[CONTRIBUTION FROM THE DIVISION OF PHYSIOLOGY, NATIONAL INSTITUTE OF HEALTH]

STUDIES IN THE ACRIDINE SERIES. V. AMINO CARBINOLS DERIVED FROM N,X-DIACETYL-9,10-DIHYDROACRIDINE[1]

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That certain α-(dialkylaminomethyl)-4-quinolinemethanols, as well as naphthalene, phenanthrene, and piperidyl amino carbinols are variously effective in controlling some types of avian malarial infections has been amply demonstrated (1).

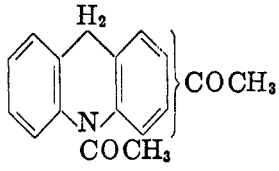
In view of the known, important, pharmacological properties of certain acridine derivatives (*e.g.*, atabrine, acriflavine), it seemed desirable to synthesize and investigate the plasmodicidal properties of diverse acridyl amino carbinols. It occurred to us that the latter could be obtained by condensing the requisite acridyl-ω-halomethyl ketones with secondary amines, followed by reduction of the resulting amino ketones to the amino carbinols. Thus far we have prepared four distinct types of these substances in which the amino carbinols may be regarded as being derived from: (I) N,x-diacetyl-9,10-dihydroacridine, (II) 6(?) and 7-acetyl-1,2,3,4-tetrahydroacridine, (III) 9-formylacridine through condensation with 3-dialkylamino-1-propylmagnesium chloride, and (IV) N,9-diacetyl-9,10-dihydroacridine. This contribution concerns itself with the first (I) of the four types mentioned; reports on the others will follow.

The idea of preparing acridyl amino carbinols is not new. As early as 1935, Eisleb (2), seeking to synthesize quinine analogs in the acridine series, prepared 9-acridyl methyl ketone by treating acridine-9-aldehyde with methylmagnesium iodide, followed by chromic acid oxidation of the resulting secondary carbinol. Interaction of the ketone in 40% HBr with bromine gave the ω-bromo ketone hydrobromide, but the latter failed to react with piperidine as expected. The failure of this condensation was unfortunate. Had it succeeded, a path would have been opened for the preparation of acridine derivatives in which the secondary carbinol group is attached to the carbon function *para* to the hetero nitrogen atom, a configuration present in, and forming an integral part of, the quinine structure. As far as can be ascertained, no further work along these lines was attempted by Eisleb.

More recently, Braz (3) reported the synthesis of several 9-acridyl-ω-halomethyl ketones. Starting with the requisite acridine-9-carboxylic acid he prepared, in turn, the acid chloride, diazo ketone and halomethyl ketone by standard procedures. Whether these halomethyl ketones were brought into reaction with amines was not disclosed, though it seems logical to infer that they were prepared for this purpose in view of the earlier experiments of Eisleb. The failure of

[1] This work was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the National Institute of Health. Communication XXVI in the series "Attempts to Find New Antimalarials." The Survey Numbers (SN) correspond to those given by Wiselogle (1).

Eisleb's bromo ketone to react with piperidine, in addition to certain other anomalous observations described in his paper, points up the, as yet, unexplained, unique behavior of both elementary and group substituents attached to the meso position in acridine. A parallel observation in the anthracene series was made recently in this Laboratory by May and Mosettig (4), who found that 9-ω-bromoacetylanthracene failed to react with secondary amines under standard conditions.



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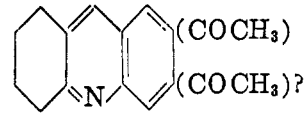

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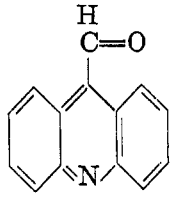

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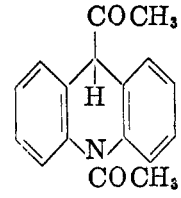

IV

In view of Eisleb's results, it was decided to explore a different approach in the preparation of acridyl halomethyl ketones. Very little appears to be recorded in regard to the Friedel-Crafts acylation of acridine or its derivatives. It is known that heterocyclic nitrogen compounds, with some exceptions, are not readily acylated by the Friedel-Crafts reaction. Thus pyridine and quinoline either do not react at all or, when forced, yield intractable products. The presence of certain substituents in the molecule, however, (notably hydroxyl or methoxyl) appears to facilitate acylation (5, 6, 7). Carbazole, an exception to the rule regarding heterocyclic nitrogen compounds, is readily acylated by acetyl chloride ($AlCl_3$) to give the 3,6-diacetylcarbazole (8). The acylation of N-acetylcarbazole takes a different course, however, and N,2-diacetylcarbazole results (9). In consideration of the foregoing, we decided to attempt the Friedel-Crafts acylation of N-acetyl-9,10-dihydroacridine employing bromoacetyl bromide. The N-acetyl derivative was chosen in order to avoid any doubt regarding N acylation; and, aware of the possibility of nuclear halogenation, bromoacetyl bromide rather than acetyl chloride was used, so as to circumvent the bromination step to the bromo ketone.

As the first step in this work, a commercial grade of acridine was purified and reduced to 9,10-dihydroacridine in the presence of Raney nickel according to Adkins and Coonradt (10). The resulting acridane was smoothly N-acetylated in excellent yield by heating with acetyl chloride. The N-acetylation of 9,10-

dihydroacridine using acetic anhydride as the acylating agent was described recently (11). Our experimental work, however, was completed prior to the appearance of this paper. The aluminum chloride-catalyzed reaction of N-acetyl-9,10-dihydroacridine with bromoacetyl bromide in carbon disulfide proceeded without difficulty to give N-acetyl-x-ω-bromoacetyl-9,10-dihydroacridine in 50% yield (average of 6 runs). No attempt was made to work up the highly-colored, oily by-products, so it is not possible to say whether any isomeric bromo ketones were formed in the reaction. The condensation of the bromo ketone with secondary amines was effected in dry ether to give, in addition to amine hydrobromide, the corresponding amino ketones. With the exception of the tetrahydroisoquinolino analog, which was obtained crystalline, all of the amino ketones prepared were viscous syrups. Some difficulty was encountered in the catalytic hydrogenation[2] of the crude amino ketones, and it was found advantageous to purify them through their hydrochlorides before reduction. With the tetrahydroisoquinolino analog, catalytic hydrogenation of the amino ketone hydrochloride gave good results.

Because of the great tendency of 9,10-dihydroacridine (acridane) and its derivatives to revert to the parent, acridine ring system under mild oxidation conditions (*e.g.*, atmospheric oxygen), several of the amino alcohols described were deacetylated at the heterocyclic nitrogen function thereby regenerating the acridane structure. Conceivably, the 9,10 hydrogen atoms could be removed enzymatically (*in vivo*), thus enabling the true acridine system to act on the parasite. It is interesting to note that a slight increase in activity was observed with the des-N-acetyl amino carbinols (12).

The elucidation of the position occupied by the ω-bromoacetyl group is being deferred until adequate reference derivatives of acridine can be prepared by unambiguous syntheses. This phase of the problem will be reported in a future communication. Of the drugs prepared in this series, SN 6087 exhibited significant activity, while SN 5698 and SN 5849 were slightly active toward *P. Gallinaceum* (blood-inoculated chick infection) (12).

Acknowledgment. The microanalyses are by E. A. Garlock, Jr., formerly of this Laboratory.

EXPERIMENTAL

The melting points given are uncorrected.

9,10-Dihydroacridine. Crude acridine (Reilly) was purified through its dichromate as outlined by Graebe (13), although the final HCl treatment, described by him, was omitted. The acridine so obtained was dissolved in dry dioxane and digested with Raney nickel according to Adkins and Coonradt (*loc. cit.*). After a second reflux with nickel, the filtered dioxane solution was shaken at room temperature for 3 hrs. in the presence of fresh nickel and an initial hydrogen pressure of 100 atmospheres. Vacuum concentration (under nitro-

[2] Catalytic, rather than aluminum isopropoxide (Meerwein-Ponndorf-Verley), reduction of the amino ketones was chosen in order to circumvent the possibility of simultaneous hydrolysis of the N-acetyl group.

gen) of the filtered solution afforded reasonably pure 9,10-dihydroacridine (m.p. 169–70°). In this manner, working with 50–75 g. batches, 300 g. of crude acridine yielded 190 g. (69%) of 9,10-dihydroacridine which, in view of its air-sensitivity, was acetylated without further purification.

N-Acetyl-9,10-dihydroacridine. Ninety grams of 9,10-dihydroacridine was covered with 178 ml. (5 moles) of acetyl chloride (redistilled from freshly fused sodium acetate) and the mixture refluxed for 30 minutes on the steam-bath. The dark color which developed as the solid dissolved soon faded to a light yellow, and hydrogen chloride was evolved copiously. Treatment of the reaction mixture with ice gave a practically colorless, crystalline precipitate which was collected, well washed with water and air-dried. The yield of crude N-acetyl derivative was 110 g. Recrystallization from methanol afforded 96.5 g. (88%) of short, stout prisms; m.p. 149–151°. Three further recrystallizations raised the m.p. to 151.5–153°.

Anal. Calc'd for $C_{15}H_{13}NO$: C, 80.7; H, 5.87.
Found: C, 80.5; H, 6.07.

The Friedel-Crafts reaction: x(ω-Bromoacetyl)-N-acetyl-9,10-dihydroacridine. Observing the usual precautions for the maintenance of anhydrous conditions, a stirred mixture of 65.2 g. (0.29 mole) of finely powdered N-acetyl-9,10-dihydroacridine and 65 g. (0.32 mole) of bromoacetyl bromide in 400 ml. of c.p. carbon disulfide was gradually treated, without cooling, during 1 hr. with 116 g. (0.87 mole) of powdered, anhydrous $AlCl_3$. Ten minutes after the initial addition of the latter, the reaction flask was immersed in a pan of warm water (55–60°) and heating continued as described below. Other than a slight, progressive darkening of the system during the early $AlCl_3$ additions, there was little sign of reaction. However, when approximately one-half of the catalyst had been added the reaction appeared to get under way, as evidenced by the evolution of HBr and the gradual separation of a light amber gum. Stirring and heating were maintained for 70 min. after the final $AlCl_3$ addition, and stirring continued for an additional 45 min. at room temp. After standing for an hour, the flask was cooled and the supernatant CS_2 decanted; it was practically devoid of reaction product. The gummy residue was decomposed by adding it, portion-wise to a stirred slurry of ice and 2 *N* HCl and the system thoroughly extracted with chloroform. Concentration (*vacuo*) of the water-washed and dried chloroform solution afforded a syrup which readily crystallized to a sticky, tan solid when rubbed with a little dry ether. After three triturations with small portions of ice-cold methanol, there remained 55 g. (55%) of practically colorless, crystalline powder, m.p. 155–158°. The bromo ketone crystallizes in small, six-sided plates from acetone, as well as from a benzene-petroleum ether (30–60°) mixture. After three recrystallizations from the latter, m.p. 161–163°.

Anal. Calc'd for $C_{17}H_{14}BrNO_2$: C, 59.3; H, 4.10; Br, 23.2.
Found: C, 59.5; H, 4.23; Br, 23.5.

x-(2-Diethylamino-1-hydroxyethyl)-N-acetyl-9,10-dihydroacridine hydrochloride (SN 6087). A mixture of 20 g. of N-acetyl-x-(ω-bromoacetyl) dihydroacridine and 9.4 g. (2.2 moles) of diethylamine in 250 ml. of dry ether was mechanically shaken for 15 hours. The resulting suspension was cooled (ice-water) and 8.7 g. of a mixture of diethylamine hydrobromide (8.3 g. or 93%) and a little unchanged bromo ketone (0.4 g.) was recovered. The water-washed and dried ethereal solution yielded, after concentration (*vacuo*), 17.6 g. of syrupy amino ketone. This was dissolved in 30 ml. of acetone and acidified with 10 ml. (excess) of 5.4 *N* alcoholic HCl. Addition of dry ether precipitated a light yellow gum which slowly became powdery when scratched. After decanting the supernatant solvent the hydrochloride was slurried with fresh, dry ether, filtered and dried in a vacuum desiccator; 19 g. (probably solvated). Because of the hygroscopic nature of the salt, no attempt was made to recrystallize it. Instead it was dissolved in cold water, basified (under ether) with 2 *N* NH_4OH and the regenerated amino ketone (14.1 g.) taken up in 170 ml. of methanol and hydrogenated in the presence of 0.25 g. of PtO_2. Hydrogen absorption virtually ceased after 39 hrs. (0.88 mole absorbed). The syrupy amino alcohol (12.5 g.) in 30 ml. of acetone was cooled and acidified with 6.8 ml. (1 equiv.) of 5.4 *N* alcoholic HCl. Dilution with dry

ether precipitated a gum which solidified to a light yellow powder (13.9 g.) when scratched. The crude hydrochloride was dissolved in 500 ml. of boiling acetone, filtered and concentrated (*vacuo*) to *ca.* 50 ml.; crystallization was spontaneous, but slow. Overnight (5°) 4.5 g. of cream-colored prisms, m.p. 173–176°, separated. The mother liquor deposited another 1.8 g. of prisms (m.p. 175–177°) after 60 hrs. at 5°. Four recrystallizations from acetone gave the constant m.p. 180–182° d.

Anal. Calc'd for $C_{21}H_{27}ClN_2O_2$: C, 67.3; H, 7.25.
Found: C, 67.1; H, 7.35.

The combined mother liquors on concentration and keeping yielded about 1 g. of impure, crystalline hydrochloride. The remaining oil could not be crystallized.

x-(2-Diethylamino-1-hydroxyethyl)-9,10-dihydroacridine (SN 5971). A suspension of 13 g. of the above, powdery amino alcohol hydrochloride (not crystallized) was heated with 200 ml. of 5% alocholic KOH for 15 min. on the steam-bath. The clear, yellow solution was poured into 1 liter of 5% aqueous NaCl and thoroughly extracted with ether. The latter, after several washings with 5% NaCl, was dried and concentrated (*vacuo*, under N_2) to give a syrup which slowly crystallized after one-half hour of alternate scratching and standing. Two recrystallizations from 70% ethanol afforded 5.5 g. of nearly colorless needles, m.p. 107–108.5°. An analytical sample, after three more recrystallizations, showed the m.p. 108–110°. The substance, as might be inferred from its structural relationship to dihydroacridine, is air-sensitive and turns brown after exposures of short duration (36–48 hrs.).

Anal. Calc'd for $C_{19}H_{24}N_2O$: C, 77.0; H, 8.16.
Found: C, 76.4; H. 8.17.

x-(2-Dimethylamino-1-hydroxyethyl)-N-acetyl-9,10-dihydroacridine hydrochloride (SN 5981). To an ice-cooled solution of 12 g. (6 moles) of dimethylamine in 250 ml. of dry ether was added 15 g. of finely powdered bromo ketone. The flask was intermittently cooled and shaken for 10 min., mechanically shaken for 5 hrs. then kept at 5° overnight. After removing dimethylamine hydrobromide (5.2 g. or 92%), the washed and dried ethereal solution gave 11.9 g. of the syrupy amino ketone. A solution of the latter in 20 ml. acetone was acidified with 9 ml. of 15% alcoholic HCl and strongly diluted with dry ether. Scratching caused the separation of the powdery hydrochloride. This was triturated twice with dry ether and the amino ketone regenerated under ether (NH_4OH). The resulting clear, amber syrup (10 g.) in 50 ml. of methanol, with 0.25 g. PtO_2, absorbed 1.05 moles of hydrogen (48 hrs.). The filtered methanol solution yielded 8.9 g. of syrupy amino alcohol. A solution of the latter in 20 ml. of acetone afforded, after acidification with 7 ml. of 15% alcoholic HCl and dilution with dry ether, 10 g. of a cream-colored, micro-crystalline powder which was dissolved in 1 liter of boiling acetone (containing a few drops of methanol) and clarified with Norit. Overnight (20°) the solution deposited 3.5 g. (crop I) of pale yellow crystals. Another 2 g. (crop II) of crystalline hydrochloride was derived from the concentrated mother liquor (60 hrs. at 20°). The salt crystallizes from acetone (containing a few drops of methanol) in clusters of 4-sided plates which are obviously solvated, m.p. 124–127° (foams). The m.p. was not changed appreciably on recrystallization. That the salt is solvated (methanol) is evident from the analytical data, but an accurate methanol determination could not be obtained owing to mechanical losses caused by frothing during vacuum drying.

Anal. Calc'd for $C_{19}H_{23}ClN_2O_2 \cdot CH_3OH$: C, 63.4; H, 7.18.
Found: C, 63.4; H, 7.01.

x-(2-Dimethylamino-1-hydroxyethyl)-9,10-dihydroacridine (SN 6779). This substance was prepared from the above-described N-acetyl amino alcohol hydrochloride by hydrolysis with ethanolic KOH as outlined under the diethylamino homolog. From 7.5 g. of crude hydrochloride 3.3 g. of deacetylated base resulted, which crystallized in needles from 70% ethanol; m.p. 120–121.5°. The base is air-sensitive.

Anal. Calc'd for $C_{17}H_{20}N_2O$: C, 76.1; H, 7.51.
Found: C, 76.6; H, 7.48.

x-(2-Di-n-propylamino-1-hydroxyethyl)-N-acetyl-9,10-dihydroacridine hydrochloride (SN 5928). This member of the series was synthesized in the same manner as the diethylamino

homolog. From 10 g. of bromo ketone and 5.9 g. (2 moles) of di-*n*-propylamine in 150 ml. of dry ether, the following were obtained in the order given: 11 g. of syrupy amino ketone; 10 g. of crude, amino ketone hydrochloride and 8.2 g. of regenerated amino ketone base. The latter, in 100 ml. of methanol with 0.35 g. PtO_2, absorbed 0.93 mole of hydrogen in 60 hrs. Conversion of the syrupy amino alcohol to its hydrochloride was accomplished in acetone with alcoholic HCl and dry ether. The crude salt (6.9 g.) was recrystallized from acetone-ether; after 48 hrs., 4.2 g. of small, colorless prisms of m.p. 186–188° d. Two additional recrystallizations raised the m.p. to 190–191.5° d.

Anal. Calc'd for $C_{23}H_{31}ClN_2O_2$: C, 68.5; H, 7.76.
Found: C, 68.4; H, 7.84.

x-(2-Di-n-propylamino-1-hydroxyethyl)-9,10-dihydroacridine (SN 5698). Alkaline hydrolysis (5% ethanolic KOH) of 8 g. of the above amino alcohol hydrochloride resulted in a syrup which slowly crystallized when scratched. Recrystallization from 70% ethanol gave 4.1 g. of air-sensitive, felted needles, m.p. 91–93°. After three recrystallizations, the m.p. was 92–94°.

Anal. Calc'd for $C_{21}H_{28}N_2O$: C, 77.7; H, 8.70.
Found: C, 77.6; H, 9.13.

x-(2-Di-n-butylamino-1-hydroxyethyl)-N-acetyl-9,10-dihydroacridine hydrochloride (SN 5934). Employing the procedure outlined above for the diethylamino compound, the condensation of 15 g. of bromo ketone with 11.3 g. (2 moles) of di-*n*-butylamine in 200 ml. of dry ether gave, in the order named: 15.4 g. of syrupy amino ketone base; 12.3 g. of crude amino ketone hydrochloride and 9 g. of regenerated amino ketone. Catalytic reduction of the latter in 100 ml. of methanol with 0.35 g. PtO_2 (1.1 moles of H_2 absorbed in 60 hrs.) gave 8.5 g. of an amber syrup. This was taken up in 25 ml. of acetone and treated with 4 ml. (1 equivalent) of 5.4 *N* alcoholic HCl. The addition of dry ether precipitated the hydrochloride as a yellow gum which gradually solidified when scratched. The crude salt (7.8 g.) was dissolved in boiling acetone, filtered, concentrated to small volume and treated with dry ether to light turbidity. After 36 hrs. 3.8 g. of clusters of practically colorless prisms separated; m.p. 178–180° d. Three crystallizations (acetone-ether) gave the constant m.p. 183–184.5° d.

Anal. Calc'd for $C_{25}H_{35}ClN_2O_2$: C, 69.7; H, 8.19.
Found: C, 69.4; H, 8.29.

Another 0.8 g. of less pure hydrochloride was recovered from the mother liquors.

x-(2-Di-n-amylamino-1-hydroxyethyl)-9,10-dihydroacridine (SN 5849). To a cooled suspension of 20 g. of bromo ketone in 250 ml. of dry ether, 18.3 g. (2 moles) of di-*n*-amylamine was added and the system mechanically shaken for 15 hrs. After chilling in ice, 12.5 g. of di-*n*-amylamine hydrobromide was removed. The ethereal solution afforded 22.5 g. of amino ketone base which, in turn, gave an oily hydrochloride when treated in cold acetone, with the calculated amount of alcoholic HCl. The hydrochloride remained gummy despite repeated triturations with fresh portions of dry ether and scratching. The regenerated amino ketone 13.5 g. (NH_4OH-ether) was reduced in 60 ml. of methanol in the presence of 0.6 g. PtO_2 (0.91 mole H_2 absorbed in 62 hrs.). The hydrochloride of the resulting amino alcohol, formed in acetone with alcoholic HCl and dry ether, appeared as a gum which could not be crystallized. The amino alcohol base was therefore deacetylated directly.

Deacetylation. Hydrolysis of 11.9 g. of the above base in 180 ml. of 5% alcoholic KOH, as described previously, afforded 7.5 g. of a syrup which slowly crystallized (2 hrs.). Recrystallization from 70% ethanol gave 6 g. of practically colorless, air-sensitive needles. The melting point, after three crystallizations, was 78–80°.

Anal. Calc'd for $C_{25}H_{36}N_2O$: C, 78.9; H, 9.54.
Found: C, 78.5; H, 9.51.

x-(2-Tetrahydroisoquinolino-1-oxoethyl)-N-acetyl-9,10-dihydroacridine. The condensation of 9 g. of bromo ketone with 6.95 g. (2 moles) of tetrahydroisoquinoline (14) in 150 ml. of dry ether gave, after 15 hrs. shaking, 14.3 g. of a colorless precipitate which proved to be a mixture consisting of a small amount of unchanged tetrahydroisoquinoline, the hydro-

bromide of the latter, and the expected amino ketone. Two triturations of the mixture with dry ether removed tetrahydroisoquinoline; the amine hydrobromide was extracted by repeated leaching with warm (40°) water. The residual, water-insoluble amino ketone was a colorless powder, 8.6 g. (84%) which crystallized from acetone-water in diamond-shaped prisms. After three crystallizations, the m.p. was 162–164.5°.

Anal. Calc'd for $C_{26}H_{24}N_2O_2$: C, 78.7; H, 6.10.
Found: C, 78.4; H, 6.30.

x-(2-Tetrahydroisoquinolino-1-hydroxyethyl)-N-acetyl-9,10-dihydroacridine hydrochloride (SN 6088). A solution of 6.2 g. of the above amino ketone in 60 ml. acetone was treated with 2.85 ml. (1 equiv.) of 5.4 *N* ethanolic HCl and the powdery hydrochloride precipitated with dry ether (6.9 g.). The salt, in 130 ml. of methanol, was digested with Norit for a few minutes and, after filtration, reduced in the presence of 0.35 g. of PtO_2 (1.05 moles H_2 absorbed in 26 hrs.). The syrupy residue, from concentration (*vacuo*) of the filtered solution, was taken up in a little acetone and strongly diluted with dry ether. The amino alcohol hydrochloride separated as a gum which quickly solidified when scratched. After a second trituration with dry ether, the pale yellow powder (5.9 g.) was dissolved in boiling acetone, to which a few drops of methanol were added, digested with Norit, filtered and concentrated to small volume. The hydrochloride crystallized spontaneously; 3.5 g. of nearly colorless, crystalline crusts. The constant m.p. 216–217° d. was obtained after three recrystallizations (acetone-ether).

Anal. Calc'd for $C_{26}H_{27}ClN_2O_2$: C, 71.8; H, 6.26.
Found: C, 71.4; H, 5.94.

x-(2-Transdecahydroquinolino-1-hydroxyethyl)-N-acetyl-9,10-dihydroacridine hydrochloride (SN 6089). Ten grams of bromo ketone shaken with 8.1 g. (2 moles) of transdecahydroquinoline (15) in 150 ml. of dry ether (15 hrs.) afforded the following intermediates: 11.2 g. of syrupy amino ketone; 11.3 g. of crude amino ketone hydrochloride, and 9.1 g. of regenerated amino ketone base. The latter in 100 ml. of methanol, in the presence of 0.3 g. PtO_2, absorbed 1 mole of H_2 (39 hrs.) to give 8.7 g. of oily amino alcohol. A solution of this in 25 ml. of acetone was treated with 4.1 ml. (1 equiv.) of 5.4 *N* ethanolic HCl and the hydrochloride precipitated as a gum with dry ether. Trituration with fresh, dry ether gave a pale-yellow powder (9.4 g.). This was dissolved in 300 ml. of boiling acetone (Norit) filtered and concentrated (*vacuo*). After 24 hrs. (20°), 6.4 g. of a colorless, microcrystalline powder was collected. Repeated recrystallization from acetone gave colorless, crystalline crusts, m.p. 175–177° d.

Anal. Calc'd for $C_{26}H_{33}ClN_2O_2$: C, 70.8; H, 7.54.
Found: C, 70.6; H, 7.82.

x-(2-Transdecahydroquinolino-1-hydroxyethyl)-9,10-dihydroacridine hydrochloride (SN 5929). A solution of 4.3 g. of the above amino alcohol hydrochloride in 55 ml. of 5% ethanolic KOH was heated for 2 hrs. (steam-bath) then poured into 500 ml. of 15% NaCl solution. The light-tan precipitate was collected, triturated 3 times with water and dried in a vacuum desiccator—yield 3 g. A filtered solution of the latter in 125 ml. of warm, absol. ethanol was acidified with 1.8 ml. (1 equiv.) of 5.4 *N* ethanolic HCl. After 24 hrs. (5°), the hydrochloride was obtained as virtually colorless, micro-needles, 2.7 g. Three recrystallizations from absol. ethanol-ether gave the constant m.p. 232–234° d.

Anal. Calc'd for $C_{24}H_{31}ClN_2O$: C, 72.3; H, 7.83.
Found: C, 72.0; H, 7.86.

SUMMARY

The aluminum chloride-catalyzed bromoacetylation of N-acetyl-9,10-dihydroacridine is described.

Several new amino carbinols derived from x-(ω-bromoacetyl)N-acetyl-9,10-dihydroacridine have been prepared.

The plasmodicidal activity of three members of this series of drugs has been noted.

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