TABLE I (*Continued*)

X	Reaction Method	Reaction Temp., C°.	Reaction Time	Yield, %	Solvent	Form	M.P., °C.	Color in Concd. H_2SO_4	Formula	Nitrogen, % Calcd.	Nitrogen, % Found
	A	80	3	0	C_6H_6	Needles	271	Red	$C_{21}H_{14}N_2O_3$[d]	8.18	8.08
	B	60	17	80							
Dihydrochloride					Dil. HCl	Prisms	267 (dec.)		$C_{21}H_{14}N_2O_3 \cdot 2HCl$	6.75	6.77

[a] Lit. m.p. 178–179°, K. Matsumura and C. Sone, *J. Am. Chem. Soc., 53*, 1492 (1931). [b] Calcd. for $C_{20}H_{18}N_2O_3$: C, 75.47; H, 5.66. Found: C, 75.19; H, 5.72. [c] In one lot, from the filtrate of recrystallization another isomer [yellow prisms, m.p. 276° (dec.), yield 20%, a red color in concd. H_2SO_4.] was isolated, but not successfully repeated.
Anal. Calcd. for $C_{19}H_{15}NO_4$: N, 4.36. Found: N, 4.37. *The hydrochloride* crystallized EtOH-HCl as yellow needles, m.p. 273–274° (dec.).
Anal. Calcd. for $C_{19}H_{15}NO_4 \cdot HCl$: N, 3.92. Found: N, 4.11.
[d] Calcd. for $C_{21}H_{14}N_2O_3$: C, 73.68; H, 4.09. Found: C, 73.92; H, 4.40.

In the case of furfural, *N* sodium hydroxide (8 ml.) was added dropwise to a cooled solution of the components.

B. In concentrated hydrochloric acid. A mixture of 5-acetyl-8-quinolinol (0.38 g., 0.002 mol.) aromatic aldehyde (0.002 mol.) and concentrated hydrochloric acid (5 ml.) was allowed to stand in a sealed tube. After different periods of reaction time, the tube was opened, acid fume removed *in vacuo*, the product filtered, dissolved in water, and free base precipitated by adding sodium acetate to it.

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5-Carboxy-8-quinolinol Derivatives

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This note describes the preparation of several derivatives of 5-carboxy-8-quinolinol in the hope that they may be of tuberculostatic activity. None of them, however, possessed any notable antituberculous activity *in vitro*.

EXPERIMENTAL

Condensation of 8-quinolinol with carbon tetrachloride. The Lippmann and Fleissner method[1] *was followed.* Starting from 20 g. of 8-quinolinol and with 13 hr. refluxing, 5.7 g. (22%) of 5-carboxy-8-quinolinol [m.p. 272° (dec.)] was isolated as the final product.

From dirty matter which was insoluble in dilute sodium carbonate, 4.7 g. of unreacted 8-quinolinol (m.p. 70–74°) was recovered by distillation with steam and 1.2 g. of 5-carboethoxy-8-quinolinol (m.p. 124.5–125.5°) isolated by carbon tetrachloride extraction of the residue of steam distillation and recrystallization of the extract from ethanol, the identity being ascertained by mixed m.p. method with an authentic specimen of 5-carboethoxy-8-quinolinol.

The hydrochloride formed light yellow needles, m.p. 263° (dec.).

Anal. Calcd. for $C_{12}H_{11}NO_3 \cdot HCl$: N, 5.53. Found: N, 5.71.

The carbon tetrachloride insoluble dark solid (*ca.* 5 g.) after three recrystallizations from dilute hydrochloric acid gave pure hydrochloride. It produced 0.62 g. of the free base on treating with dilute sodium carbonate.

It formed colorless prisms, m.p. 282–283° when recrystallized from nitrobenzene and then glacial acetic acid. The analytical figures corresponded to those of *bis*-8-quinolinol-5-yl ketone.

Anal. Calcd. for $C_{19}H_{12}N_2O_3$: C, 72.15; H, 3.80; N, 8.86. Found: C, 72.26; H, 3.79; N, 8.61.

The hydrochloride crystallized from dilute hydrochloric acid as light yellow columns, m.p. 309–311° (dec.).

Anal. Calcd. for $C_{19}H_{12}N_2O_3 \cdot 2HCl$: N, 7.20. Found: N, 7.02.

Diacetyl derivative crystallized from dilute acetic acid as colorless prisms, m.p. 201–202°. In dilute ethanol, it gives no color reaction with ferric chloride but develops a green color on standing or warming.

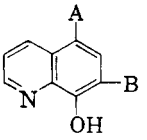
Anal. Calcd. for $C_{23}H_{16}N_2O_5$: N, 7.00. Found: N, 7.21.

8-Hydroxy-(XII) *and 8-chloro-*(XIII) *5-carbamoylquinoline.* A mixture of 5-carboxy-8-quinolinol (1.9 g., 0.01 mol.), phosphorus pentachloride (2.2 g., 0.011 mol.) and phosphorus oxychloride (2.9 g.) was heated at 100–105°

(1) E. Lippmann and F. Fleissner, *Ber.*, 19, 2467 (1886).

TABLE I

DERIVATIVES OF 5-CARBOXY-8-QUINOLINOL



Compound	A	B	M.P., °C.	Form	Solvent	Formula	Nitrogen Calcd.	Nitrogen Found
I[a]	$-COOC_4H_9$	H	83	Slightly yellow rhombs	EtOH	$C_{14}H_{15}NO_3$	5.71	5.52
II[b]	$-COOC_2H_5$	$-NO_2$	285 (dec.)	Yellow needles	C_6H_6	$C_{12}H_{10}N_2O_5$	10.69	10.30
III[b]	$-COOC_4H_9$	$-NO_2$	220 (dec.)	Yellow columns	C_6H_6	$C_{14}H_{14}N_2O_5$	9.66	10.12
IV[c]	$-COOC_2H_5$	$-NH_2$	132–132.5	Garnet colored needles	Ether	$C_{12}H_{12}N_2O_3$	12.07	12.05
V[c]	$-COOC_4H_9$	$-NH_2$	139–140	Garnet colored columns	Ether	$C_{14}H_{16}N_2O_3$	10.77	10.81
VI[d]	IV Dihydrochloride		254 (dec.)	Orange needles	Dil. HCl	$C_{12}H_{12}N_2O_3 \cdot 2HCl$	9.18	8.76
VII[d]	V Dihydrochloride		211 (dec.)	Orange columns	Dil. HCl	$C_{14}H_{16}N_2O_3 \cdot 2HCl$	8.41	8.94
VIII[e]	$-COOC_2H_5$	$-NH^1COCH_3$	192	Slightly pink needles	C_6H_6	$C_{14}H_{14}N_2O_4$	10.22	10.24
IX[e]	$-COOC_4H_9$	$-NH^1COCH_3$	185–186	Slightly pink needles	C_6H_6	$C_{16}H_{18}N_2O_4$	9.27	9.41
X[f]	$-CONH^1NH_2$	H	268 (dec.)	Colorless needles	MeOH	$C_{10}H_9N_3O_2$	20.69	20.32
XI[d]	I Hydrochloride		239–240 (dec.)	Colorless needles	Dil. HCl	$C_{14}H_{15}NO_3 \cdot HCl$	4.97	5.20

[a] Made by heating a mixture of 5-carboxy-8-quinolinol (1.14 g.), butanol (5 ml.) and concentrated sulfuric acid (0.6 g.) at 120° for 16 hr. until clear dissolution effected, adding water and sodium acetate (2 g.) to the solution, removing butanol by steam distillation, dissolving the residual oil which soon solidified, in dilute hot hydrochloric acid (250 ml.) (just acid to congo red), filtering from dark green amorphous matter and precipitating the free ester (1.08 g., 73%) by sodium carbonate.

Anal. Calcd. for $C_{14}H_{15}NO_3$: C, 68.57; H, 6.12. Found: C, 68.14; H, 6.37.

[b] Made by heating a mixture of the corresponding ester (0.001 mol.) and 10% nitric acid (4 ml.) at 80° with stirring for 1 hr., yield 88% II and 84% III. [c] Made by stirring a mixture of the corresponding nitro compound (0.001 mol.), ethanol (10 ml.) 2% ammonium hydroxide (14 ml.) and sodium hydrosulfite (2 g.) for 1 hr. at room temperature, removing ethanol by evaporation on a water bath and filtering the resulting crystals on cooling, yield 60% IV and 80% V. [d] Made by concentrating a solution of the corresponding base in dilute hydrochloric acid *in vacuo* over potassium hydroxide at room temperature until crystals began to separate. [e] Made by adding acetic anhydride (0.11 g.) and freshly fused sodium acetate (0.25 g.) to a solution of the corresponding amine (0.001 mol.) in ether (65 ml.), letting the mixture stand at room temperature for 4 days, then evaporating the ether and washing the residue with water in almost quantitative yield. [f] Made by heating a mixture of I (0.25 g.) and 80% hydrazine hydrate (0.5 g.) at 100° for 13 hr. and washing the product with cold benzene, yield 59%.

for 1 hr., phosphorus oxychloride removed *in vacuo* and the residue treated with cold acetone (60 ml.) which had been saturated with ammonia at 0°. The reaction product on treating with dilute ammonia, 0.72 g. of 5-carboxy-8-quinolinol was recovered and the crude XII, when purified through the hydrochloride and finally recrystallized from 90% ethanol gave colorless glistening plates, m.p. 275–276° (dec.),[2] yield 0.32 g. It gives a deep green color with ferric chloride.

Anal. Calcd. for $C_{10}H_8N_2O_2$: N, 14.89. Found: N, 14.63.

On heating 5 hr. instead of 1 hr., the reaction product, on recrystallization from ethanol gave XII (0.17 g.) and from the filtrate of recrystallization XIII (0.4 g.) respectively. XIII gave colorless columns, m.p. 230–231° and no color reaction with ferric chloride.

Anal. Calcd. for $C_{10}H_7ClN_2O$: C, 58.11; H, 3.39; Cl. 17.19. Found: C, 57.91; H, 2.91; Cl, 17.27.

The picrate crystallized from ethanol as plates, m.p. 200–202°.

Anal. Calcd. for $C_{10}H_7ClN_2O \cdot C_6H_3N_3O_7$: N, 16.07. Found: N, 15.51.

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(2) Lit. m.p. 264–265° (dec.). G. R. Clemo and R. Howe, *J. Chem. Soc.*, **1955**, 3552.

Synthesis of *N*-Acetyl-5-methoxytryptamine

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Lerner has reported the isolation[1] from pineal glands and peripheral nerves of an indole derivative, melatonin, which is the most potent agent

(1) A. B. Lerner, J. D. Case, Y. Takahashi, T. H. Lee, and W. Mori, *J. Am. Chem. Soc.*, **80**, 2587 (1958).