309. *The Constitution of the Supposed Aliphatic Keto-anils.*

By Wilfrid H. Cliffe.

Knoevenagel and Jaeger (*Ber.*, 1921, **54**, 1723) stated that acetone and aniline interact in the presence of iodine to form a product which regenerates the parent substances on hydrolysis with dilute mineral acids and is therefore to be regarded as a true acetoneanil. Short and Watt (J., 1930, 2293) concluded that the anil is in tautomeric equilibrium with a large proportion of the corresponding enamine ($>CH\cdot C:N \rightleftharpoons >C:C\cdot NH$), a conclusion criticised by von Auwers and Wunderling (*Ber.*, 1932, **65**, 70). Reddelien and Thurm (*ibid.*, p. 1511) have stated that the supposed anil is a secondary base not hydrolysed by acid and is, in fact, 2 : 2 : 4-trimethyl-1 : 2-dihydroquinoline, a conclusion which has now been accepted by Short (Murray, Short, and Stansfield, *J. Amer. Chem. Soc.*, 1933, **55**, 2805).

The present author commenced a reinvestigation of the work of Knoevenagel and Jaeger in 1930 and had reached a conclusion similar to that of Reddelien and Thurm: namely, that "acetoneanil" and its homologues are secondary bases stable to acid hydrolysts. In consequence, many observations difficult to reconcile with the Knoevenagel formulation have been satisfactorily explained.

What led the author to such a belief was primarily the ready formation of *N*-nitroso-compounds which are reducible to the initial bases. Further indications were afforded by the preparation of acetyl derivatives, substituted ureas with phenyl *iso*cyanate, and by the reactions of the bases with alkyl magnesium halides, confirming the results described by Short and Watt. Yet it was considered that such results were not conclusive evidence, as the possibility of ready enolisation in presence of such reagents as acetic anhydride and methylmagnesium iodide was not excluded (compare Grignard and Savard, *Compt. rend.*, 1924, **179**, 1573; 1926, **182**, 422).

In order to devise a practicable method of establishing the constitution of "acetoneanil," or of differentiating it from the structure assigned to it by Knoevenagel and Jaeger, only reactions of a mild character, and hence least likely to disturb a possibly mobile system, were held to be trustworthy. For example, the most direct evidence was sought by a comparison of the behaviours of "acetoneanil," methylaniline, and benzylideneaniline on treatment with *p*-toluenediazonium chloride. Whereas "acetoneanil" and methylaniline reacted smoothly with the formation of diazoamino-compounds, the true Schiff's base remained unaffected under precisely the same conditions. Confirmatory evidence was available by comparative instantaneous brominations, since the enolising effect of bromine is generally accepted to be very slow. Equimolecular proportions of benzylideneaniline and "acetoneanil" in solution in methyl alcohol were brominated by very rapid addition of the halogen in the same solvent. The Schiff's base was found to destroy three molecules of bromine. On the other hand, "acetoneanil" and "acetone-*m*-tolil" destroyed quantities of bromine which, on the assumption that these compounds possessed the structure assigned to them by Knoevenagel and Jaeger, would correspond to four molecular proportions. Such results are quite inconsistent with the early formulation, though not inconsistent with the conclusions of Reddelien and Thurm. On the assumption that the formulæ proposed by Reddelien and Thurm are correct, the bromine destroyed corresponds to five molecular proportions, and the composition of the product from "acetoneanil" corresponds to a dibromotrimethyldihydroquinoline dibromide (p. 1329).

In addition, the following results were difficult to reconcile with the Knoevenagel–Jaeger structure. "Acetone-*m*-chloroanil" and "acetone-*p*-chloroanil" (both well-crystallised solids) were found on analysis to contain chlorine contents in total disagreement with the calculated figures for a true acetonechloroanil. The figures, however, are in good accord with those calculated for a chloro-2 : 2 : 4-trimethyl-1 : 2-dihydroquinoline. Furthermore, reduction of the so-called acetone-*m*-chloroanil with sodium and butyl alcohol, and subsequent determination of the chloride, disclosed an amount more than 26% below the expected, but in approximate agreement with that which would be required by an assumption of the quinoline structure. All these results are in complete accordance with the conclusions of Reddelien and Thurm.

It has been definitely demonstrated by Reddelien and Thurm that catalytic reduction of " acetoneanil " to the supposed tetramethylindoline is not accompanied by simultaneous formation of a molecular proportion of aniline, as was originally proclaimed by Knoevenagel and Jaeger.

Similarly, the author has repeatedly failed to discover more than a small quantity of primary amine after reduction with sodium and alcohols, though its virtual absence was not regarded as very suggestive on account of the presence of resinous material which is invariably the result of reduction in such a manner.

The aliphatic " keto-anils " derived from methyl ethyl ketone have been examined for the sake of comparison. In the first instance Knoevenagel's directions for the preparation of " ethyl methyl ketoneanil " were accurately followed and repeated on many occasions, but the product was always found to contain 2-methyl-4-ethylquinoline, the formation of which was not recorded by Knoevenagel. In a similar manner a homologue of aniline with the same ketone yielded the corresponding homologue of this quinoline. The " anils " of the acetone series are known to lose methane fairly readily to pass into quinoline derivatives under the influence of condensing agents or by heating under pressure (Knoevenagel, Bähr, and Wagner, *Ber.*, 1923, **56**, 2414; D.R.-P. 363582 and 363583). In the methyl ethyl ketone series, however, the conversion appears to take place under conditions during which the " anils " from acetone are quite stable. Replacement of the iodine used as a catalyst in Knoevenagel's preparation by sulphanilic acid partially or wholly obviates the production of the quinoline. The yield of " anil," however, is adversely affected by this weaker acid catalyst, and no reaction took place between methyl ethyl ketone and aniline in absence of a catalyst. Though separation of " anil " and quinoline may be effected by acetylation of the former and purification by repeated washing with dilute mineral acid, attempts to regenerate the pure base have proved fruitless, as hydrolysis of the acetyl compound—even by alkali—is sufficient to cause appreciable conversion into the quinoline.

EXPERIMENTAL.

2 : 2 : 4-Trimethyl-1 : 2-dihydroquinoline (" acetoneanil ") was more conveniently prepared by a modification of Knoevenagel's method. To equimolecular proportions of acetone and aniline containing 1% of iodine was added 10% of the combined weight of ligroin, in order that there might possibly be formed a ternary mixture with the water produced. The vapour was deprived of its moisture during the course of the reaction by contact with calcium carbide or chloride contained in a Soxhlet apparatus, and a rapid return of the condensed vapour was facilitated by short circuiting the syphoning arrangement of the apparatus. As a result, the time was reduced from 40 to 5 hours and the yield slightly raised. The " anil " was a triboluminescent solid, b. p. 260°/762 mm. (Found : C, 82·6; H, 8·8; N, 7·8. Calc. for $C_{12}H_{15}N$: C, 83·2; H, 8·7; N, 8·1%. Calc. for $C_9H_{11}N$: C, 81·2; H, 8·3; N, 10·5%).

1-*Acetyl*-2 : 2 : 4-*trimethyl*-1 : 2-*dihydroquinoline* (" *Acetylacetoneanil* ").—A solution of " acetoneanil " (1 pt.) in acetic anhydride (2 pts.) was boiled for ½ hour and poured after cooling into excess of sodium carbonate solution. The pale brown crust which quickly formed was collected, washed, dried in a vacuum (yield, almost theoretical), and crystallised from light petroleum, forming colourless plates, or distilled; m. p. 54° (Reddelien and Thurm gave 53°), b. p. 174—175°/23 mm. (Found: C, 78·5; H, 8·0; N, 6·6. Calc. for $C_{14}H_{17}ON$: C, 78·1; H, 7·9; N, 6·5%. Calc. for $C_{11}H_{13}ON$: C, 75·4; H, 7·4; N, 8·0%). It was rapidly hydrolysed by boiling dilute hydrochloric acid. An attempt to acetylate the " anil " by the method of Chattaway (J., 1931, 2495) was unsuccessful.

1-*Phenylcarbamyl*-2 : 2 : 4-*trimethyl*-1 : 2-*dihydroquinoline*.—A solution of equimolecular proportions of " acetoneanil " and phenyl *iso*cyanate in dry ether was refluxed for 6 hours, the solvent distilled, and the residue treated with fresh ether. The solution was filtered from a trace of carbanilide, and the ether again distilled to leave the substantially pure urea in 97% yield. It crystallised from ligroin (b. p. 60—80°) in needles, m. p. 124° (Reddelien and Thurm gave 125°) (Found: C, 78·3; H, 7·0; N, 9·2. Calc. for $C_{19}H_{20}ON_2$: C, 78·1; H, 6·9; N, 9·6%. Calc. for $C_{16}H_{16}ON_2$: C, 76·2; H, 6·3; N, 11·1%).

1-Nitroso-2 : 2 : 4-trimethyl-1 : 2-dihydroquinoline separated as an orange-red oil when a solution of " acetoneanil " in ice-cold dilute hydrochloric acid was treated below the surface with sodium nitrite. It was isolated by means of ether, and, on treatment with tin and hot hydrochloric acid, regenerated the " anil," but the reduction could not be effected without heat.

3 : 4 : 6 : 8-*Tetrabromo*-2 : 2 : 4-*trimethyl*-1 : 2 : 3 : 4-*tetrahydroquinoline*, obtained by the addition of excess of bromine to a solution of " acetoneanil " in methyl alcohol, crystallised from ligroin in white silky needles, m. p. 160° (Found : C, 30·0; H, 2·4; N, 2·9; Br, 66·0. $C_{12}H_{13}NBr_4$ requires C, 29·3; H, 2·6; N, 2·9; Br, 65·2%). There was also obtained a small quantity of a second substance which separated from alcohol in pale yellow plates, m. p. 181—182° (Found : Br, 64·7%).

1 : 2 : 2 : 4-Tetramethyl-1 : 2-dihydroquinoline (the *iso*propenylmethylaniline of Knoevenagel, Bähr, and Wagner; *Ber.*, 1923, **56**, 2416) was prepared in the manner devised by these authors. It was a pale yellow mobile oil, b. p. 144°/14 mm. (Found : N, 7·8. Calc. for $C_{13}H_{17}N$: N, 7·5%. Calc. for $C_{10}H_{13}N$: N, 9·5%). The picrate had m. p. 147°, and the quaternary iodide (from alcohol) m. p. 158°.

2 : 2 : 4-*Trimethyl*-1 : 2-*dihydroquinoline*-7-*sulphonic Acid*.—" Acetoneanil " (13·3 g.) was gradually added to ice-cold 20% fuming sulphuric acid (94 g.), and the solution kept at room temperature for 16 hours before being poured over ice. The sulphonic acid (9·8 g.), which separated in white micro-prisms after a short time, was washed free from mineral acid and recrystallised from hot water, in which it was sparingly soluble. It decomposed above 360° and was identified as a *m*-acid by treatment with excess of bromine, the sulpho-group not being displaced. The resulting bromo-sulphonic acid was a white solid, almost insoluble in cold water.

1 : 2 : 2 : 4-Tetramethyl-1 : 2-dihydroquinoline-7-sulphonic acid, prepared in a similar manner to the above from the so-called *iso*propenylmethylaniline of Knoevenagel, formed white prisms (from water), decomp. 323°.

6 : 6′-*Bis*-(2 : 2 : 4-*trimethyl*-1 : 2-*dihydroquinolino*)*methane*.—" Acetoneanil " (1·33 g.) and formaldehyde (2·5 g. of 36%) were allowed to react at room temperature in presence of *N*-sulphuric acid (0·2 c.c.), water (1 c.c.), and a trace of sulphanilic acid as a catalyst. After 2 days the solid product was washed with water and remained as an almost white solid with a tendency to oxidise on exposure to the air. The yield was high, but the base was difficult to obtain in a crystalline condition. It was best purified from aqueous alcohol and melted indefinitely. It was oxidised to the greenish-blue hydrol by lead dioxide in acetic acid.

6 : 6′-Bis-(1 : 2 : 2 : 4-tetramethyl-1 : 2-dihydroquinolino)methane, similarly obtained from "*iso*propenylmethylaniline," differed but little from the above compound in its general properties.

6 : 6′-*Bis*-(2 : 2 : 4-*trimethyl*-1 : 2-*dihydroquinolino*)*phenylmethane*.—A mixture of " acetoneanil," benzaldehyde, and freshly fused zinc chloride was heated near 100° for 2 hours. Volatile impurities were removed in steam, and the clean, pale green, almost non-basic powder dried in the steam-oven (yield, nearly theoretical). It was purified once from alcohol and then melted at 158°. The dye obtained by oxidation of this leuco-compound with lead dioxide dyed tannin-mordanted cotton deep green.

Similar dyes were obtained from " acetoneanil " and *o*-methoxybenzaldehyde, and from " *iso*propenylmethylaniline " and benzaldehyde, whilst " acetoneanil " and *p*-dimethylaminobenzaldehyde gave a leuco-compound oxidisable to a dye like crystal-violet.

2 : 2 : 4 : 7-Tetramethyl-1 : 2-dihydroquinoline (Knoevenagel and Jaeger's " acetone-*m*-tolil ") was prepared in superior yield from acetone and *m*-toluidine by their method as a low-melting crystalline solid (Found : C, 83·6; H, 9·3; N, 7·4. Calc. for $C_{13}H_{17}N$: C, 83·4; H, 9·1; N, 7·5%. Calc. for $C_{10}H_{13}N$: C, 81·6; H, 8·9; N, 9·5%). The white crystalline hydrochloride and nitrate melted at 224° and 149—151° respectively. On being treated near its b. p. with hydrogen chloride, the compound was converted into 2 : 4 : 7-trimethylquinoline, identical with that obtained by Yamaguchi (*J. Pharm. Soc. Japan*, 1924, No. 503, 8).

The acetyl derivative (from the base and acetic anhydride) separated from aqueous alcohol or light petroleum in white prisms, m. p. 85°. The benzoyl derivative (from the base and benzoic anhydride) was obtained as an oil which rapidly became solid. It crystallised from aqueous alcohol or light petroleum as a pale yellow solid, m. p. 108·5°.

1 : 2 : 2 : 4 : 7-Pentamethyl-1 : 2-dihydroquinoline was obtained, by the action of " acetone-*m*-tolil " on methyl sulphate in presence of a little alcohol, decomposition of the methosulphate with 15% sodium hydroxide solution, and distillation of the liberated oil under reduced pressure,

in almost theoretical yield as a pale yellow oil, b. p. 162—163°/18 mm. Picrate, m. p. 171° (from alcohol). Hydriodide, m. p. 242·5° (from alcohol).

1-Phenylcarbamyl-2 : 2 : 4 : 7-tetramethyl-1 : 2-dihydroquinoline, obtained from "acetone-*m*-tolil" and phenyl *iso*cyanate, as described in the case of "acetoneanil," formed white needles from ligroin, m. p. 149°.

7-Chloro-2 : 2 : 4-trimethyl-1 : 2-dihydroquinoline ("*Acetone-*m*-chloroanil*").—*m*-Chloroaniline (128 g.), acetone (29 g.), and iodine (1·5 g.) were heated under reflux for 30 hours, and then shaken with water, whereby were extracted 3 g. of *m*-chloroaniline hydrochloride, identified by comparison of both itself and the benzoyl derivative of the base with authentic specimens. The oil was dried over sodium sulphate and fractionated under reduced pressure, the "acetone-*m*-chloroanil" (34·3 g.) being collected at 165—175°/20 mm. A further quantity (6·5 g.) was obtained by redistillation of the intermediate fraction. The pure *substance* distilled at 172°/18 mm. as a pale yellow oil which solidified, and crystallised from light petroleum in large, flat, transparent plates, m. p. 38·5° (Found : C, 69·4; H, 6·9; N, 7·3; Cl, 16·3. $C_{12}H_{14}NCl$ requires C, 69·4; H, 6·7; N, 6·7; Cl, 17·1%. $C_9H_{10}NCl$ requires C, 64·5; H, 6·0; N, 8·4; Cl, 21·2%). The "chloroanil" was stable to boiling hydrochloric acid and formed a sparingly soluble salt, m. p. 202° (decomp.) after crystallising from absolute alcohol in transparent rectangular plates. The sparingly soluble nitrate (shining transparent plates from alcohol) melted at 131—132° (decomp.).

Addition of methyl sulphate to the "chloroanil" in dry ether slowly afforded clusters of small white needles, m. p. 139°, or 140° after purification from light petroleum–alcohol. The hydriodide of the *N*-methyl derivative of the "chloroanil" was prepared from the "anil" and methyl iodide in a sealed tube at 100°, and had m. p. 142—144° (from alcohol).

The acetyl derivative of the "chloroanil" was prepared by boiling the base with twice its weight of acetic anhydride for 1 hour. It formed long white shining needles, m. p. 76—77°, from light petroleum.

The substituted urea, made from the "chloroanil" and phenyl *iso*cyanate in dry ether, was obtained in white silky needles, m. p. 160°.

6-Chloro-2 : 2 : 4-trimethyl-1 : 2-dihydroquinoline ("acetone-*p*-chloroanil"), prepared similarly from *p*-chloroaniline (the yield was lower), crystallised from aqueous alcohol in long white needles, m. p. 61·5° (Found : C, 69·3; H, 6·9; N, 7·1; Cl, 16·5. $C_{12}H_{14}NCl$ requires C, 69·4; H, 6·7; N, 6·7; Cl, 17·1%. $C_9H_{10}NCl$ requires C, 64·5; H, 6·0; N, 8·4; Cl, 21·2%). The hydrochloride (m. p. 196° with decomp.) was sparingly soluble, whilst the nitrate and sulphate were easily soluble.

8-Chloro-2 : 2 : 4-trimethyl-1 : 2-dihydroquinoline ("acetone-*o*-chloroanil") was also prepared, but in very poor yield, probably owing to the steric effect of the *o*-substituent.

2-Methyl-2 : 4-diethyl-1 : 2-dihydroquinoline ("ethyl methyl ketoneanil") was prepared according to the directions of Knoevenagel and Jaeger (*Ber.*, 1921, **54**, 1729) and was always found to contain about 10% of 2-methyl-4-ethylquinoline, which could largely be removed as the picrate (m. p. 191°, from alcohol) or as the tartrate (m. p. 149°, from alcohol) (Found : N, 7·3. Calc. for $C_{14}H_{19}N$: N, 7·0%. Calc. for $C_{10}H_{13}N$: N, 9·5%).

Complete separation of the "anil" and the quinoline impurity could be effected by acetylation or nitrosation of the former and extraction of the latter with acid, but the pure "anil" could not be regenerated from either the acetyl or the nitroso-derivative without formation of a variable proportion of 2-methyl-4-ethylquinoline.

The acetyl compound (b. p. 173—179°/12·5 mm.) was a pale yellow, viscous oil which did not crystallise during 8 months. The nitrosoamine formed a thick red oil, resistant to reduction in the cold with tin and hydrochloric acid.

2 : 6-Dimethyl-2 : 4-diethyl-1 : 2-dihydroquinoline (Knoevenagel and Jaeger's "ethyl methyl ketone-*p*-tolil") was prepared by long refluxing of *p*-toluidine (107 g.) with methyl ethyl ketone (36 g.) and iodine (1·5 g.) and fractionation of the product under reduced pressure. The compound (25 g.) boiled at 164—166°/18 mm. (Found : C, 83·9; H, 9·9; N, 6·9. Calc. for $C_{15}H_{21}N$: C, 83·7; H, 9·8; N, 6·5%. Calc. for $C_{11}H_{15}N$: C, 82·0; H, 9·3; N, 8·7%).

The compound contained a small amount of 2 : 6-dimethyl-4-ethylquinoline, identified by its tartrate (white silky needles, m. p. 173°, from alcohol) and picrate (m. p. 185°, from alcohol).

2 : 8-Dimethyl-2 : 4-diethyl-1 : 2-dihydroquinoline ("methyl ethyl ketone-*o*-tolil") was also prepared, though in poor yield, and was similarly found to contain about 10% of a quinoline derivative, assumed to be 2 : 8-dimethyl-4-ethylquinoline.

2 : 6 : 8-Trimethyl-2 : 4-diethyl-1 : 2-dihydroquinoline ("methyl ethyl ketone *m*-xylidil") was prepared from methyl ethyl ketone and *m*-xylidine in presence of iodine. The yield was

poor, and the product, after fractionation, contained a quinoline derivative, probably 2 : 6 : 8-trimethyl-4-ethylquinoline.

The author expresses his thanks to Professor A. Lapworth, F.R.S., for his continued encouragement and advice, and to Imperial Chemical Industries Ltd. for gifts of chemicals.

THE UNIVERSITY, MANCHESTER. [*Received, July* 26*th*, 1933.]