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# SYNTHESIS OF QUINO(4,3–c)QUINOLINE DERIVATIVES AND POLYCARBOCYCLIC QUINO(4,3–c)QUINOLINES

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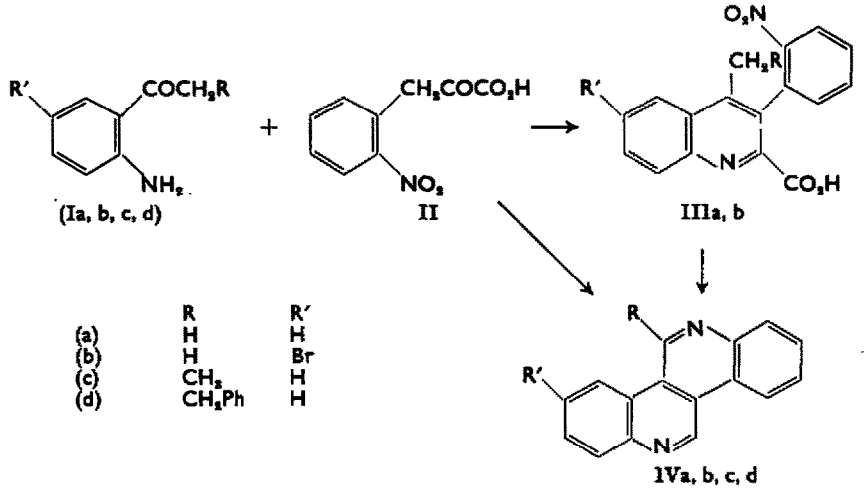
**Abstract**—Several quino(4,3-c)quinoline derivatives and polycarbocyclic quino(4,3-c)quinolines have been synthesized by the new ring-closure reaction between methyl (or methylene) and nitro groups.

IT HAS been found[1] that the condensation of *o*-aminoacetophenone (Ia) with *o*-nitrophenylpyruvic acid (II) in the presence of an excess of zinc chloride at 140–150° yields directly quino(4,3-c)quinoline (IVa) and, at a low temperature of 80°, the intermediate, 3-(*o*-nitrophenyl)lepidine-2-carboxylic acid (IIIa) is produced. The cyclization reaction of IIIa to quino-quinoline (IVa) takes place in the presence of zinc chloride at 160°.



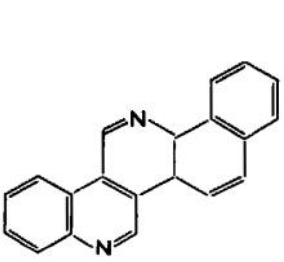

As an extension of the new ring-closure reaction between methyl (or methylene) and nitro groups, several quino(4,3-c)quinoline derivatives and polycarbocyclic quino(4,3-c)quinolines has been prepared.

Similarly, *o*-aminopropiophenone (Ic) or *o'*-aminophenyl phenylethyl ketone (Id) condense directly with *o*-nitrophenylpyruvic acid (II) to give 5-methylquino(4,3-c)-quinoline (IVc) and 5-benzylquino(4,3-c)quinoline (IVd).

Polycarbocyclic quino-quinolines, 8,14-diazapicene (V), 1,2,3,4-tetrahydro 8,14-diazapicene (VI) and 1,2,3,4-tetrahydro 8,14-diaza benzo[a]picene (VII), have been prepared by condensation of *o*-aminoacetophenone with 1-nitronaphthyl-2-pyruvic acid, 5-amino-6-acetyltetrahydronaphthalene with *o*-nitrophenylpyruvic acid and

[1] T. Kobayashi and R. Kikumoto, *Tetrahedron* **18**, 813 (1962).

5-amino-6-acetyltetrahydronaphthalene with 1-nitronaphthyl-2-pyruvic acid in the presence of zinc chloride at 170–190°.



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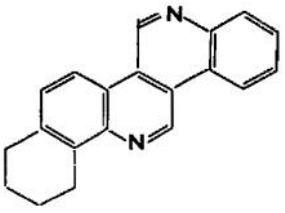

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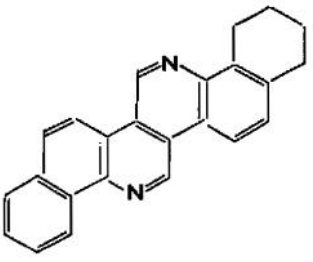
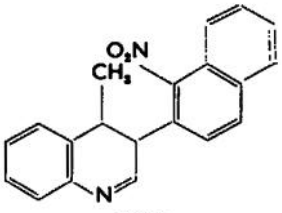
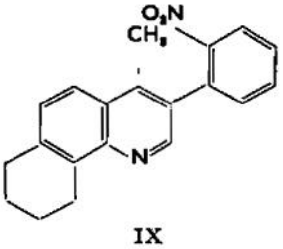


VII

Intermediates in the above described condensation reaction, i.e., 3-(1′-nitronaphthyl)lepidine (VIII) and 3-(*o*-nitrophenyl)-7,8,9,10-tetrahydro benzo[h]lepidine (IX), were prepared at a low temperature of 140–150°.



VIII



IX

## EXPERIMENTAL

*3-Bromoquino(4,3-c)quinoline* (IVb). To a solution of Ib[2] (0·8 g) and *o*-nitrophenylpyruvic acid[3] (0·8 g) (II) in dry toluene (15 ml) anhydrous $ZnCl_2$ (2·5 g) was added and the mixture refluxed for 1½ hr on an oil-bath. The solution was allowed to boil off freely during ½ hr and the mixture then heated on the oil-bath for 4 hr at 160–170° with frequent stirring. The dark product was dissolved in acetic acid (15 ml), treated with charcoal and poured into excess NaOH aq for basification. The precipitate was filtered, washed with water, dried and distilled *in vacuo* (13 mm). The distillate recrystallized from pyridine and EtOH in yellow needles, 0·14 g, mp 325°. (Found: C, 62·29; H, 3·11; N, 8·99. $C_{16}H_9BrN_2$ requires: C, 62·16; H, 2·93; N, 9·06%.)

The intermediate IIIb of IVb, was also obtained by the condensation of Ib with II in the presence of excess anhydrous $ZnCl_2$ at 140° for 4 hr. The yield after recrystallization from EtOH, was 0·35 g (24 %) of colourless needles, mp 196–197° (dec), from Ib (0·8 g) and II (0·8 g). (Found: C, 52·67; H, 3·25; N, 7·11. $C_{17}H_{11}BrN_2O_4$ requires: C, 52·74; H, 2·86; N, 7·24%.) The decarboxylation of this acid (IIIb) by distillation *in vacuo* (2 mm) gave 6-bromo-3-(*o*-nitrophenyl)lepidine. The product was recrystallized from EtOH to give colourless plates, mp 150–151°. (Found: C, 56·28; H, 3·01; N, 8·09. $C_{16}H_{11}BrN_2O_2$ requires: C, 56·00; H, 3·23; N, 8·16%.)

*5-Methylquino(4,3-c)quinoline* (IVc). Anhydrous $ZnCl_2$ (2·5 g) was added to a solution of Ic[4] (0·45 g) and II (0·63 g) in dry benzene (10 ml). After removal of benzene by evaporation on an oil-bath, the residue was heated at 150–155° for 3½ hr, dissolved in acetic acid (13 ml) and the solvent treated with charcoal. The solution was then poured into an excess cold NaOH aq and the precipitated crystals filtered off and distilled *in vacuo* (2 mm). The distillate was recrystallized from EtOH and dried yielding 0·08 g, yellow needles, mp 287–290°. (Found: C, 83·97; H, 5·34; N, 11·36. $C_{17}H_{12}N_2$ requires: C, 83·58; H, 4·95; N, 11·47%.)

[2] J. C. E. Simpson, C. M. Atkinson, K. Schofield and O. Stephenson, *J. Chem. Soc.* 646 (1945).
[3] F. J. Dicaio, *J. Amer. Chem. Soc.* **66**, 1420 (1944).
[4] K. R. Aurwers and M. Duesberg, Ber., **53**, 1208 (1920).

*5-Benzylquino(4,3-c)quinoline* (IVd). The reaction was carried out as described for IVc.

A mixture of Id (0·22 g) II (0·21 g) and anhydrous $ZnCl_2$ (2 g) in dry benzene (5 ml) was heated at 160° for 4 hr, and the product dissolved in acetic acid (5 ml). After filtration (charcoal), the solution was basified with NaOH aq. The yellow product obtained by distillation *in vacuo* (3 mm) crystallized from acetic acid in yellow needles, 0·04 g, mp 280–282°. (Found: C, 86·03; H, 5·49; N, 8·54. $C_{22}H_{16}N_2$ requires: C, 86·22; H, 5·03; N, 8·74%.)

Compound Id was prepared from *o'*-nitrochalcone[5] by hydrogenation in EtOH with 10% Pd–C as catalyst. Recrystallization from MeOH gave colourless plates, mp 74–76°. (Found: C, 79·97; H, 6·71; N, 6·22. $C_{15}H_{13}NO$ requires: C, 80·36; H, 7·00; N, 6·10%.)

8,14-*Diazapicene* (V). To a suspension of *o*-aminoacetophenone (0·54 g) and 1-nitronaphthyl-2-pyruvic acid[6] (1·04 g) in dry xylene (10 ml) anhydrous $ZnCl_2$ (5 g) was added. After evaporating the solvent, the residue was heated on an oil-bath at 180–195° for 3½ hr with frequent stirring and then boiled with acetic acid (15 ml) and water (50 ml). The insoluble product was collected by filtration, washed with water, dried and distilled *in vacuo* (2 mm). Two recrystallizations from EtOH gave yellow needles, 0·11 g, mp 285–288°. (Found: C, 85·36; H, 4·52; N, 10·16. $C_{20}H_{12}N_2$ requires: C, 85·69; H, 4·32; N, 9·90%.)

3-(1'-*Nitronaphthyl*)*lepidine* (VIII) (*intermediate of* V). A mixture of *o*-aminoacetophenone (0·21 g) 1-nitronaphthyl-2-pyruvic acid (0·42 g) and anhydrous $ZnCl_2$ (2 g) in dry xylene (25 ml) was refluxed for 4 hr. After removal of solvent by steam-distillation, the residue was distilled *in vacuo* (2 mm). The distillate recrystallized from EtOH to yield 0·12 g, yellow needles, mp 186–187°. (Found: C, 76·28; H, 5·09; N, 8·91. $C_{20}H_{14}N_2O_2$ requires: C, 76·42; H, 4·49; N, 8·91%.)

1,2,3,4-*Tetrahydro*-8,14-*diazapicene* (VI). To a solution of 5-amino 6-acetyltetrahydronaphthalene[7] (0·59 g) and *o*-nitrophenylpyruvic acid (0·63 g) in dry toluene (20 ml) anhydrous $ZnCl_2$ (5 g) was added. After evaporation of the solvent, the residue was heated at 180–190° for 4½ hr and dissolved in acetic acid (charcoal) and the solution poured into excess NaOH aq for basification. The precipitate was filtered, washed with water, dried and then distilled *in vacuo* (4 mm). It was recrystallized once from EtOH, and once from acetic acid to obtained 0·09 g, yellow needles, mp 278–280·5°. (Found: C, 84·32; H, 5·81; N, 10·02. $C_{20}H_{16}N_2$ requires: C, 84·48; H, 5·67; N, 9·82%.)

3-(*o-Nitrophenyl*)-7,8,9,10-*tetrahydro benzo*[h]*lepidine* (IX) (*intermediate of* VI). Anhydrous $ZnCl_2$ (1·5 g) was added to a solution of 5-amino-6-acetyltetrahydronaphthalene (0·19 g) and *o*-nitrophenylpyruvic acid (0·21 g) in dry toluene (6 ml). After evaporating the solvent, the residue was heated at 150–160° for 4½ hr, the dark product dissolved in hot acetic acid (6 ml) (charcoal) and then added to excess NaOH aq. The precipitate was collected by filtration, washed with water, dried and distilled *in vacuo* (2 mm). Crystallization from acetic acid afforded 0·07 g pale yellow needles, mp 143–144·5°. (Found: C, 74·65; H, 5·56; N, 8·96. $C_{20}H_{18}N_2O_2$ requires: C, 74·45; H, 5·70; N, 8·80%.)

1,2,3,4-*Tetrahydro*-8,14-*diazabenzo*[a]*picene* (VII). To a suspension of 5-amino-6-acetyltetrahydronaphthalene (0·19 g) and 1-nitronaphthyl-2-pyruvic acid (0·26 g) in dry toluene (18 ml) anhydrous $ZnCl_2$ (2·5 g) was added. After evaporating the solvent on an oil-bath, the residue was heated at 180–190° for 3 hr and dissolved in hot acetic acid (25 ml) (charcoal), and the filtrate poured into excess NaOH aq for basification. After cooling, the resulting precipitate was filtered, washed with water, dried and distilled *in vacuo* (2 mm). Recrystallization of the distillate from acetic acid gave 0·05 g, yellow needles, m.p. 306°. (Found: C, 85·91; H, 5·43; N, 8·77. $C_{24}H_{16}N_2$ requires: C, 86·20; H, 5·43; N, 8·38%.)

[5] R. P. Barnes, J. A. Graham and M. A. S. Qureshi, *J. Org. Chem.* **28**, 2891 (1963).
[6] F. Mayer and T. Oppenheimer, *Ber. Dtsch. Chem. Ges.* **49**, 2140 (1916).
[7] W. Borsche and A. Bodenstein, *Ber. Dtsch. Chem. Ges.* **59**, 1915 (1926).