[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, SWARTHMORE COLLEGE]

Quinoline Analogs of Podophyllotoxin. II. Friedländer Reactions with Tetronic Acid: A General Method for the Preparation of 2-Hydroxymethyl-3-quinolinecarboxylic Acid Lactones[1]

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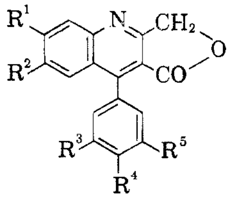
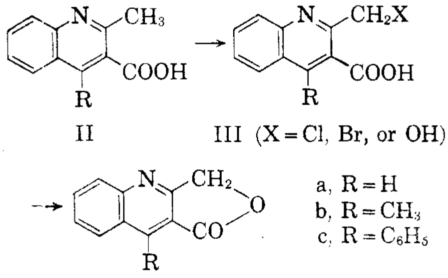
A variation of the Friedländer reaction in which an *o*-amino aromatic carbonyl compound is condensed with the cyclic β-ketoester, tetronic acid, instead of the usual acyclic active methylene carbonyl compound, has been found to provide a convenient general method for the preparation of 2-hydroxymethyl-3-quinolinecarboxylic acid lactones. Three representative quinoline lactones derived from *o*-aminobenzaldehyde, *o*-aminoacetophenone, and *o*-aminobenzophenone have been prepared by this method, and the products have been characterized by means of their ultraviolet absorption spectra and by oxidative degradation to known quinolinecarboxylic acids.

In a continuation of the work described in the preceding paper in this series,[2] it became necessary to prepare certain quinoline lactones of type I. Since a search of the literature failed to reveal any examples of compounds containing the 2-hydroxymethyl-3-quinolinecarboxylic acid lactone moiety, we undertook to develop a general method for the preparation of this new class of compounds. The results of this work are described in the present communication.



I

Consideration was first given to routes involving the lactonization of intermediates such as III, derived from the corresponding quinaldinecarboxylic acids (II), but the inaccessibility of some of the required 4-substituted 3-quinaldinecarboxylic acids did not make this method appear very promising.



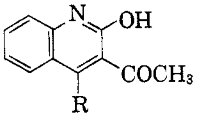
II

III (X = Cl, Br, or OH)

IV

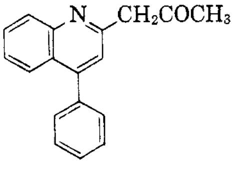
a, R = H
b, R = CH_3
c, R = C_6H_5

One of the most generally useful methods for the synthesis of Py-substituted quinolines is the Friedländer method, in which an *o*-amino aromatic carbonyl compound is condensed with a carbonyl compound having an active α-methylene group.[3] Thus IIa may readily be prepared by the condensation of *o*-aminobenzaldehyde with ethyl acetoacetate and subsequent hydrolysis of the resultant ester.[4] The applicability of this method to the preparation of 4-alkyl and 4-aryl quinolines of type II, however, is seriously limited by the tendency of the *o*-aminoaryl ketones to react abnormally with all but the simplest methyl ketones.[5] Thus *o*-aminoacetophenone and *o*-aminobenzophenone yield only the carbostyrils Va and Vb, respectively, on treatment with ethyl acetoacetate,[6] and, even more surprisingly, *o*-aminobenzophenone condenses with acetylacetone to give 2-acetonyl-4-phenylquinoline (VI) instead of the expected 3-acetyl-2-methyl-4-phenylquinoline (VII).[5,7]

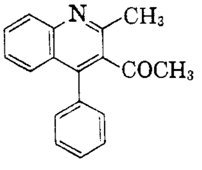


V

a, R = CH_3
b, R = C_6H_5



VI



VII

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(1) This investigation was supported by research grant CY-2726(C) from the National Cancer Institute of the National Institutes of Health, U. S. Public Health Service.

(2) E. A. Fehnel, *J. Org. Chem.*, **23**, 432 (1958).

(3) For general discussions of the Friedländer reaction, see R. C. Elderfield, *Heterocyclic Compounds*, John Wiley and Sons, Inc., New York, 1952, vol. 4, pp. 45–47, 203–204, 209–210; R. H. Manske, *Chem. Revs.*, **30**, 113 (1942); C. Hollins, *The Synthesis of Nitrogen Ring Compounds*, D. Van Nostrand and Co., New York, 1924, pp. 283–286.

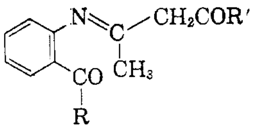
(4) P. Friedländer and C. F. Gohring, *Ber.*, **16**, 1833 (1883).

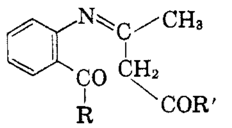
(5) *Cf.* W. Borsche and F. Sinn, *Ann.*, **538**, 283 (1939).

(6) E. A. Fehnel and A. S. Penn, unpublished work; see also W. Borsche and F. Sinn.[5]

(7) *o*-Aminobenzaldehyde behaves normally in the reaction with acetylacetone, giving 3-acetyl-2-methylquinoline [J. Eliasberg and P. Friedländer, *Ber.*, **25**, 1752 (1892)].

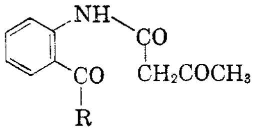
It seems unlikely that these marked differences in the behavior of the *o*-amino aromatic aldehydes and ketones arise merely from the diminished electrophilic reactivity of the carbonyl group in the ketones. The classical Friedländer reaction appears to involve two distinct steps: (1) a reversible condensation between the aromatic amino group and a carbonyl group in the active α-methylene compound to produce an anil, followed by (2) an irreversible intramolecular Claisen-type condensation between the aromatic *o*-carbonyl group and an α-methylene or α-methyl group in the azomethine side chain of the anil. With polyfunctional α-methylene carbonyl compounds which present the possibility of alternative reaction paths in one or both of these steps, the nature of the final products must depend upon the relative rates of the various competing reactions. In most Friedländer-type reactions involving *o*-aminoaryl aldehydes the observed products are those that would be expected on the basis of electronic effects alone, uncomplicated by any overwhelming steric factors; anil formation occurs at the most reactive carbonyl group in a polyfunctional α-methylene carbonyl component and cyclization of the resultant anil occurs at the more reactive α-carbon atom if two α-methylene groups of different degrees of reactivity are present in the azomethine side chain. In the "abnormal" reactions of the *o*-aminoaryl ketones, on the other hand, steric factors appear to outweigh electronic factors in determining the nature of the final products. When, for example, in the reaction of *o*-aminobenzophenone with acetylacetone the aromatic carbonyl group is observed to condense with the relatively unreactive terminal α-methyl group rather than the more reactive central α-methylene group in the intermediate anil, it becomes difficult to escape the conclusion that, in this case at least, the course of the reaction is governed by influences other than the relative electrophilic and nucleophilic activities of the reactive centers. An examination of scale models of stereoisomeric *syn*- and *anti*-methyl anils of types VIII and IX (or the corresponding eneamines[8]) strongly suggests that the crucial factor may be the extent to which the group R interferes sterically with the attainment of the transition state conformations required for ring closure. If the energy barrier involved in the formation of structures of type IX (or the corresponding cyclic transition states) when R is phenyl is so great as to preclude the appearance of these species in the reaction of *o*-aminobenzophenone with acetylacetone or ethyl acetoacetate, the failure to obtain the "normal" Friedländer reaction products in these cases is understandable.


VIII


IX

$R = H, CH_3, \text{ or } C_6H_5$
$R' = CH_3 \text{ or } OC_2H_5$

In Friedländer reactions involving β-ketoesters, an alternative reaction path is obviously available in which condensation with the aromatic amine occurs at the ester function to produce an anilide, rather than at the ketone function to produce an anil. The occurrence of both types of reaction and the facile interconvertibility of the products has been amply demonstrated in the case of several simple aromatic amines, including *o*-toluidine.[9] There can be little doubt, therefore, that in the first stage of the reactions of *o*-aminoaryl carbonyl compounds with ethyl acetoacetate anilides of type X must be present in reversible equilibrium with the anils VIII and IX. When steric interference to nucleophilic attack on the aromatic carbonyl group is minimal (*i.e.*, when R = H), so that any of the three conformations VIII, IX, or X may be attained without excessive strain, ring closure would be expected to proceed more readily with either IX or X than with VIII because of the much greater reactivity of the appropriately oriented α-methylene groups in IX and X. The observation that *o*-aminoaryl aldehydes generally yield 3-quinolinecarboxylic esters on reaction with ethyl acetoacetate implies either that ring closure occurs more rapidly with the anil IX than with the anilide X or that anil formation occurs more rapidly than anilide formation under the reaction conditions usually em-


X

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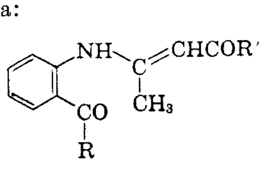
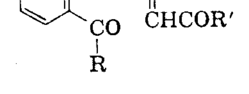
[8] The available evidence indicates that anils derived from β-dicarbonyl compounds exist predominantly in the tautomeric eneamine forms, with the carbon-carbon double bond in conjugation with the carbonyl group. It is probable, therefore, that the anils under discussion are involved in the following equilibria:

VIII ⇄



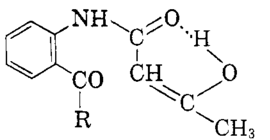
IX ⇄



The two eneamine structures thus represented might, of course, be configurationally equivalent (*e.g.*, if the arylamino and —COR′ groups are *trans* in both cases), but they would still be conformationally different and would presumably be subject to the same steric considerations as the corresponding azomethine structures.

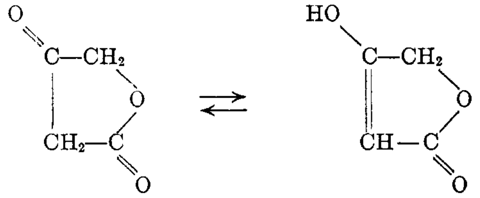
[9] C. R. Hauser and G. A. Reynolds, *J. Am. Chem. Soc.*, **70**, 2402 (1948).

ployed.[10] If, in the case of the anils derived from the *o*-aminoaryl ketones (R = CH_3 or C_6H_5), structure VIII is highly favored over structure IX for steric reasons as suggested above, only the *syn*-methyl anil VIII and the anilide X need be considered as potential precursors of the final product. Presumably here the much greater reactivity of the doubly activated methylene group in the anilide as compared with the relatively feeble reactivity of the methyl group in the *syn*-methyl anil governs the subsequent course of the reaction. The apparent failure of the terminal acetyl group to interfere sterically with the ring closure of the anilide may be due to the well known tendency of β-dicarbonyl compounds to exist in chelate enol forms,[11] which in this case (see structure XI) would have a very favorable effect upon the geometry of the conformation required for ring closure.

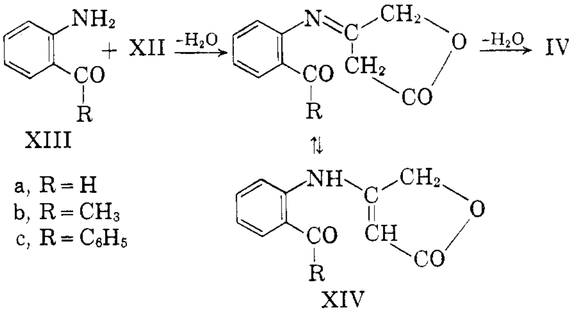


XI

These considerations led us to investigate the possibility of using the β-ketolactone, tetronic acid (XII), as the active α-methylene carbonyl component in Friedländer-type reactions. Steric factors should play a negligible role in determining the relative stabilities of the cyclic transition state conformations of the anils formed from this cyclic carbonyl compound, and the unusually high reactivity of the α-methylene group, as manifested by the extensive enolization and strongly acidic nature of this substance, should facilitate the desired ring closure. Subsequent experiments confirmed these expectations and showed this variation of the Friedländer method to be a practical and convenient route to quinoline lactones of type IV.



XII



XIII

a, R = H
b, R = CH_3
c, R = C_6H_5

XIV

o-Aminobenzaldehyde reacts readily with tetronic acid in boiling ethanol, producing the lactone IVa directly in a single operation and rendering unnecessary the isolation of the intermediate anil. The *o*-aminoaryl ketones (XIIIb, XIIIc), on the other hand, yield only the corresponding anils (XIVb, XIVc) when heated on a steam bath with an equivalent amount of tetronic acid either in ethanol or in the absence of a solvent. Cyclization of these anils to the quinoline lactones (IVb, IVc) is easily accomplished, however, by dissolving them in cold concentrated sulfuric acid, from which the desired products may be isolated in almost quantitative yield by dilution with water and neutralization with ammonium hydroxide. The over-all yields of purified quinoline lactones obtained from these three representative *o*-amino aromatic carbonyl compounds (XIIIa, XIIIb, XIIIc) were all above 70%.

The structures of the three quinoline lactones (IVa, IVb, IVc) were established by a comparison of their ultraviolet absorption spectra with those of closely related quinoline derivatives of known structure and by oxidative degradation of each lactone to the corresponding 3-quinolinecarboxylic acid. Strong family resemblances are noted among all the spectra in this series of compounds (Figs. 1–3), the most characteristic features being an intense short wave-length band with a maximum in the 225–245 mμ region and a less intense broad band at longer wave lengths with a suggestion of fine structure and with a shoulder (which in one case emerges as a distinct peak) in the 320–340 mμ region. The principal effect of the lactone ring is to shift the absorption toward somewhat longer wave lengths and higher intensities relative to the spectra of analogous carboxylic acid derivatives.

Oxidation of IVa and IVc with selenium dioxide and of IVb with potassium permanganate led, *via*

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[10] The latter assumption seems much more reasonable than the former. In the first place, generalized experience suggests that the appropriately oriented α-methylene group in the anilide X would be more reactive than the corresponding group of the anil IX. Furthermore, the previously cited studies of Hauser and Reynolds[9] are consistent with the view that anilide formation becomes significant only under much more drastic conditions than are required for anil formation.

It is interesting to note in this connection that in at least two cases involving substituted *o*-aminobenzaldehydes it has been possible to obtain either the 3-quinolinecarboxylic esters or the 3-acylcarbostyrils, depending upon the conditions under which the condensations with the β-ketoesters were carried out [J. Tröger and C. Cohaus, *J. prakt. Chem.*, **117**, 97 (1927); J. Tröger and J. Bohnekamp, *J. prakt. Chem.*, **117**, 161 (1927)]. The 3-quinolinecarboxylic esters formed readily on refluxing an ethanolic solution of the *o*-aminoaryl aldehyde and the β-ketoester in the presence of a trace of sodium hydroxide. The carbostyrils were obtained only after the components had been heated together at 160° in the absence of both solvent and catalyst for several hours.

[11] *Cf.* the enol content of acetoacetanilide in various solvents: 8.9–9.5% (MeOH), 15.3–15.5% (EtOH), 25% (EtOAc), 12.0–14.4% (C_6H_6), 41.7–43.3% (Et_2O) [K. H. Meyer, *Ber.*, **47**, 826 (1914)].

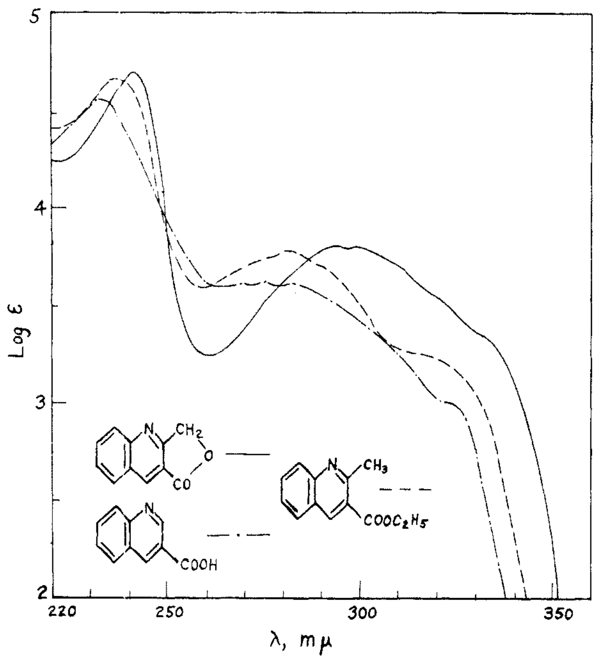
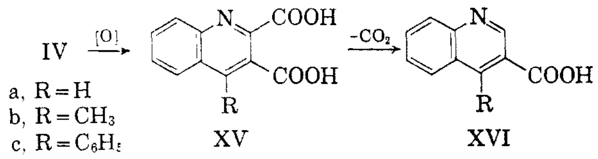


Fig. 1. Ultraviolet absorption spectra of 2-hydroxymethyl-3-quinolinecarboxylic acid lactone (IVa), ——; ethyl 2-methyl-3-quinolinecarboxylate, – – –; and 3-quinolinecarboxylic acid (XVIa), —·—·—; all in absolute ethanol

the corresponding acridinic acids (XV), to the previously known 3-carboxylic acids (XVI), which were identified in the case of XVIa and XVIb by the melting points of the acids and their picrate derivatives and in the case of XVIc by a mixed melting point with an authentic sample of the acid. The 4-phenylquinoline lactone IVc was further characterized by conversion to the previously unknown 4-phenylacridinic anhydride, the spectrum of which is included for comparison with those of the parent lactone and the corresponding 3-carboxylic acid in Fig. 3.



XV XVI

EXPERIMENTAL[12]

2-Hydroxymethyl-3-quinolinecarboxylic acid lactone (IVa). A solution of 2.16 g. (0.0178 mole) of freshly prepared *o*-aminobenzaldehyde[13] in 12 ml. of absolute ethanol was added to a solution of 1.78 g. (0.0178 mole) of tetronic acid[14] in 12 ml. of absolute ethanol, and the mixture was refluxed for 1 hr. The resultant yellow suspension was cooled and the precipitate was collected, washed with a little ethanol, and dried to give 2.41 g. (73%) of pale yellow crystals, m.p. 217–219°. Treatment with Nuchar and recrystallization from benzene provided colorless needles which melted at 219–220°; λ_{max}^{EtOH} 242 mμ (log ε 4.70), 294 mμ (log ε 3.80), 298 mμ (log ε 3.80).

Anal. Calcd. for $C_{11}H_7NO_2$: C, 71.34; H, 3.81; N, 7.56. Found: C, 71.35; H, 3.95; N, 7.60.

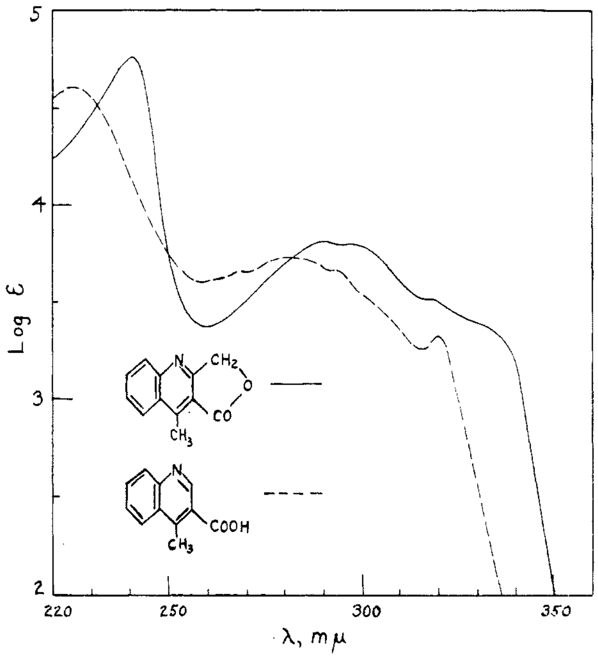


Fig. 2. Ultraviolet absorption spectra of 2-hydroxymethyl-4-methyl-3-quinolinecarboxylic acid lactone (IVb), ——; and 4-methyl-3-quinolinecarboxylic acid (XVIb), - - -; all in absolute ethanol

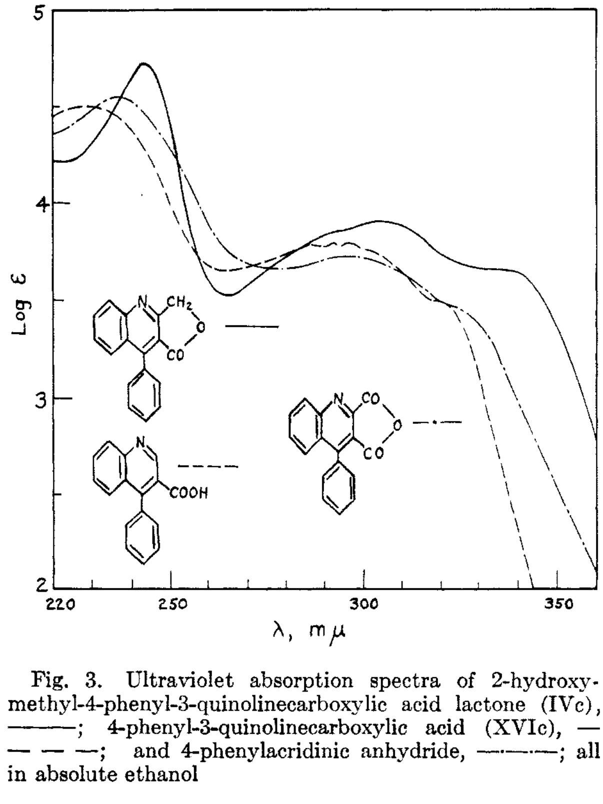


Fig. 3. Ultraviolet absorption spectra of 2-hydroxymethyl-4-phenyl-3-quinolinecarboxylic acid lactone (IVc), ——; 4-phenyl-3-quinolinecarboxylic acid (XVIc), — — —; and 4-phenylacridinic anhydride, —·—·—; all in absolute ethanol

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[12] Microanalyses are by Clark Microanalytical Laboratory, Urbana, Ill.

[13] L. I. Smith and J. W. Opie, *Org. Syntheses*, Coll. Vol. III, 56 (1955).

[14] L. A. Duncanson, *J. Chem. Soc.*, 1207 (1953).

The *picrate* of IVa was prepared in the usual way,[15] except that the product could not be recrystallized from ethanol without decomposition. The crude product was therefore washed with ether and dried to give yellow crystals, m.p. 172–174° (dec.), which were analyzed without further purification.

Anal. Calcd. for $C_{17}H_{10}N_4O_9$: C, 49.28; H, 2.43. Found: C, 49.64; H, 2.57.

Oxidative degradation of IVa to 3-quinolinecarboxylic acid (XVIa). A mixture of 1.78 g. (0.0096 mole) of IVa, 2.22 g. (0.020 mole) of selenium dioxide, 13 ml. of dioxane, and 0.7 ml. of water was refluxed for 5 hr., after which the hot reaction mixture was filtered to remove the precipitated selenium. On cooling, the dark red filtrate deposited a pale pink solid, which was collected, washed with a little ether, and dried; yield, 0.49 g. This material was mixed with a few ml. of water, evaporated to dryness on a steam bath, and finally heated at 120–130° on an oil bath for 90 min.[16] The solid residue was treated with Nuchar and recrystallized from ethanol to give a colorless microcrystalline powder, m.p. 273–274° (dec.),[17] $\lambda_{\max}^{\mathrm{EtOH}}$ 233 mμ (log ε 4.56), 275 mμ (log ε 3.62), inflection 322 mμ (log ε 3.02).[18] The picrate of this compound, prepared in the usual way[15] and recrystallized from ethanol, melted at 218–220° with previous sintering.[19]

β-(o-Acetylphenylimino)butyrolactone (XIVb). A mixture of 5.02 g. (0.0371 mole) of *o*-aminoacetophenone and 3.71 g. (0.0371 mole) of tetronic acid[14] was heated in a boiling water bath until the initially homogeneous melt had completely solidified (*ca.* 5–10 min.). The resultant yellow solid was taken up in *ca.* 300 ml. of boiling ethanol; on cooling, the solution deposited 6.27 g. (78%) of yellow leaflets, m.p. 178–181° Further recrystallization from ethanol raised the m.p. to 180–182°; $\lambda_{\max}^{\mathrm{EtOH}}$ 251 mμ (log ε 4.17), 288 mμ (log ε 4.26), 345 mμ (log ε 3.90).

Anal. Calcd. for $C_{12}H_{11}NO_3$: C, 66.35; H, 5.11; N, 6.45. Found: C, 66.21; H, 4.98; N, 6.53.

2-Hydroxymethyl-4-methyl-3-quinolinecarboxylic acid lactone (IVb). Finely powdered XIVb (6.45 g.) was added in small portions over a 15-min. period to 65 ml. of cold concentrated sulfuric acid. The resultant solution was poured onto 100 g. of cracked ice, and 200 ml. of concentrated ammonium hydroxide was added cautiously while stirring and cooling the mixture in an ice bath. The precipitate was collected, washed thoroughly with water, and dried in an oven at 110°; yield, 5.83 g. (98%) of white powder, m.p. 208–210°. Recrystallization from benzene gave colorless crystals melting at 209–210°; $\lambda_{\max}^{\mathrm{EtOH}}$ 241 mμ (log ε 4.76), 291 mμ (log ε 3.81).

Anal. Calcd. for $C_{12}H_9NO_2$: C, 72.35; H, 4.55; N, 7.03. Found: C, 72.52; H, 4.50; N, 7.11.

The *picrate* of IVb, prepared in the usual way,[15] was washed with ether and dried to give silky yellow needles melting at 188–189°.

Anal. Calcd. for $C_{18}H_{12}N_4O_9$: C, 50.47; H, 2.83. Found: C, 50.21; H, 2.92.

Oxidative degradation of IVb to 4-methyl-3-quinolinecarboxylic acid (XVIb). A suspension of 2.10 g. of IVb in 100 ml. of 0.1*M* aqueous sodium hydroxide was heated and stirred while 5.6 g. of potassium permanganate was added in small portions over a 1-hr. period. The mixture was then cooled, saturated with sulfur dioxide, and filtered to remove a small amount of unreacted lactone. The filtrate was made strongly acidic by the addition of a small amount of hydrochloric acid and was concentrated to a small volume by distillation under reduced pressure. The resultant precipitate was collected, washed with water, and dried to provide 1.04 g. of pale yellow microcrystalline powder melting at *ca.* 185–190° (dec.). A solution of this material in 5 ml. of glacial acetic acid was refluxed for 2 hr. and was then evaporated to dryness on the steam bath. The brown crystalline residue was recrystallized from methanol to give pale yellow crystals which melted at 231–233° (dec.) alone and when mixed with an authentic sample of 4-methyl-3-quinolinecarboxylic acid[20] (m.p. 232–233° dec.); $\lambda_{\max}^{\mathrm{EtOH}}$ 226 mμ (log ε 4.60), 268 mμ (log ε 3.66), 282 mμ (log ε 3.72), 320 mμ (log ε 3.33).

β-(o-Benzoylphenylimino)butyrolactone (XIVc). An intimate mixture of 1.97 g. (0.0100 mole) of *o*-aminobenzophenone and 1.00 g. (0.0100 mole) of tetronic acid[14] was heated in a boiling water bath until the initially homogeneous melt had completely solidified (*ca.* 10 min.). The resultant yellow solid was taken up in *ca.* 150 ml. of boiling methanol; on cooling, the solution deposited 2.08 g. (75%) of yellow crystals, m.p. 178–180°. Dilution of the mother liquor with an equal volume of water provided an additional 0.38 g. of product of comparable purity, giving a total yield of 88%. Recrystallization of this material from methanol afforded silky yellow needles melting at 182–183°; $\lambda_{\max}^{\mathrm{EtOH}}$ 258 mμ (log ε 4.32), 330 mμ (log ε 3.64), inflection *ca.* 280 mμ (log ε 4.13).

Anal. Calcd. for $C_{17}H_{13}NO_3$: C, 73.10; H, 4.69; N, 5.02. Found: C, 72.86; H, 4.70; N, 5.03.

2-Hydroxymethyl-4-phenyl-3-quinolinecarboxylic acid lactone (IVc). Finely powdered XIVc (4.60 g.) was added in small portions over a 15-min. period to 25 ml. of cold concentrated sulfuric acid. The resultant solution was poured onto 50 g. of ice, and 75 ml. of concentrated ammonium hydroxide was added cautiously while the mixture was stirred and cooled in an ice bath. The precipitate was collected, washed thoroughly with water, and dried at 110° to give 4.25 g. (99%) of pale yellow microcrystalline powder, m.p. 201–203°. Treatment with Nuchar and recrystallization from benzene provided colorless crystals melting at 204–205°; $\lambda_{\max}^{\mathrm{EtOH}}$ 244 mμ (log ε 4.71), 305 mμ (log ε 3.90), inflection *ca.* 330 mμ (log ε 3.66).

Anal. Calcd. for $C_{17}H_{11}NO_2$: C, 78.14; H, 4.24; N, 5.36. Found: C, 78.36; H, 4.43; N, 5.14.

The *picrate* of IVc was prepared in the usual way[15] and was recrystallized from ethanol to give yellow-orange crystals melting at 171–172°.

Anal. Calcd. for $C_{23}H_{14}N_4O_9$: C, 56.33; H, 2.88. Found: C, 56.60; H, 2.75.

Oxidative degradation of IVc to 4-phenyl-3-quinolinecarboxylic acid (XVIc). A mixture of 1.96 g. (0.0075 mole) of IVc, 1.67 g. (0.015 mole) of selenium dioxide, 10 ml. of dioxane, and 0.7 ml. of water was refluxed for 90 min., after which the hot reaction mixture was filtered to remove the precipitated selenium. The filtrate was diluted with *ca.* 200 ml. of water and allowed to stand for several hours. The resultant gelatinous suspension was filtered and the precipitate was washed with water and dried; yield, 1.42 g. (65%) of crude 4-phenylacridinic acid, m.p. *ca.* 200–210°

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(15) R. L. Shriner, R. C. Fuson, and D. Y. Curtin, *The Systematic Identification of Organic Compounds*, 4th ed., John Wiley & Sons, Inc., New York, N. Y., 1956, p. 229, method A.

(16) *Cf.* C. Graebe and H. Caro, *Ber.*, **13**, 99 (1880), for the conversion of acridinic acid to 3-quinolinecarboxylic acid. The indefinite m.p. of acridinic acid makes it unsuitable as a derivative for identification purposes.

(17) Melting point of 3-quinolinecarboxylic acid, 274–275° [W. Borsche and R. Manteuffel, *Ann.*, **526**, 22 (1936)], 270–272° [H. Gilman and S. M. Spatz, *J. Am. Chem. Soc.*, **62**, 446 (1940)].

(18) *Cf.* the spectrum of 3-quinolinecarboxylic acid given by S. Chiavarelli and G. B. Marini-Bettòlo, *Gazz. chim. ital.*, **82**, 86 (1952).

(19) Melting point of 3-quinolinecarboxylic acid picrate, 217–218° (W. Borsche and R. Manteuffel, ref. cited in footnote 17).

(20) L. Marion, R. H. F. Manske, and M. Kulka, *Can. J. Research*, **24B**, 224 (1946). The sample was kindly supplied by Dr. Manske.

(dec.).[21] When 0.45 g. of this material was heated at 200–210° for 5 min. and the product was recrystallized from ethanol, there was obtained 0.19 g. of almost colorless powder, m.p. 226–228°. Further recrystallization from ethanol gave small colorless needles, m.p. 231–232°[22]; $\lambda_{\text{max}}^{\text{EtOH}}$ 228 mμ (log ε 4.49), 293 mμ (log ε 3.79), 296 mμ (log ε 3.79), inflection 318 mμ (log ε 3.50). The picrate of this compound melted at 198–199°.[23]

4-Phenylacridinic anhydride. A mixture of 1.42 g. of the crude 4-phenylacridinic acid described above and 3.0 ml. of acetic anhydride was heated at 120° for 10 min., after which the temperature was gradually raised to 150° over a 30-min. period. On cooling, the precipitate was collected, washed with carbon tetrachloride, and dried *in vacuo* to provide 0.95 g. (71%) of pale yellow crystals which melted at 250–255° with previous sintering. Recrystallization from benzene raised the m.p. to 264–266°; $\lambda_{\text{max}}^{\text{EtOH}}$ 236 mμ (log ε 4.54), 296 mμ (log ε 3.72), inflection 320 mμ (log ε 3.50).

Anal. Calcd. for $C_{17}H_9NO_3$: C, 74.16; H, 3.30; N, 5.09. Found: C, 74.41; H, 3.34; N, 5.01.

Ultraviolet absorption spectra. The ultraviolet absorption spectra were determined with a Beckman Model DU spectrophotometer, readings being made at intervals of 5 mμ or less (1 mμ in the vicinity of absorption maxima) with a nominal band width of approximately 1 mμ. Absolute ethanol was used as the solvent. The ethyl 2-methyl-3-quinolinecarboxylate required as a reference compound for comparison of the spectra in Fig. 1 was prepared by the condensation of ethyl acetoacetate with *o*-aminobenzaldehyde according to the directions of Friedländer and Gohring[4]; the product was obtained in the form of colorless crystals, m.p. 69–70°, after recrystallization from aqueous ethanol (reported[4] m.p. 71°); $\lambda_{\text{max}}^{\text{EtOH}}$ 237 mμ (log ε 4.67), 281 mμ (log ε 3.78), inflection *ca.* 310 mμ (log ε 3.27).

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(21) The m.p. of 4-phenylacridinic acid prepared by the oxidation of 9-phenylacridine, is reported to be 200–215° [A. Claus and C. Nicolaysen, *Ber.*, **18**, 2706 (1885)]. The indefinite m.p. makes this compound unsuitable as a derivative for identification purposes.

(22) The m.p. of 4-phenyl-3-quinolinecarboxylic acid is reported to be 226–228° [W. Borsche and F. Sinn, *Ann.*, **538**, 283 (1939)].

(23) W. Borsche and F. Sinn (ref. cited in footnote 22) give 196° for the m.p. of 4-phenyl-3-quinolinecarboxylic acid picrate.