Non-benzenoid Aromatic Heterocycles. V[*,1]*. An Attempted Synthesis of 4, 7-Dihydro-4, 7-phenanthroline Derivatives*

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Heptalene (I) was first proposed by Baker[2] in 1945 as a possible aromatic, wholly conjugated compound. Many synthetic trials of its derivatives have since been carried out[3], and yet their synthesis has not been successful with only one exception of condensed heptalene derivative II[4], while this compound should rather be regarded as an azulene derivative. The results of a few theoretical treatments[5] on this compound I also do not coincide with one another in the stability of this hydrocarbon.

In connection with this problem, the authors attempted the synthesis of 4, 7-dihydro-4, 7-phenanthroline derivatives III. These compounds are planar without undue strain and are wholly conjugated, and they have seven π-electrons in each hetero-ring. In this respect, these compounds are similar in their electronic structure to the supposed hydrocarbon heptalene (I).

As a possible route to III, the hydrogenation of 4, 7-phenanthroline dimethiodide (IV) was first attempted. The reduction of 4, 7-phenanthroline 4, 7-dimethiodide was reported by Karrer et al.[6] They used sodium hyposulfite and obtained a red substance, to which the formula V was suggested. The present authors attempted the reduction of IV by catalytic hydrogenation or by zinc powder. In neither case was the expected III (R, R''=Me, R', R'''=H) obtained, but instead an intense red solution, presumably the same substance as reported by Karrer, was formed.

Next, the dehydrogenation of tetrahydro-4, 7-phenanthroline was attempted. It has been found[7] with quinoline that the methiodide reacts with Grignard reagents to form 1, 2-dihydroquinoline derivative, and the present authors expected a reaction of the same type in 4,7-phenathroline dimethiodide. 4,7-Phenanthroline 4, 7-dimethiodide reacted with methylmagnesium iodide as expected, to give the desired 3, 4, 7, 8-tetrahydro-3, 4, 7, 8-tetramethyl-4, 7-phenanthroline (VI). It is markedly unstable to air and quickly combines with oxygen on being kept in air and an intensely green substance was formed. When VI was treated with chloranil, a dark precipitate (presumably an addition complex) was rapidly formed, and even after four hours' reflux in xylene, no tetrachlorohydroquinone was formed, which showed that no dehydrogenation had occurred in tetrahydrophenanthroline (VI). When VI was treated with concentrated sulfuric acid, the starting material was recovered accompanied by an intensely green substance.

Finally, an addition of organometallic compounds to 4, 7-phenanthroline (VII) was attempted. It has been reported that phenazines give *N,N'*-disubstituted *N,N'*-dihydrophenazines by the action of Grignard reagents or organolithium compounds, followed by alkyl halides[8]. Hence, if the structure III is sufficiently stable, the organometallic compounds should add to VII to form 4, 7-disubstituted 4, 7-dihydro-4, 7-phenanthrolines (III). Although phenanthroline was recovered unchanged by the action of phenylmagnesium bromide, when it was treated with phenyllithium followed by methyl iodide, a yellow compound of a formula $C_{19}H_{16}N_2$ with strong green fluorescence (VIII) was obtained. Evidently, the addition of phenyllithium took place, but structures VIIIa and VIIIb would be possible to this substance because the addition of phenyllithium to 1, 2-position of pyridines and quinolines has been reported[9]. The yellow color of this substance suggests that it is not the expected 4, 7-dihydro-4, 7-phenanthroline derivatives. Further, the hydrochloride and the picrate of VIII are red, while Karrer et al.[6] reported that *N*-methyl-1, 2, 3, 4-tetrahydro-4, 7-phenanthroline hydrochloride also is red. This fact also throws doubt on the supposed structure VIIIa. The

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[*] Presented at the Meeeting of the Chemical Society of Japan, Tokyo, October, 1960.

[1] Part IV. H. Kato and M. Ohta, This Bulletin, **34**, 357 (1961).

[2] W. Baker, *J. Chem. Soc.*, **1945**, 258.

[3] Cf. for example, W. Baker and J. F. W. McOmie, "Non-benzenoid Aromatic Compounds", in "Progress in Organic Chemistry", Vol. 3, Butterworths Scientific Publications, London (1955), p. 44.

[4] K. Hafner and J. Schneider, *Ann.*, **624**, 37 (1959).

[5] R. B. Brown, *Trans. Faraday Soc.*, **45**, 296 (1949); **46**, 146 (1950); D. P. Craig, *J. Chem. Soc.*, **1951**, 3175, etc.

[6] P. Karrer, A. Pletscher and W. Manz, *Helv. Chim. Acta*, **30**, 1146 (1947).

[7] W. Bradly and F. Jeffrey, *J. Chem. Soc.*, **1954**, 2770.

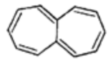
[8] H. Gilman and Dietrich, *J. Am. Chem. Soc.*, **79**, 6178 (1957).

[9] K. Ziegler and H. Zeiser, *Ber.*, **63**, 1847 (1930); *Ann.*, **485**, 174 (1931).

structure of VIII was proved to be VIIIb by treating 4, 7-phenanthroline monomethiodide (IX) with phenylmagnesium bromide to give the indentical product with VIII.

In connection with this reaction, the reaction of phenyllithium to 4, 7-phenanthroline was studied in more detail. When two or more molar equivalents of phenyllithium was used, no disubstituted tetrahydrophenanthroline derivative was formed, and the dihydro-derivative VIIIb was the sole product. When the addition product of phenyllithium was hydrolyzed with water, 3-phenyl-4, 7-phenanthroline (X) was formed, probably via the dihydro compound.

From these facts, one may reasonably assume that the compound of the type III, although planar and wholly conjugated, are not stable and of which no aromaticity can be expected.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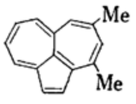

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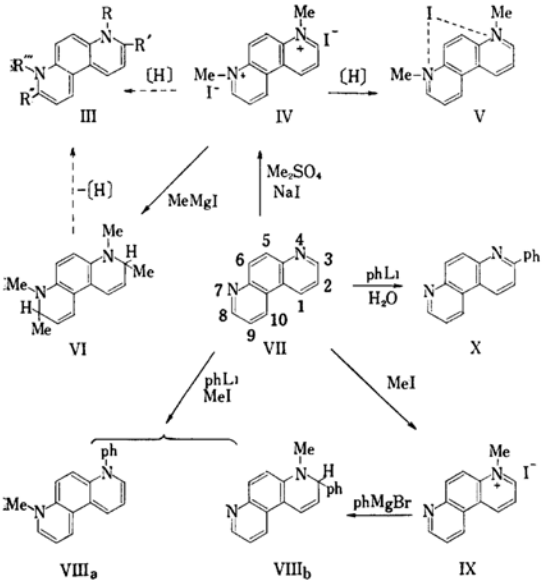

Experimental

4, 7-Phenanthroline (VII).—a) To a mixture of 6-aminoquinoline (12 g.), orthoarsenic acid (13 g.) and glycerol (36 g.), there was added dropwise concentrated sulfuric acid (32 g.) with stirring and heating at 130~140°C. The mixture was heated and stirred for four hours and then poured into a solution of potassium hydroxide in ice-water. The black resinous residue and the aqueous layer were extracted continuously for fifteen hours with benzene, and the benzene extract was treated with a large quantity of charcoal. On evaporation of benzene, practically pure 4, 7-phenanthroline was obtained (11 g.), m. p. 170~173°C[10]. This substance was used directly for the following reactions.

b) To a mixture of *p*-phenylenediamine (60 g.), orthoarsenic acid (150 g.) and glycerol (300 g.), there was added dropwise concentrated sulfuric acid (150 g.), with stirring and heating at 130~140°C. The mixture was heated and stirred for six hours; then the mixture was diluted with ice-water and neutralized with ammonia. The black resinous product was extracted several times with hot benzene, and the benzene extract was treated with charcoal. On evaporation of benzene, crude 4, 7-phenanthroline (48 g.) was obtained, m. p. 165~169°C. Recrystallization from benzene afforded pale yellow needles, m. p. 173°C.

4, 7-Phenanthroline Monomethiodide (IX). — A benzene solution of 4, 7-phenanthroline (2 g.) and methyl iodide was gently refluxed for thirty minutes; then methyl iodide was added further and reflux was continued for another half an hour. The yellow crystals which separated out (3 g.) were collected and recrystallized from water to give bright yellow needles (2 g.), m. p. 270°C[12].

4, 7-Phenanthroline Dimethiodide (IV). — A mixture of 4, 7-phenanthroline (20 g.) and dimethyl sulfate (40 g.) was heated at 160°C for two hours and then diluted with water, and sodium iodide (50 g.) was added. The brown precipitate which separated out was collected and recrystallized from water to give pale brown plates (18 g.), m.p. 264°C[13].

Reduction of 4, 7-Phenanthroline Dimethiodide. —To a solution of 4, 7-phenanthroline dimethiodide (2.3 g.) in water (50 ml.), there was added zinc powder (0.7 g.) in small portions with stirring and warming. The solution quickly turned to an intense wine-red color. The colored substance could not be extracted with ether, benzene, chloroform, etc.

When this reaction was carried out in cold water, or in aqueous or absolute ethanol, the same result was observed. When 4, 7-phenanthroline dimethiodide was hydrogenated with Pd-C (5%) or Pd-$CaCO_3$ (2%) in water, ethanol or acetone, the same coloration took place accompanied by the starting material.

3, 4, 7, 8-Tetrahydro-3, 4, 7, 8-tetramethyl-4, 7-phenanthroline (VI).—To an ether solution (25 ml.) of methylmagnesium iodide (prepared from 1 g. of magnesium and 5.7 g. of methyl iodide), there was added portionwise fine powdered 4, 7-phenanthroline dimethiodide (2.3 g.) with stirring and under an atmosphere of nitrogen. Stirring was continued for an additional two hours after the addition was complete, while heat was evolved slightly and the dimethiodide gradually dissolved. The solution was decomposed with aqueous ammonium chloride and extracted with ether. The ether extract was dried over potassium carbonate, the ether was evaporated under nitrogen and the residue was washed with methanol and ether to give a dark

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[10] Reported m. p.[11] 173°C.

[11] I. Heilbron, "Dictionary of Organic Compounds", Vol. IV, Oxford University Press, New York (1953), p. 87.

[12] Reported m. p.[11] 268~269°C.

[13] Reported m. p.[11] 265°C.

yellow powder (0.7 g.), m. p. 113~117°C. Recrystallization from ether afforded yellow prisms (0.2 g.), m. p. 147°C. This compound is very sensitive to air and rapidly turns intense green on standing.

Found: C, 79.80; H, 8.68; N, 11.76. Calcd. for $C_{16}H_{20}N_2$ (VI): C, 79.95; H, 8.39; N, 11.66%.

Air Oxidation of VI. — A current of air was bubbled into an ethanolic solution of VI (0.1 g.) for two days. The resultant intensely green substance (0.07 g.) was purified by chromatography (alumina-benzene) to give a dark green amorphous powder. This compound does not show a definite m. p. but melts at about 230°C.

Found: C, 65.68; H, 6.92%.

When it was allowed to stand in air for a long time, it became practically insoluble in most solvents.

Attempted Dehydrogenation of VI with Chloranil. — Chloranil (0.2 g.) and VI (0.2 g.) were refluxed for four hours in xylene (10 ml.). A black precipitate was rapidly formed. This precipitate (0.4 g.) was scarcely soluble in most organic solvents and is positive to Beilstein's halogen test. On treatment of the filtrate with aqueous potassium hydroxide, no tetrachlorohydroquinone was obtained.

Treatment of VI with Concentrated Sulfuric Acid. — A solution of VI (0.2 g.) in concentrated sulfuric acid (10 ml.) was warmed at 60~70°C for an hour and was kept standing overnight at room temperature. The starting material was recovered unchanged accompanied by a small amount of green insoluble substance.

3, 4-Dihydro-4-methyl-3-phenyl-4,7-phenanthroline (VIIIb).—a) An ether solution (20 ml.) of phenyllithium (prepared from 3.14 g. of bromobenzene and 0.3 g. of lithium) was added dropwise under an atmosphere of nitrogen into a tetrahydrofuran solution (30 ml.) of 4,7-phenanthroline (3 g.) with cooling and stirring. The solution turned wine-red. After half an hour, a tetrahydrofuran solution (10 ml.) of methyl iodide (3 g.) was added to the solution with cooling and stirring. The solution turned greenish yellow after the addition was complete. After two hours, the solution was decomposed by addition of an aqueous solution of ammonium chloride and the resultant solution was extracted with ether followed by chloroform and each extract was dried over calcium chloride.

The ether extract was concentrated to give a yellow residue (2.8 g.). Recrystallization from acetone afforded yellow fine needles with strong green fluorescence, m. p. 155°C.

Found: C, 83.50; H, 6.08; N, 10.53. Calcd. for $C_{19}H_{16}N_2$ (VIIIb): C, 83.79; H, 5.92; N, 10.27%.

The same compound was obtained when two or more molar equivalents of phenyllithium were reacted with 4,7-phenanthroline.

This compound turns red-colored on addition of hydrochloric acid.

Picrate: red needles (from aqueous dimethylformamide), m. p. 173°C.

Found: N, 13.85. Calcd. for $C_{25}H_{19}N_5O_7$: N, 13.97%.

The chloroform extract in the above experiment was concentrated and the residue (0.5 g.) was recrystallized from benzene to give white needles, m. p. 171~172°C, undepressed on admixture with an authentic specimen of 4,7-phenanthroline.

When 4,7-phenanthroline was treated with phenylmagnesium bromide followed by methyl iodide, the starting material was recovered.

b) To an ether solution (30 ml.) of phenylmagnesium bromide (prepared from 3.2 g. of bromobenzene and 0.5 g. of magnesium), there was added fine powdered 4,7-phenanthroline monomethiodide with stirring. After an hour, this solution was poured into aqueous ammonium chloride, extracted with ether and benzene and the extract was dried over calcium chloride. The solvent was removed and the residue (1.2 g., m. p. 152~154°C) was recrystallized from acetone to give yellow fine needles with strong green fluorescence, m. p. 155°C. Picrate, red needles, m. p. 173°C. Neither melting point was depressed on admixture with the specimens prepared by procedure a).

3-Phenyl-4,7-phenanthroline (X). — An ether solution (40 ml.) of phenyllithium (prepared from 6.3 g. of bromobenzene and 0.6 g. of lithium) was added dropwise under an atmosphere of nitrogen into a tetrahydrofuran solution (30 ml.) of 4,7-phenanthroline (3 g.) with stirring and cooling. After thirty minutes, the reaction mixture was decomposed by addition of aqueous ammonium chloride and extracted with ether, the ether extract was dried over calcium chloride, and the solvent was removed. Recrystallization of the residue from acetone afforded yellow fine needles with green fluorescence (1 g.), m. p. 187°C[14].

Found: C, 83.85; H, 4.92; N, 10.81; Mol. wt. (Rast) 260. Calcd. for $C_{18}H_{12}N_2$ (X): C, 84.35; H, 4.72; N, 10.85%; Mol. wt. 255.

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[14] Reported m. p.[11] 183°C.

[15] C. Willgerodt and S. Jabolinsky, *Ber.*, 33, 2918 (1900).