Tetrahedron, 1963, Vol. 19, pp. 1685 to 1690. Pergamon Press Ltd. Printed in Northern Ireland

1,2-DIHYDROQUINOLINE STUDIES—I

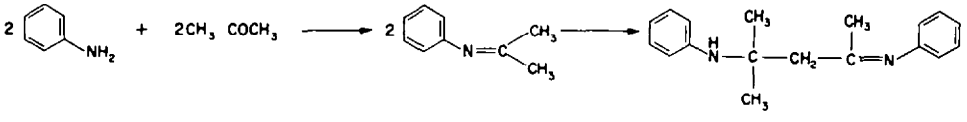
THE STRUCTURE OF THE ARYLAMINE-ACETONE CONDENSATION PRODUCTS

C. C. TUNG

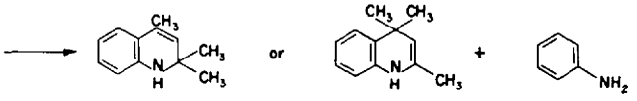
(*Received* 15 *April; revised form* 21 *May* 1963)

Abstract—Authentic samples of 1,2-dihydro-2,2,4-trimethylquinoline (III) and 6-ethoxy-1,2-dihydro-2,2,4-trimethylquinoline (IX) were synthesized. Their infrared, ultraviolet and N.M.R. spectra and derivatives were shown to be identical with those of the corresponding aromatic amine-acetone condensation product. Some reactions of *p*-phenetidine-acetone anil (X) were described in support of the mechanism for the formation of 1,2-dihydroquinolines.

THE acid catalyzed aniline-acetone condensation product, which was mistakenly proposed by Knoevenagel[1] as acetone anil I, was suggested by Reddelien and Thurm[2] as 1,2-dihydro-2,2,4-trimethylquinoline (III), although an alternative structural assignment as 1,4-dihydro isomer IV could not be entirely excluded. Rosser and Ritter[3] proposed that the formation of III or IV could result from aldolization of I to II followed by cyclization with elimination of aniline.



I II

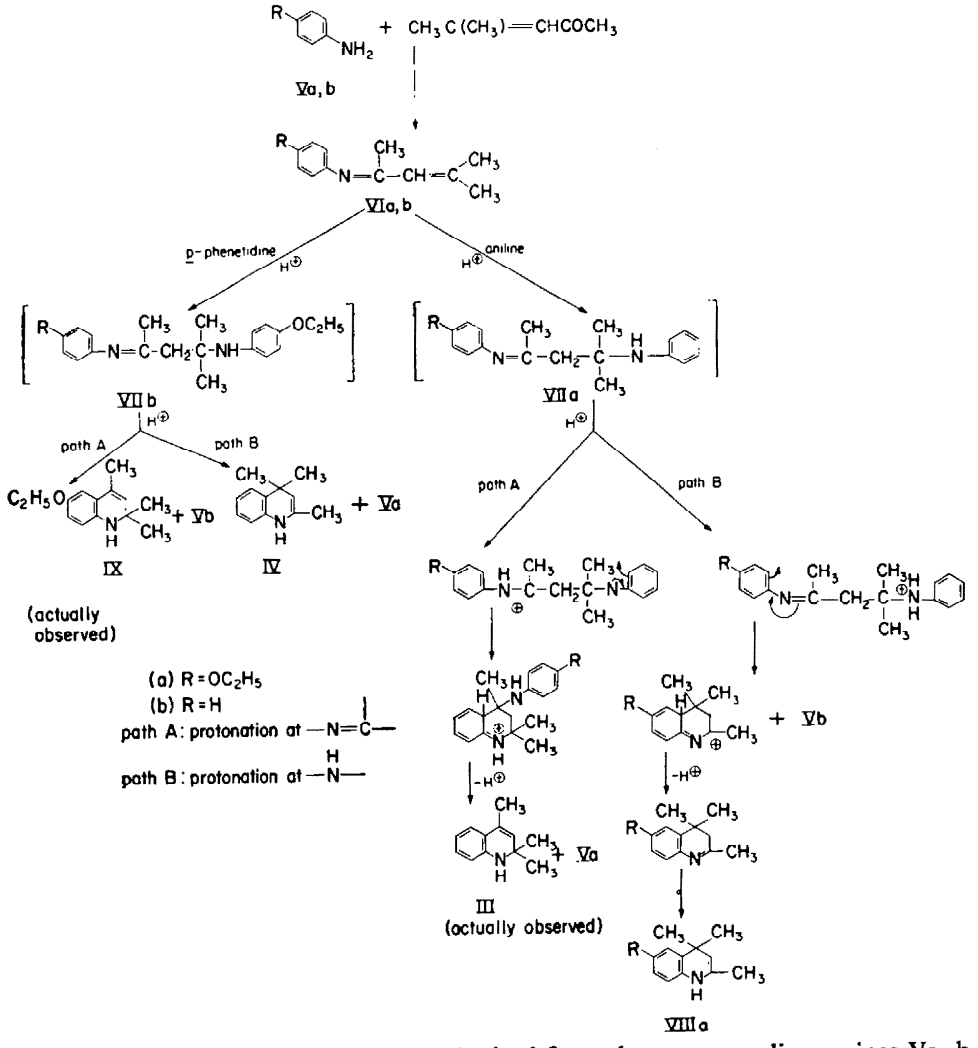


III IV

Johnson and Buell[4] suggested the structure of aniline acetone condensation product is III on the basis that its ultraviolet spectrum was strikingly similar to that of 1,2-dihydroquinoline. Recently, elucidative work on the structure of the condensate as III by chemical evidence has been reported. For example, Brown[5] confirmed the structure of the condensate as III on the ground that isobutylene and 2-guanidino-4-methyl quinazoline were formed by the reaction of "acetone anil" with dicyandiamide. Elliott and Yates[6] also confirmed the structure of III by the oxidative degradation of the acetyl derivative of "acetone anil".

[1] E. Knoevenagel, *Ber.*, **54B**, 1722 (1921).
[2] G. Reddelien and A. Thurm, *Ber.*, **65B**, 1511 (1932).
[3] C. M. Rosser and J. J. Ritter, *J. Amer. Chem. Soc.*, **59**, 2179 (1937).
[4] W. S. Johnson and B. G. Buell, *J. Amer. Chem. Soc.*, **74**, 4517 (1952).
[5] J. P. Brown, *Chem. & Ind.*, **9**, 233 (1960).
[6] I. W. Elliott, Jr., and P. Yates, *J. Org. Chem.* **26**, 1287 (1961).

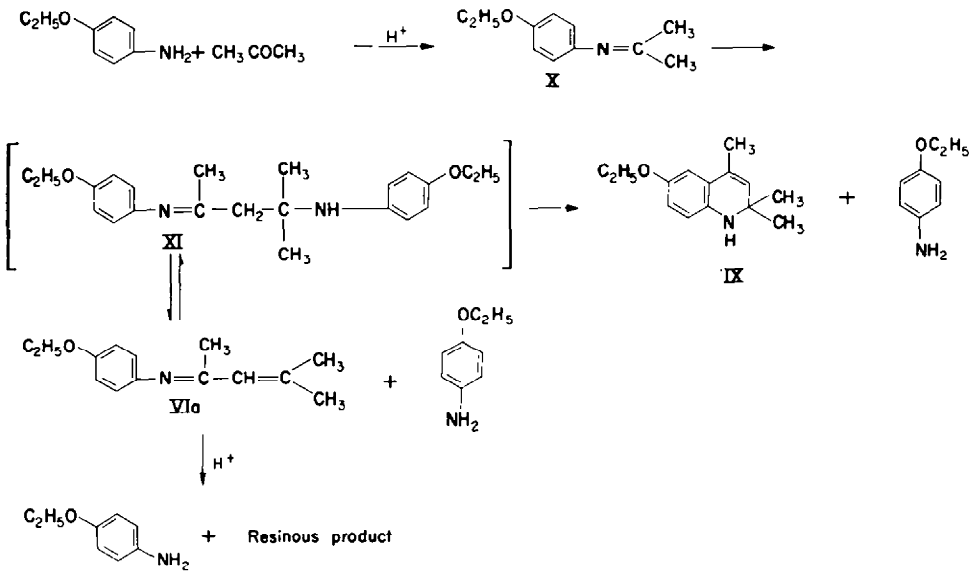
This paper describes the synthesis of authentic samples of 1,2-dihydro-2,2,4-trimethylquinoline[7] (III) and 6-ethoxy-1,2-dihydro-2,2,4-trimethylquinoline[8] (IX). A comparison of these authentic samples with the products prepared from the corresponding aromatic amines and acetone clearly demonstrates that the latter possess the 1,2-dihydroquinoline structure rather than 1,4-dihydro.



Mesityloxide anils VIa, b were synthesized from the corresponding amines Va, b and mesityloxide in benzene solution. The anil VIa was allowed to react with aniline in the presence of an acid catalyst to form the intermediate VIIa which is related to II. Protonation of VIIa (path A or B) with cyclization could then lead to two easily distinguishable groups of products; 1,2-dihydro-2,2,4-trimethylquinoline (III) and *p*-phenetidine (path A) or 6-ethoxy-1,4-dihydro-2,4,4-trimethylquinoline (VIIIa) and aniline (path B).

[7] Flectol A, a rubber antioxidant, trademark of Monsanto Chemical Company, St. Louis, Mo.
[8] Santoquin, a feed additive antioxidant, trademark of Monsanto Chemical Company, St. Louis, Mo.

The fact that equimolar quantities of dihydroquinoline III and *p*-phenetidine were obtained from this reaction indicates that path A was favored. The identity of the dihydroquinoline III to that obtained from aniline–acetone condensation was demonstrated by mixed melting point determinations of their carbanilates and hydrochloride salts and by infrared, ultraviolet and N.M.R. spectra. Similarly, the anil VIb was reacted with *p*-phenetidine to give equimolar quantities of dihydroquinoline



IX and aniline. IX was found to be identical with the product obtained from the *p*-phenetidine–acetone condensation. Hence, the structure of the aromatic amine-acetone condensation product is conclusively 1,2-dihydro-2,2,4-trimethylquinoline. The reaction of VIa with *p*-phenetidine and VIb with aniline gave IX and III respectively.

Support for the mechanism of the aromatic amine–acetone condensation was achieved from the reaction of X and VIa with *p*-phenetidine. That the final product was IX in each case strongly suggested that the precursor was the anil XI.

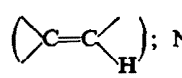
Since X gave 25% yield of IX but an 81% yield in excess *p*-phenetidine, one can reasonably assume an equilibrium between XI and VIa and *p*-phenetidine. The detection of VIa and *p*-phenetidine from X after standing at room temperature for some time also substantiates an equilibrium.

Attempts to cyclize VIa, b in the presence of acid catalyst were unsuccessful. *p*-Phenetidine (from VIa) and aniline (from VIb) and non-distillable products (300°/0·1 mm) were obtained.

EXPERIMENTAL

1,2-*Dihydro*-2,2,4-*trimethylquinoline from aniline and acetone.* The procedure of Craig[9] was used. The following properties were recorded for the condensation product: b.p. 130° (5 mm); m.p. 26–27°; U.V.: λ_{max} 230 mμ (log ϵ 4·48), 270 (3·35), 340 (3·40); I.R.: 2·90 μ (>N—H), 6·04 μ

[9] D. Craig, *J. Amer. Chem. Soc.*, **60**, 1458 (1938).

 ; N.M.R.[10]: ring protons (multiplet) at τ2·91–3·88, olefinic proton (quartet with a coupling constant of 1·2–1·3 c/s) at τ4·88, amine proton (singlet) at τ6·63, 4-methyl protons (doublet with a coupling constant of 1·2–1·3 c/s) at τ8·14, 2,2-dimethyl protons (singlet) at τ8·90, in an intensity ratio of 4:1:1:3:6; hydrochloride salt, m.p. 214–215°; 3,4-dichlorocarbanilate, m.p. 135–136°.

6-Ethoxy-1,2-dihydro-2,2,4-trimethylquinoline from p-phenetidine and acetone. The procedure of Craig[9] was used. The following properties were obtained for the condensation product: b.p. 155° (5 mm); 137° (2 mm); N_D^{25}: 1·57; U.V.: λ_{max} 228 mμ (log ε 4·41), 350 (3·40); I.R.: 3·02 μ  , 6·10 μ  ; N.M.R.[10]; ring protons (multiplet) at τ3·36–3·83 olefinic proton (quartet with a coupling constant of 1·2–1·3 c/s) at τ4·80, ethoxy methylene protons (quartet with a coupling constant of 7·0 c/s) at τ6·15, amine proton (singlet) at τ6·54, 4-methyl protons (doublet with a coupling constant of 1·2–1·3 c/s) at τ8·13, ethoxy methyl protons (triplet with a coupling constant of 7·0 c/s) at τ8·72, 2,2-dimethyl protons (singlet) at τ8·86 in an intensity ratio of 3:1:2:1:3:3:6; hydrochloride salt, m.p. 192–193°; 3,4-dichlorocarbanilate, m.p. 139–140°.

p-Phenetidine-mesityloxide anil (VIa). A mixture containing 137·2 g (1·0 mole) of *p*-phenetidine and 300·0 g (3·1 moles) of mesityloxide in 100 ml of benzene was heated at reflux temperature (104°) for 24 hr. The solvent and excess of mesityloxide were removed *in vacuo* and the residue distilled. There was obtained 76·0 g (35%) of *p*-phenetidine mesityloxide anil VIa, b.p. 115–116° (1 mm). The product solidified into a light yellow colored solid, m.p. 55–56°. I.R.: 1540 cm^{-1} (C=N str.). (Found: C, 77·24; H, 8·82; N, 6·29; M.W., 218. Calc. for $C_{14}H_{19}NO$: C, 77·37; H, 8·81; N, 6·45; M.W., 217.)

Aniline mesityloxide anil (VIb). The anil VIb, prepared by the procedure for VIa, was obtained in 25% yield; b.p. 78–79° (1 mm) (reported[8] b.p. 125° at 16 mm), n_D^{25}: 1·5498. I.R.: 1540 cm^{-1} (C=N str.). (Found: C, 83·12; H, 8·69; N, 8·01; M.W., 178. Calc. for $C_{12}H_{15}N$: C, 83·18; H, 8·72; N, 8·07; M.W., 173.)

1,2-Dihydro-2,2,4-trimethylquinoline (III) *from* VIa *and aniline.* A mixture of 18·2 g (0·084 mole) of VIa, 66·2 g (0·71 mole) of aniline and 0·1 g of toluenesulfonic acid was heated at 130–140° for 4 hr. Distillation afforded the following fractions: (1) aniline recovered, 56·0 g (aniline used 10·2 g, 0·11 mole); (2) *p*-phenetidine, 8·9 g, 0·065 mole; (3) 1,2-dihydro-2,2,4-trimethylquinoline, 11·6 g (80%, 0·067 mole), b.p. 130° (5 mm). Fraction (3) has properties identical with aniline-acetone condensation product.

6-Ethoxy-1,2-dihydro-2,2,4-trimethylquinoline (IX) *from* (VIb) *and p-phenetidine.* A mixture of 20·4 g (0·118 mole) of VIb, 161·5 g (1·18 mole) of *p*-phenetidine and 0·1 g of toluenesulfonic acid was heated at 130–140° for 3 hr. The following fractions were obtained from distillation: (1) aniline: 9·1 g (0·10 mole); (2) *p*-phenetidine recovered, 146·2 g (*p*-phenetidine used 15·3 g, 0·12 mole); (3) 6-ethoxy-1,2-dihydro-2,2,4-trimethylquinoline; 21·3 g (83%, 0·098 mole). Fraction (3) has properties identical with *p*-phenetidine acetone condensation product.

6-Ethoxy-1,2-dihydro-2,2,4-trimethylquinoline (IX) *from* (VIa) *and p-phenetidine.* A mixture of 12·0 g (0·055 mole) of VIa, 75·0 g (0·55 mole) of *p*-phenetidine and 0·1 g of toluenesulfonic acid was heated at 130–140° for 3 hr. The following fractions were obtained from distillation: (1) *p*-Phenetidine recovered, 79·5 g (0·58 mole, *p*-phenetidine gain 0·03 mole; (2) 6-ethoxy-1,2-dihydro-2,2,4-trimethylquinoline, 9·6 g (81%, 0·04 mole).

1,2-Dihydro-2,2,4-trimethylquinoline (III) *from* (VIb) *and aniline.* A mixture of 16·7 g (0·095 mole) of VIb, 63·3 g (0·68 mole) of aniline and 0·1 g of toluenesulfonic acid was heated at 130–140°C for 4 hr. Distillation afforded the following fractions: (1) Aniline: 65·8 g (0·71 mole, aniline gain 0·03 mole); (2) 1,2-Dihydro-2,2,4-trimethylquinoline: 12·5 g (77%, 0·072 mole).

p-Phenetidine acetone anil (X)

One liter of acetone was added dropwise to 137·2 g. (1·0 mmole) of *p*-phenetidine at 135–140° over a period of thirteen hours. The unreacted acetone was collected through the condenser and

[10] Spectra were measured at 60 Mc/s. on a modified Varian Model A-60 spectrometer in chloroform solution with tetramethylsilane as an internal reference.

discarded. Fractional distillation gave 181·6 g of light yellow liquid, b.p. 72–73°/0.4 mm. Infrared data indicated this product contains about 80% of *p*-phenetidine acetone anil (X) and 20% of unreacted *p*-phenetidine. Anil X was separated as a colorless solid m.p. 65–66°, by Beckman Magachrom Preparative Gas Chromatography.[11]

X discolored in air on standing to give brown colored semisolid which indicated the presence of VIa and *p*-phenetidine by gas chromatogram. Analysis was made on the freshly prepared colorless solid.

Anal. Calcd. for $C_{11}H_{15}NO$: C, 74·59; H, 8·54; N, 7·90; M.W., 177.
Found: C, 74·26; H, 8·96; N, 7·91; M.W., 173.

6-Ethoxy-1,2-dihydro-2,2,4-trimethylquinoline (IX) *from* (X)

(*a*) *With no* p-*phenetidine.* A mixture of 4·0 g (0·0226 mole) of X and 0·05 g. of toluenesulfonic acid was heated at 130–140° for four hours. The mixture was fractionally distilled to give 1·8 g (0·0131 mole) of *p*-phenetidine and 0·60 g (0·00276 mole) of IX (25%). The residue was not distillable at 300° (0·1 mm).

(*b*) *With excess of* p-*phenetidine.* A mixture of 12·3 g (0·0695 mole) of X, 0·05 g of toluenesulfonic acid and 51·7 g (0·378 mole) of *p*-phenetidine under the same conditions as described in (a) gave 6·4 g (0·030 mole) of IX (85% yield) and 54·8 g (0·40 mole) of *p*-phenetidine.

Attempted ring closure of VIa.

(a) A mixture of 19·9 g (0·092 mole) of VIa and 0·2 g of toluenesulfonic acid was heated at 135–140°C for 3 hr. The mixture was distilled *in vacuo* to obtain 11·7 g (0·068 mole) of *p*-phenetidine and 8·2 g of residue which was not distillable at 300° (0·1 mm).

(b) To a solution containing 0·2 g of toluenesulfonic acid in 150 ml of *p*-xylene at reflux temperature (138°) was added a solution of 15·0 g (0·069 mole) of VIa in 50 ml of *p*-xylene over a period of 1 hr. The mixture was heated at reflux temperature for an additional 1½ hr. The solvent was removed under *vacuo* and the residue was distilled. The only distillable product, 4·9 g (0·0358 mole) was identified as *p*-phenetidine and the residue was not distillable at 300° (0·1 mm).

Attempted ring closure of VIb

A mixture of 15·9 g (0·092 mole) of VIb and 0·2 g of toluenesulfonic acid was treated under the same conditions as described for VIa. The mixture was distilled to obtain 2·9 g (0·032 mole) of aniline and the residue was not distillable at 300° (0·1 mm).

[11] A column packed with Apiezon on ground firebrick was used.