostatic attraction. The " phenaz-

FIG. 1.




*Absorption spectra of* 3 : 4-*benzacridine* (———), *of* 5 : 10-*dihydro*-3 : 4-*benzacridine* (– – – – –), *and of the complex* (. . . . . ), *all in alcoholic solution. The spectra are plotted on a* $\epsilon^{1\%}_{1\,cm.}$ *scale and show four isosbestic points* (*at* 2280, 2950, 3350, *and* 3920 Å).

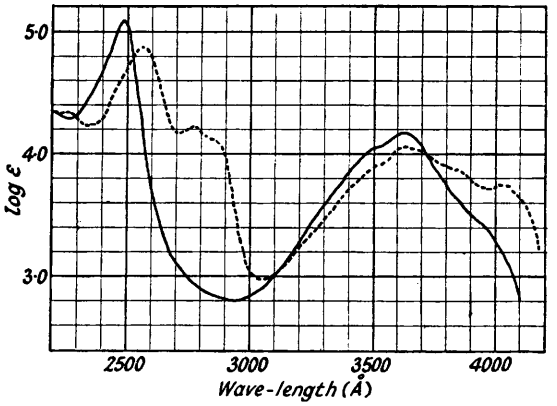
hydrins " are deeper in colour than the acridine complexes, and this seems reasonable in view of the fact that the former compounds have twice as many nitrogen atoms and increased possibilities of resonance.

For the preparation of 3 : 4-benzacridone and of 5-chloro-3 : 4-benzacridine, *o*-chlorobenzoic acid was first condensed with 2-naphthylamine (Bachman and Picha, *J. Amer. Chem. Soc.*, 1946, **68**, 1599), and the resulting naphthylanthranilic acid cyclised. 3 : 4-Benzacridone was obtained by Ullmann's method (*Annalen*, 1907, **355**, 312), but 5-chloro-3 : 4-benzacridine was obtained directly by use of phosphorus oxychloride. As already mentioned, dehalogenation with hydrogen and Raney nickel gave a mixture of the 3 : 4-benzacridine–5 : 10-dihydro-3 : 4-benzacridine complex and 5 : 10-dihydro-3 : 4-benzacridine. The latter was smoothly oxidised to 3 : 4-benzacridine with dichromate (compare Albert and Willis, *J. Soc. Chem. Ind.*, 1946, **65**, 26), and the present synthesis of this compound constitutes a distinct improvement on Ullmann's method (*loc. cit.*).

Several methods for the preparation of phenanthridone were investigated. The Schmidt reaction on fluorenone (Walls, *J.*, 1935, 1405; Smith, *J. Amer. Chem. Soc.*, 1948, **70**, 320) gave a good yield, but the method is not very suitable on a large scale. The same criticism applies to the formation of phenanthridone by the action of hydrazoic acid on diphenic acid, although the yield is good (cf. Caronna, *Gazzetta*, 1941, **71**, 475; Stephenson, *J.*, 1949, 2620). The most satisfactory method proved to be that of Oyster and Adkins (*J. Amer. Chem. Soc.*, 1921, **43**, 208) involving the conversion of diphenic acid into its anhydride, and then into diphenamic acid and phenanthridone.

There seems to be no really satisfactory method for the conversion of phenanthridone into phenanthridine on a large scale. Albert, Brown, and Duewell (*J.*, 1948, 1284) obtained phenanthridine by dehalogenation of 9-bromophenanthridine with hydrogen and Raney nickel, and it seemed that a modification of this method would be suitable. Accordingly, 9-chlorophenanthridine was prepared by an improved process involving the addition of dimethylaniline to the reaction mixture; but all attempts to dehalogenate this compound either with very " reactive " Raney nickel (Adkins and Billica, *J. Amer. Chem. Soc.*, 1948, **70**, 695) and hydrogen, or with catalyst prepared by the ordinary method (*Org. Synth.*, 1941, **21**, 15) and " aged " for some weeks, gave 9 : 10-dihydrophenanthridine. Attempts to interrupt the hydrogenation did not give satisfactory results. Another dehalogenation method tried involved the use of toluene-*p*-sulphonhydrazide, as suggested by Albert and Royer (*J.*, 1949, 1148) for the dehalogenation of 5-chloroacridines. The method proved rather unsatisfactory in this case, and phenanthridine was obtained in only 30% yield. The use of lithium aluminium hydride was also investigated. 9-Chlorophenanthridine was reduced to 9 : 10-dihydrophenanthridine with lithium aluminium hydride, and the reduction of phenanthridone to dihydrophenanthridine proceeded very smoothly and in good yield. At first sight the latter result appears to be at variance with the work of de Mayo and McKee (*Nature*, 1950, **166**, 1075), who obtained phenanthridine on reduction of phenanthridone with lithium aluminium hydride. However,

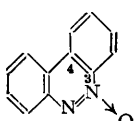
FIG. 2.




*Absorption spectra of* 1′ : 2′ : 3′ : 4′-*tetrahydro*-1 : 2-*benzophenazine* (– – – – –) *and of phenazine* (———), *both in alcoholic solution.*

these workers evidently used only the theoretical quantity of lithium aluminium hydride. In the present work, a large excess was used, and the fact that dihydrophenanthridine was obtained is in agreement with the work of Wooten and McKee (*J. Amer. Chem. Soc.*, 1949, **71**, 2946), who found that phenanthridine is reduced to 9 : 10-dihydrophenanthridine under these conditions. In no case was evidence of a phenanthridine–dihydrophenanthridine complex noted, and a complex was not formed by crystallisation from a solution containing equimolecular quantities of the two substances.

Lithium aluminium hydride has also been used in some synthetical experiments leading to 3 : 4-benzocinnoline. This substance had previously been obtained in one stage by electrolytic reduction of 2 : 2′-dinitrodiphenyl (Wohlfart, *J. pr. Chem.*, 1902, **65**, 295). It has also been obtained previously by a two-stage reduction of the same substance. The reduction to the *N*-oxide (V) was carried out with sodium sulphide, and this was reduced to 3 : 4-benzocinnoline with stannous chloride and hydrochloric acid (Ullmann and Dieterle, *Ber.*, 1904, **37**, 23; King and King, *J.*, 1945, 824). In our hands the latter process gave only indifferent results, but the reduction of benzocinnoline *N*-oxide was effected without difficulty by using zinc dust and acetic acid. It has also been found that 2 : 2′-dinitrodiphenyl is smoothly reduced to 3 : 4-benzocinnoline with lithium aluminium hydride, and the same reagent also reduced 3 : 4-benzocinnoline *N*-oxide, in good yield.



(V)

Many attempts were made to obtain 9 : 10-dihydro-1 : 2-benzophenazine. Unchanged material was recovered after attempted reduction with sodium and methyl alcohol, sodium and *iso*amyl alcohol, ammonium sulphide, sodium sulphide, and lithium aluminium hydride. With

hydrogen and Raney nickel, however, reduction took place to give 1′ : 2′ : 3′ : 4′-tetrahydro-1 : 2-benzophenazine, and the same tetrahydro-derivative was obtained by reduction with hydrogen and palladium. The structure of this compound follows from the similarity of its absorption spectrum (Fig. 2) to that of phenazine.

## Experimental.

*The* 3 : 4-*Benzacridine*–5 : 10-*Dihydro*-3 : 4-*benzacridine Complex.*—(i) 5-Chloro-3 : 4-benzacridine (5 g.; prepared by Bachman and Picha's method, *loc. cit.*) was suspended in absolute ethanol (150 c.c.), and potassium hydroxide (1·5 g.) and Raney nickel catalyst (3·5 g.) were added. After hydrogenation in the usual way the alcoholic solution was separated from the catalyst and concentrated to 80 c.c. Water was added to the boiling solution until crystallisation started, and pale yellow flakes (2·5 g.) of 5 : 10-dihydro-3 : 4-benzacridine which separated were collected. Similar treatment of the mother-liquor gave bright orange crystals (1·5 g.) not identical with the above. These were dissolved in benzene and the solution was passed through a column of alumina. The column was developed and eluted with chloroform, an orange band being the first to pass through the column. Removal of the solvent and recrystallisation from aqueous alcohol gave the *complex* as orange needles, m. p. 140° (Found : C, 88·5; H, 5·2. $C_{34}H_{24}N_2$ requires C, 88·7; H, 5·2%). A portion of this compound was treated with concentrated hydrochloric acid and water (1 : 1), and the suspension warmed. The insoluble part was recrystallised from aqueous alcohol. It formed very pale yellow crystals, m. p. 165°, alone or mixed with authentic 5 : 10-dihydro-3 : 4-benzacridine (Lehmstedt, Bruns, and Klee, *Ber.*, 1936, **69**, 2399, give m. p. 158° for this substance). The acid solution was basified with ammonia, and the colourless precipitate recrystallised from aqueous alcohol. It formed colourless crystals, m. p. 130—131°, alone or mixed with authentic 3 : 4-benzacridine.

(ii) The same complex, m. p. 140°, was obtained by gradual addition (40 minutes) of a suspension of lithium aluminium hydride (0·2 g.) in anhydrous dioxan (15 c.c.) to 3 : 4-benzacridone (0·25 g.; Ullmann, *loc. cit.*) in anhydrous dioxan, followed by refluxing for 7 hours. After the addition of water to decompose the complex, the mixture was filtered and the filtrate concentrated. The crude product was recrystallised from aqueous alcohol, from which the complex separated in almost quantitative yield.

(iii) The same orange complex, m. p. 140°, was obtained on mixing ethanolic solutions of equimolecular quantities of 3 : 4-benzacridine and 5 : 10-dihydro-3 : 4-benzacridine.

3 : 4-*Benzacridine.*—This was obtained in almost quantitative yield by the oxidation of the crude 5 : 10-dihydro-3 : 4-benzacridine, obtained as in (i) above, with potassium dichromate and sulphuric acid as described by Albert and Willis (*loc. cit.*) for the oxidation of acridan. 3 : 4-Benzacridine formed colourless needles from aqueous alcohol, and had m. p. 131°, in agreement with Ullmann (*loc. cit.*).

*Phenanthridone from Diphenic Acid.*—The following method gave a better yield of phenanthridone than that of Stephenson (*loc. cit.*). A mixture of diphenic acid (2·4 g.), sulphuric acid (20 c.c.), and chloroform (40 c.c.) was treated with powdered sodium azide (2·6 g.) at such a rate that the temperature was maintained at 45—50°. The addition took 30 minutes, the temperature being kept at 50° ± 2° for a further 80 minutes. The mixture was poured on ice, the chloroform layer separated and evaporated, and the insoluble phenanthridone, m. p. 287° (1·1 g.), collected (lit., m. p. 293°, corr.). The acid filtrate was basified with sodium hydroxide, giving 2 : 2′-diaminodiphenyl, m. p. 80—80·5° (0·3 g.) (lit., m. p. 81°).

9-*Chlorophenanthridine.*—Graebe and Wander's method (*Annalen*, 1893, **276**, 245) proved very tedious and gave only small yields of the desired compound. The following method proved satisfactory, however, and gave almost quantitative yields. A mixture of phenanthridone (19 g.), phosphorus oxychloride (150 c.c.), and dimethylaniline (6 c.c.) was refluxed for 3 hours (compare Kenner *et al.*, *J.*, 1943, 574). The excess of phosphorus oxychloride was removed *in vacuo*, and the residue poured on ice. The product was extracted with ether, and the ethereal solution washed with sodium carbonate, dried, and evaporated. The residual 9-chlorophenanthridine had m. p. 116° after recrystallisation from aqueous alcohol.

9 : 10-*Dihydrophenanthridine.*—(i) A mixture of 9-chlorophenanthridine (1·0 g.), potassium hydroxide (0·5 g.), and Raney nickel catalyst (1·5 g.) in alcohol (30 c.c.) was shaken with hydrogen at room temperature and pressure. When hydrogenation became very slow the solution was separated from the catalyst, concentrated to a small volume, and treated with a little water. The material which separated was recrystallised from alcohol, giving 9 : 10-dihydrophenanthridine (0·83 g.) as colourless plates, m. p. 125° (de Diesbach and Aeschbach, *Helv. Chim. Acta*, 1945, **28**, 1396, give m. p. 125°) (Found : C, 86·4; H, 6·0. Calc. for $C_{13}H_{11}N$ : C, 86·2; H, 6·2%).

(ii) A suspension of lithium aluminium hydride (0·5 g.) in dioxan (15 c.c.) was gradually added to a boiling suspension of phenanthridone (0·5 g.) in anhydrous dioxan (30 c.c.). The refluxing was continued for 8 hours, after which water was added to decompose the complex. After removal of the inorganic material by filtration, the liquors were diluted with water, and the product collected and recrystallised from aqueous alcohol. The dihydrophenanthridine (0·4 g.) was identified by direct comparison with an authentic specimen prepared as above.

(iii) 9 : 10-Dihydrophenanthridine was also obtained by reduction of 9-chlorophenanthridine with lithium aluminium hydride.

*Phenanthridine.*—(i) Dehydrogenation of 9 : 10-dihydrophenanthridine (1·0 g.) was effected by palladised charcoal at 260° (20 minutes). The resulting phenanthridine, crystallised from aqueous alcohol, formed fine white needles (0·93 g.), m. p. 106° (Albert, Brown, and Duewell, *loc. cit.*, give m. p. 107—108°).

(ii) Dry hydrogen chloride was passed into a solution of toluene-*p*-sulphonhydrazide (1·5 g.) and 9-chlorophenanthridine (1·0 g.) in chloroform (20 c.c.). After 3 days at room temperature the yellow precipitate was collected and added to a solution of sodium hydroxide (4·0 g.) in water (30 c.c.) and

ethylene glycol (80 c.c.). The mixture was heated on the water-bath for 3½ hours, poured into water (200 c.c.), and kept in the refrigerator overnight. The resulting precipitate was collected and dissolved in acid, from which the phenanthridine separated on basification. Purification from aqueous alcohol gave phenanthridine, m. p. 106°, in 30% yield.

3 : 4-*Benzocinnoline.*—A mixture of benzocinnoline *N*-oxide (5·0 g.; King and King, *loc. cit.*) in glacial acetic acid (50 c.c.) was heated very gently, and zinc dust (5 g.) added slowly during 5 minutes. After being heated for a further 10 minutes the solution was filtered and the filtrate poured into ammonia. The resulting 3 : 4-benzocinnoline (4·3 g.) separated from benzene as pale yellow blades, m. p. 156° in agreement with Ullmann and Dieterle (*loc. cit.*).

(ii) A solution of lithium aluminium hydride (3·0 g.) in anhydrous ether (15 c.c.) was added to a solution of 2 : 2′-dinitrodiphenyl (4·0 g.) in anhydrous benzene (35 c.c.), and the mixture refluxed for 4 hours. A brown precipitate formed during the reaction. Water (5 c.c.) was added to the cold solution, the inorganic material was filtered off, and the ether–benzene layer washed with 5% sodium carbonate solution and then water, and dried ($Na_2SO_4$). Removal of the solvent and recrystallisation of the residue from benzene gave 3 : 4-benzocinnoline (2·7 g., 92% yield) as pale yellow blades, m. p. 156°.

*Reduction of* 1 : 2-*Benzophenazine.*—Attempted reduction of 1 : 2-benzophenazine (Ullmann and Heisler, *Ber.*, 1909, **42**, 4263) with sodium and methyl alcohol, with sodium and *iso*amyl alcohol, with ammonium sulphide and sodium hydroxide in boiling aqueous alcohol, and with alkaline sodium sulphide, all gave unchanged material. It was, however, reduced catalytically, as follows. A solution of 1 : 2-benzophenazine (1·0 g.) in alcohol (150 c.c.) was hydrogenated over Raney nickel catalyst until the rate of hydrogenation became very slow. The solution was filtered from the catalyst, concentrated, and allowed to cool. The crystals which separated were orange-red, and were purified by passage (in benzene solution) through a column of alumina. A narrow, dark red band formed at the top of the column, and a broad pale yellow band moved rapidly through the column on elution with benzene. Concentration of the eluate gave 1′ : 2′ : 3′ : 4′-*tetrahydro*-1 : 2-*benzophenazine*, which on further crystallisation formed pale yellow needles, m. p. 125° (Found : C, 82·4; H, 5·7. $C_{16}H_{14}N_2$ requires C, 82·05; H, 6·0%). The dark red band was also eluted but gave only a small amount of a dark red oil on removal of the solvent.

The same tetrahydro-1 : 2-benzophenazine, m. p. 125°, was also obtained by reduction of 1 : 2-benzophenazine with hydrogen over palladised charcoal.

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