tures (200 ml. and 250 ml.). The solids resulting were collected by filtration, washed with water, and crystallized from acetone and 95% ethanol, respectively. Long, colorless needles of II *c* (4.6 grams, 94.6%; m.p. 161° to 162° C.) and pale yellow needles of II *d* (2.1 grams, 88%; m.p. 219° to 220° C.) formed. II *d* thus obtained did not depress the melting range of II *d* from the nitration of II *c*.

Anal. Calcd. for $C_{11}H_{10}ClNO$: Cl, 17.07; N, 6.75. Found: Cl, 16.99; N, 6.75.

Reduction of II *a* to II *f*. II *a* (5 grams in a minimum amount of absolute ethanol) was reduced with hydrogen (Raney nickel; 35 p.s.i.g.; 2 hours). After removal of catalyst, and after removal of ethanol under reduced pressure, the residual amine was dissolved in ethyl ether. Dry hydrogen chloride was passed into the ether solution (dried previously over sodium hydroxide pellets) causing precipitation of red amine hydrochloride. The amine was liberated from its hydrochloride by grinding in sodium hydroxide-water solution. Crystallization from ethanol-water solution gave fine, pale yellow needles; 2.3 grams, 53%; m.p. 69° to 70° C.

Anal. Calcd. for $C_{11}H_{11}ClN_2$: Cl, 17.16; N, 13.56. Found: Cl, 17.07; N, 13.42.

Acetylation and Benzoylation of II*f*. II *f* (0.5 gram and 0.5 gram) was acetylated and benzolated and benzoylated according to conditions previously reported for preparation of such derivatives of 8-bromo–6-ethylquinoline; yields: 0.3 gram of II *g* (50%), m.p. 183° to 185° C.; 0.52 gram of II *h* (69.4%), m.p. 221° to 222° C.

Anal. Calcd. for $C_{13}H_{14}ClN_2O$: Cl, 14.20; N, 11.22. Found: Cl, 14.21; N, 11.21.

Calcd. for $C_{18}H_{15}ClN_2O$: Cl, 11.41; N, 9.01. Found: Cl, 11.38; N, 8.89.

RECEIVED fore review September 7, 1962. Accepted October 12, 1962.

6-Bromo–8-Ethylquinoline and Some Derivatives

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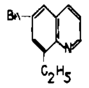
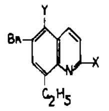
Hydrolysis of 6-bromo-2-chloro-8-ethylquinoline and 6-bromo-2-chloro-8-ethyl-5-nitroquinoline, as prepared by the action of a mixture of phosphorus pentachloride and phosphoryl chloride on the corresponding 2-quinolones, gave 2-quinolinols. The 2-quinolones resulted from the oxidation of the 1-methylquinolinum salts in basic media. Nitration of 6-bromo-, 6-bromo-2-chloro-, and 6-bromo-2-hydroxy- derivatives of 8-ethylquinoline yielded the corresponding 5-nitro compounds that were compared with authentic samples prepared by alternate routes. Amines resulting from the reduction of the nitro compounds were acetylated and benzoylated.

SOME NEW REACTIONS of 6-bromo–8-ethylquinoline (I) are recorded. Various derivatives (II) were prepared.


I


II

		Y		X	Y
a	H	NO_2	*h*	OH	NH_2
b	Cl	H	*i*	H	NHAc
c	OH	H	*j*	Cl	NHAc
d	OH	NO_2	*k*	OH	NHAc
e	Cl	NO_2	*l*	H	NHBz
f	H	NH_2	*m*	Cl	NHBz
g	Cl	NH_2	*n*	OH	NHBz

The 2-chloro compounds (II *b*, *e*) were made (from I, II *a*) by quaternizing the quinoline compound with methyl sulfate, oxidizing with alkaline ferricyanide or with alkaline peroxide, and finally treating with a mixture of phosphorus pentachloride and phosphoryl chloride. Acid hydrolysis of the 2-chloro compounds yielded the 2-quinolinols (II *c*, *d*). Other reactions used were conventional: reduction of nitro to amino and acylation or aroylation of amino to amido.

Nitroquinolines (II *a*, *e* and *d*). Cold solutions of fuming nitric acid (35 ml. and 1.5 ml.; sp. gr. 1.5) and sulfuric acid (40 ml. and 1.5 ml.; sp. gr. 1.84) were added dropwise with stirring independently to cold solutions of I (68.9 grams) and II *b* (0.4 gram) in sulfuric acid (80 ml. and 1.5 ml.; sp. gr. 1.84) at temperatures below 5° C. and 0° C., respectively. These solutions were then kept overnight at 25° C. before heating to 75° and 65° C. for 30 and 5 minutes. After cooling, these solutions were then poured into cracked ice and water mixtures causing the formation of solids that were collected and washed with water prior to purifying; yields were 78 grams (92%) from 95% ethanol, m.p. 87° to 88° C. and 0.46 gram from acetone-water, m.p. 131.5° to 132° C. A mixture of II *e* by this procedure with II *e* derived from II *a* also melted at 131.5° to 132° C.

A cold solution of nitric acid (4.1 ml.; sp. gr. 1.42) in sulfuric acid (8 ml.; sp. gr. 1.84) was added dropwise with stirring to a cold solution of II *c* (1.6 grams) in sulfuric acid (8 ml.; sp. gr. 1.84) below 0° C. The cooling bath was removed 1 hour later; and after warming to room temperature and pouring the solution into water and ice mixture, the resulting solid was collected, washed with water, and crystallized from 95% ethanol; fine, dense, yellow needles liquified at 245° C., with decomposition.

Anal. Calcd. for $C_{11}H_9BrN_2O_3$: (Br + Cl), 26.90; N, 9.43. Found: (Br + Cl), 26.99; N, 9.63.

2-Chloroquinolines (II *b*, *e*). QUATERNIZATIONS. Compound I (44.2 grams) and methyl sulfate (80 ml.) were heated together in an oil bath maintained at 120° to 125° C. for 2 hours. Water (160 ml.) was added the next day prior to extracting with ethyl ether (3 portions).

Compound II *a* (15 grams) and methyl sulfate (70 ml.) were heated together in an oil bath maintained at 135° to 140° C. for 2.5 hours. Water (85 ml.) was added after cooling, followed by extraction with ethyl ether (3 × 40 ml.).

Oxidations to Quinolones. The aqueous solution from quaternization of I was mixed with potassium ferricyanide (225 grams) in water (1500 ml.) before increasing internal temperature to 65° C. and dropping in, with stirring, a solution of potassium hydroxide (50 grams) in water (450 ml.). The crude quinolone (35.3 grams) was recovered (after stirring for 30 additional minutes) by extracting with ethyl ether on the following day, drying the extract over anhydrous sodium sulfate, and removing the ether by distillation under reduced pressure.

Finely ground potassium iodide (13 grams) was added with stirring to the aqueous solution from the quaternization of II *a*. The resulting orange-red solid was collected by filtration, suspended in boiling 95% ethanol (100 ml.), and then potassium hydroxide (15 grams) dissolved in water was added dropwise with stirring. The internal temperature was adjusted to 55° to 60° C. before dropping in hydrogen peroxide (125 ml.; 30%) and keeping at 55° to 60° C. for 0.5 hour. The quinolone (24.6 grams) was recovered by extraction with ether as for the quinolone from I.

Quinolones of Chloroquinolines. The crude quinolone fractions from compounds I and II *a* were each independently dissolved in cold phosphoryl chloride (75 ml., −10° C. and 44 ml., 0° C.) and phosphorus pentachloride (37 grams and 30 grams) was introduced prior to heating in an oil bath (125° to 135° C. and 120° to 125° C.) for 3 hours under reflux, respectively. After cooling, each of the mixtures was poured into cracked ice and water (2 kg. and 1 kg.) and the resulting solids were washed with water after separation. Compound II *b* was crystallized from acetone (needles; 11.1 grams; m.p. 46° to 47° C.) while II *e* was crystallized from acetone-water solution (fine needles; 5.3 grams; m.p. 131° to 132° C.

Anal. Calcd. for $C_{11}H_9BrClN$: (Br + Cl), 42.64; N, 5.18. Found: (Br + Cl), 42.90; N, 5.30.

Calcd. for $C_{11}H_8BrClN_2O_2$: (Br + Cl), 36.56; N, 8.88. Found: (Br + Cl), 36.60; N, 8.70.

Compound II *d* (1.0 gram) as derived from the nitration of II *c* was dissolved in phosphoryl chloride (15 ml.; 0° C.), phosphorus pentachloride (1.5 grams) was added and the mixture heated in an oil maintained at 130° to 135° C. for 2 hours. When the mixture had cooled, it was poured with stirring into cracked ice and water (50 ml.) containing 10% hydrochloric acid (10 ml.). The solid that formed was collected, washed with water, and crystallized from ethanol-water solution; yield 0.83 gram; m.p. 131° to 132° C. A mixture with sample of II *e* derived from II a also melted at 131° to 132° C.

Conversion of 2-Chloroquinolines into 2-Quinolinols. II *b* and II *e* (0.24 gram and 1.0 gram) were mixed with solutions of sulfuric acid (11.5 ml. and 7.5 ml.; sp. gr. 1.84) in water (7.9 ml. and 7.5 ml.) and refluxed for 2.5 and 1 hour respectively. The resulting mixtures were poured, after cooling to room temperature, into cracked ice-water mixtures (100 ml.). The solids resulting were collected by filtration, washed with water, and crystallized, after giving decolorizing carbon treatments, from acetone-water solution and 95% ethanol respectively. Colorless needles of II *c* (m.p. 231° to 233° C.) and yellow needles II *d* (liquifying at 244° C.) formed. A mixture of II *d* thus obtained with II *d* from the nitration of II *c* also liquified at 244° C. A better comparison was possible after converting each sample into the 2-chloroquinoline.

Anal. Calcd. for $C_{11}H_9BrNO$: Br, 31.83; N, 5.56. Found: Br, 31.76; N, 5.50.

Reduction of Nitroquinolines to Aminoquinolines. The nitroquinolines II *a* (4 grams in acetone), II *e* (2.5 grams in absolute ethanol), and II *d* (3.6 grams suspended in hot absolute ethanol) were reduced by shaking with hydrogen at 40 p.s.i.g. in presence of Raney nickel. Dry hydrogen chloride was passed into the amine solutions after separating the catalyst, yielding precipitates of the amine hydrochlorides. The solid amine hydrochlorides were decomposed with sodium hydroxide or ammonium hydroxide solutions in water before filtering off the amines, washing them with water, and dissolving in 95% ethanol. Decolorizing carbon treatments were applied prior to allowing the amines to crystallize. It was necessary to add water to the alcoholic solution of II *f* to bring about crystallization. II *f* (3.2 grams of tan powder; m.p. 77° to 78° C.), II *g* (1.5 grams of fine, white needles; m.p. 120° to 122° C.), and II *h* (2.0 grams; m.p. 202° to 204° C. with decomposition) formed.

Anal. Calcd. for $C_{11}H_{11}BrN_2$: Br, 31.83; N, 11.15. Found: Br, 32.03; N, 11.21.

Calcd. for $C_{11}H_{10}BrClN_2$: (Br + Cl), 35.22; N, 9.81. Found: (Br + Cl), 35.27; N, 9.72.

Calcd. for $C_{11}H_{11}BrN_2O$: Br, 29.93; N, 10.02. Found: Br, 30.06; N, 10.14.

Acetylation of Aminoquinolines. The aminoquinolines II *f* (0.5 gram in 5 ml. glacial acetic acid plus 3 ml. acetic anhydride), II *g* (0.4 gram in 10 ml. glacial acetic acid plus 4 ml. acetic anhydride), and II *h* (0.4 gram in 10 ml. glacial acetic acid plus 6 ml. acetic anhydride) were heated to refluxing temperature of solvent mixture for 0.5 hour prior to pouring with stirring into cracked ice-water mixture. Ammonium hydroxide was then added to neutralize acids, prior to collecting the crude solid acetamido quinolines and washing with water. Decolorizing carbon treatments were applied to solutions of II *i*, II *j* and II *k* in ethanol, ethanol and acetone, respectively. II *i* was crystallized from ethanol-water, II *j* from ethanol-water followed by petroleum ether, and II *k* from acetone yielding solids melting at 178.5° to 179.5° C., 230° to 231° C. with decomposition, and 255° to 255.5° C. with decomposition.

Anal. Calcd. for $C_{13}H_{13}BrN_2O$: Br, 27.26; N, 9.56. Found: Br, 27.43; N, 9.38.

Calcd. for $C_{13}H_{12}BrClN_2O$: (Br + Cl), 35.22; N, 8.55. Found: (Br + Cl), 35.27; N, 8.36.

Calcd. for $C_{13}H_{13}BrN_2O_2$: Br, 25.85; N, 9.06. Found: Br, 25.93; N, 9.11.

Benzoylation of Aminoquinolines. II *f* as its hydrochloride (1.5 grams), II *g* (0.25 gram), and II *h* (0.2 gram) were mixed independently with benzoyl chloride (8 ml.; 1.5 ml.; 2 ml.) and aqueous sodium hydroxide solution (15 ml. of 5%; 2 ml. of 10%; 5 ml. of 10%). The resulting mixtures were shaken while additional aqueous sodium hydroxide was added at intervals to maintain alkalinity. The solids that formed were collected by filtration, washed with water and sodium bicarbonate solution and finally recrystallized after applying decolorizing carbon treatments. II *l* crystallized from 95% ethanol as fine, colorless (white) needles; yield 1.6 grams, m.p. 185.5° to 186° C. II *m* crystallized from ethanol-water solution as fine, colorless (white) needles; yield 0.3 gram, m.p. 210° to 212° C. II *n* resulted after dissolving the purified solid formed from the benzoylation of II *h* in a solution of sodium hydroxide (5 grams) in 95% ethanol (75 ml.) at room temperature, allowing this to stand overnight, and carefully neutralizing with dilute hydrochloric acid while stirring. The resulting solid was collected by filtration, washed with water and crystallized from 95% ethanol as fine, colorless (white) needles; yield 0.2 gram, m.p. 303° to 304° C. with decomposition.

Anal. Calcd. for $C_{18}H_{15}BrN_2O$: Br, 22.50; N, 7.89. Found: Br, 22.35; N, 7.71.

Calcd. for $C_{18}H_{14}BrClN_2O$: (Br + Cl), 29.61; N, 7.19. Found: (Br + Cl), 29.68; N, 7.25.

Calcd. for $C_{18}H_{15}BrN_2O_2$: Br, 21.53; N, 7.55. Found: Br, 21.58; N, 7.40.

Received for review June 22, 1962. Accepted September 7, 1962.