TABLE I[10]

X-RAY DIFFRACTION DATA OF DERIVATIVES

D-Glucose, d (Å.)	D-Mannose, d (Å.)	D-Arabinose, d (Å.)	Hydroxymethyl furfuraldehyde, d (Å.)
(1) 15.55	(2) 13.55	10.80	(2) 9.08
(4) 9.60	6.65	8.56	(3) 8.36
7.28	5.11	5.37	7.66
6.17	(1) 4.84	4.92	7.06
5.54	4.52	4.35	(1) 5.83
5.28	4.18	4.00	5.43
4.95	3.92	3.62	5.00
(2) 4.45	(3) 3.31	3.39	4.51
(3) 4.16	3.13	3.20	4.22
3.86	2.86	3.03	3.97
3.64	2.74	2.62	3.69
3.19	2.41	2.23	3.49
2.81	2.33		3.33
2.70	2.21		3.21
2.40	2.12		2.82
	2.00		2.63
			2.51
			2.36
			2.09
			1.94
			1.82

for the 2-aminobenzenethiol, and Louis Lang of the National Sugar Refining Company for the hydroxymethylfurfural.

(10) Numbers in parenthesis indicate relative order of intensities.

NEW YORK SUGAR TRADE LABORATORY, INC.
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Some Derivatives of 6,8-Dichloroquinoline[1]

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This investigation was conducted as part of a general study concerning the synthesis and establishment of molecular structures of various previously unreported derivatives of quinoline.

6,8-Dichloroquinoline (I), as prepared from either 2,4-dichloroaniline (II) or 2,4-dichloroacetanilide by a Skraup ring-closure, was nitrated to give the same compound obtained from ring-closure of 2,4-dichloro-5-nitroaniline[2] (III). III was produced by nitrating II with a solution of sodium nitrate in fuming sulfuric acid (20% oleum); its structure was verified by removing the amino grouping prior to reduction and subsequent bromination to yield 6-bromo-2,4-dichloroaniline, which was also obtained by brominating an authentic sample of II for comparison purposes.

An authentic sample of 2,6,8-trichloro-5-nitroquinoline (VII), synthesized from 6,8-dichloro-5-nitroquinoline *via* 6,8-dichloro-1-methyl-5-nitro-2-quinolone, was shown to be the same as the direct nitration-product of 2,6,8-trichloroquinoline (VI). Since the hydrolysis of VII gave the same compound as obtained by the nitration of 6,8-dichloro-2-hydroxyquinoline (IX), which resulted from the hydrolysis of VI, the chief nitration-product of IX was established as being 6,8-dichloro-2-hydroxy-5-nitroquinoline.

Hydrogen in presence of Raney nickel or metallic tin and hydrochloric acid under the usual conditions served for the reduction of the three nitroquinolines to the corresponding amines. Conditions previously reported for converting certain substituted aminoquinolines into arsonic acids, acetamido and benzamido derivatives[3] were employed successfully in preparing derivatives of these amines.

Experimental

6,8-Dichloroquinoline (I).—2,4-Dichloroacetanilide was subjected to a Skraup ring-closure under conditions similar to those reported by Richter and Smith[4] for synthesizing certain substituted quinolines; yield 35%; m.p. 103–104°.

6,8-Dichloro-5-nitroquinoline (IV) (A).—Nitration of 6,8-dichloroquinoline under conditions similar to those employed by de Arce, Greene and Capps[3] for the nitration of 8-bromo-6-methylquinoline gave IV in yields of 66–78%; m.p. 125.5–126.5°.

Anal. Calcd. for $C_9H_4Cl_2N_2O$: Cl, 29.18; N, 11.53. Found: Cl, 29.21; N, 11.65.

(B).—2,4-Dichloro-5-nitroaniline (5.0 g.), arsenic pentoxide (5.5 g.), acetic anhydride (3 ml.), anhydrous glycerol (6.9 g.) and sulfuric acid (3.4 ml.) were mixed well and heated together under a reflux condenser by means of an oil-bath maintained at 155–160° for five hours. The cooled mass was poured with stirring into cracked ice–water mixture and finally filtered. Extraction of the water-washed and dried residue with boiling benzene removed the 6,8-dichloro-5-nitroquinoline that was deposited upon evaporation of the benzene. The crude product was purified by a combination of decolorizing carbon treatments and crystallizations from 95% ethanol; yield 3 g.

2,4-Dichloro-5-nitroaniline (III).—2,4-Dichloroaniline (5 g.) dissolved in fuming sulfuric acid (20% oleum, 50 ml.) was added dropwise, with mechanical stirring, to a solution of sodium nitrate (2.6 g.) in fuming sulfuric acid (20% oleum, 25 ml.) maintained at 0°. When an additional 30 minutes had elapsed, the temperature of the system was slowly increased to 40° and maintained for 15 minutes. An orange-colored solid formed upon pouring the reaction mixture into cracked ice and water (800 ml.). The acid was neutralized with sodium hydroxide prior to filtering and washing the residue with water. A combination of dissolutions in 95% ethanol and decolorizing carbon treatments followed by addition of water (30% by volume) gave yellow needles; 2.7 g.; m.p. 107–108°.

The molecular structure of III as obtained by procedure listed above was verified by deamination according to conditions reported by Morton and McGookin,[5] for changing 4-amino-2,3-dinitrotoluene into 2,3-dinitrotoluene, followed by reduction of the resulting 2,4-dichloronitrobenzene with tin and hydrochloric acid to 2,4-dichloroaniline and bromination in hydrochloric acid solution (sp. gr. 1.19) to give 6-bromo-2,4-dichloroaniline.

6,8-Dichloro-1-methyl-2-quinolone (V).—6,8-Dichloroquinoline (40 g.) was converted into V (43 g., m.p. of crude, 80–86°) according to modifications of conditions employed by de Arce, Greene and Capps[3] for synthesis of 8-bromo-1,6-dimethyl-2-quinolone. Dimethyl sulfate (100 ml.) acted upon 6,8-dichloroquinoline at 140–150° (temperature of oil-bath) for three hours and oxidation with potassium ferricyanide was conducted at 60–65°.

Super-heated steam distillation of some of the crude quinolone gave a solid in distillate that was analyzed.

Anal. Calcd. for $C_{10}H_7Cl_2NO$: N, 6.14. Found: N, 6.33.

2,6,8-Trichloroquinoline (VI).—Crude 6,8-Dichloro-1-methyl-2-quinolone (21 g.) was converted into VI (12.7 g., m.p. 165–166°) by treatment with phosphorus pentachloride according to the procedure of Perkin and Robinson[6] for

(1) Condensed in part from a thesis presented by Clyde E. Smith, Jr., to the Graduate School of the Alabama Polytechnic Institute in partial fulfillment of the requirements for the degree of Master of Science.

(2) See *C. A.*, **5**, 1270 (1911).

(3) H. Diaz de Arce, J. L. Greene, Jr., and J. D. Capps, THIS JOURNAL, **72**, 2971 (1950).

(4) F. Richter and G. F. Smith, *ibid.*, **66**, 396 (1944).

(5) A. Morton and A. McGookin, *J. Chem. Soc.*, 910 (1934).

(6) W. H. Perkin and R. Robinson, *ibid.*, **103**, 1977 (1913).

changing 1-methyl-2-quinolone into 2-chloroquinoline. Recrystallization from acetone combined with decolorizing carbon treatments was used in purification of VI.

Anal. Calcd. for $C_9H_4Cl_3N$: N, 6.03. Found: N, 5.90.

2,6,8-Trichloro-5-nitroquinoline (A).—2,6,8-Trichloroquinoline (22 g.) dissolved in sulfuric acid (sp. gr. 1.84, 105 ml.) was added dropwise, with stirring, to nitric acid (sp. gr. 1.42, 52 ml.) maintained at 0°. After keeping for an additional hour at 0–5°, temperature of system was allowed to increase to 25° and was finally gradually increased by application of heat to 70°. Twenty minutes later the solution, at 70°, was poured with stirring into cracked ice–water mixture (1000 ml.). The solid which separated was collected by filtration, washed with water, and purified by applying decolorizing carbon treatments along with alternate crystallizations from acetone and 95% ethanol; yield 21.5 g.; m.p. 151.5–153°.

Anal. Calcd. for $C_9H_3Cl_3N_2O_2$: Cl, 38.34; N, 10.10. Found: Cl, 38.44; N, 9.99.

(B).—6,8-Dichloro-1-methyl-5-nitro-2-quinolone (1.4 g.) was treated with phosphorus oxychloride–phosphorus pentachloride mixture under essentially the same conditions as those employed by de Arce, Greene and Capps[3] for converting 8-bromo-1,6-dimethyl-5-nitro-2-quinolone into 8-bromo-2-chloro-6-methyl-5-nitroquinoline. The temperature of oil-bath was maintained at 140–150° for 1.5 hours, and purification was by a combination of decolorizing carbon treatments and recrystallizations from 95% ethanol.

6,8-Dichloro-1-methyl-5-nitro-2-quinolone.—6,8-Dichloro-5-nitroquinoline was converted into the corresponding dimethyl sulfate addition-product and oxidized with 30% hydrogen peroxide under conditions similar to those previously reported by Capps[7] for changing 6-methyl-8-nitroquinoline into 1,6-dimethyl-8-nitro-2-quinolone. The period of heating with dimethyl sulfate at 125–130° was for three hours and the oxidation was carried out at 55–65°. 6,8-Dichloro-1-methyl-5-nitro-2-quinolone crystallized from methanol as needles; m.p. 144–145°.

Anal. Calcd. for $C_{10}H_6Cl_2N_2O_3$: N, 10.26. Found: N, 10.07.

6,8-Dichloro-2-hydroxyquinoline.—2,6,8-Trichloroquinoline (5 g.) was mixed with 20 ml. of 3:1 by volume sulfuric acid (sp. gr. 1.84)–water solution, and the resulting system was placed in an oil-bath maintained at 170–210° for 3.5 hours before pouring system with stirring into 200 ml. of cold water. The crude 6,8-dichloro-2-hydroxyquinoline was collected by filtration, washed with water and recrystallized from 95% ethanol (400 ml.); yield almost theoretical; m.p. 255–256°.

Anal. Calcd. for $C_9H_5Cl_2NO$: N, 6.57. Found: N, 6.50.

6,8-Dichloro-2-hydroxy-5-nitroquinoline (A).—Nitric acid (sp. gr. 1.42, 5 ml.) was added slowly with shaking to a solution of 6,8-dichloro-2-hydroxyquinoline (2.0 g.) in sulfuric acid (sp. gr. 1.84, 5 ml.) prior to gradually increasing temperature to 55° and maintaining at 55° for five minutes. After spontaneously cooling to room temperature, the solution obtained was poured with stirring into 250 ml. of cold water. The resulting solid was collected by filtration, washed with water and recrystallized from 95% ethanol (400 ml.); 2.0 g. yield; m.p. 255–257°. It was later shown that 2-ethoxyethanol (Cellosolve) is a good recrystallizing solvent to employ in the purification of this compound.

Anal. Calcd. for $C_9H_4Cl_2N_2O_3$: N, 10.81. Found: N, 10.60.

(B).—6,8-Dichloro-2-hydroxy-5-nitroquinoline was obtained in nearly theoretical yield from 2,6,8-trichloro-5-nitroquinoline by the application of the same conditions as employed by de Arce, Greene and Capps[3] for hydrolyzing 8-bromo-2-chloro-6-methyl-5-nitroquinoline.

5-Amino-2,6,8-trichloroquinoline and 5-Amino-6,8-dichloro-2-hydroxyquinoline.—2,6,8-Trichloro-5-nitroquinoline and 6,8-dichloro-2-hydroxyquinoline were reduced in reagent grade acetone and absolute ethanol, respectively, with hydrogen in presence of Raney nickel catalyst at 50°; m.p. of 5-amino-2,6,8-trichloroquinoline, 207–208°, and of 5-amino-6,8-dichloro-2-hydroxyquinoline, 259–260.5° dec.

Anal. Calcd. for $C_9H_5Cl_3N_2$: N, 11.32. Found: N, 11.24. Calcd. for $C_9H_5Cl_2N_2O$: N, 12.23. Found: N, 12.12.

(7) J. D. Capps, THIS JOURNAL, **69**, 176 (1947).

5-Amino-6,8-dichloroquinoline.—6,8-Dichloro-5-nitroquinoline (13 g.) was reduced with tin and hydrochloric acid under the usual conditions and the resulting amine was extracted with boiling acetone from the solid obtained after making the reaction mixture basic with sodium hydroxide. The acetone extract was treated with decolorizing carbon prior to diluting with water at boiling point of solution and slowly cooling to cause precipitation of amine as needles; yield 7.4 g.; m.p. 181–182°.

Anal. Calcd. for $C_9H_6Cl_2N_2$: N, 13.15. Found: N, 13.29.

5-Acetamido-6,8-dichloroquinoline, 5-Acetamido-2,6,8-trichloroquinoline and 5-Acetamido-6,8-dichloro-2-hydroxyquinoline.—5-Amino-6,8-dichloroquinoline, 5-amino-2,6,8-trichloroquinoline and 5-amino-6,8-dichloro-2-hydroxyquinoline were acetylated under conditions similar to those employed by de Arce, Greene and Capps[3] for acetylation of 5-amino-8-bromo-6-methylquinoline to give the respective acetamido derivatives melting at 247–248.5°, 299–300° and above 310°. 5-Acetamido-6,8-dichloroquinoline was recrystallized from 95% ethanol; 5-acetamido-2,6,8-trichloroquinoline was recrystallized from 50% by volume acetone–ethanol; and impurities were extracted from 5-acetamido-6,8-dichloro-2-hydroxyquinoline with boiling ethanol, its solubility in ethanol being too low for recrystallization.

Anal. Calcd. for $C_{11}H_8Cl_2N_2O$: N, 10.98. Found: N, 10.82. Calcd. for $C_{11}H_7Cl_3N_2O$: N, 9.67. Found: N, 9.72. Calcd. for $C_{11}H_8Cl_2N_2O_2$: N, 10.33. Found: N, 10.40.

5-Benzamido-2,6,8-trichloroquinoline.—5-Amino-2,6,8-trichloroquinoline was benzoylated according to instructions recorded by de Arce, Greene and Capps[3] for benzoylation of 5-amino-8-bromo-6-methylquinoline; m.p. 259–260° from 95% ethanol.

Anal. Calcd. for $C_{16}H_9Cl_3N_2O$: N, 7.96. Found: N, 8.11.

6,8-Dichloro-5-quinolinearsonic Acid and 2,6,8-Trichloro-5-quinolinearsonic Acid.—5-Amino-6,8-dichloroquinoline (8.9 g.) and 5-amino-2,6,8-trichloroquinoline (8.0 g.) were diazotized and converted into arsonic acids according to procedure reported by Capps and Hamilton[8] for changing certain 2-chloroaminoquinolines into 2-chloroquinolinearsonic acids. 6,8-Dichloro-5-quinolinearsonic acid and 2,6,8-trichloro-5-quinolinearsonic acid resulted in yields of 30 and 8.9%, respectively, melting at 292–293° and above 310°.

Anal. Calcd. for $C_9H_6Cl_2NAsO_3$: As, 23.96. Found: As, 23.07. Calcd. for $C_9H_5Cl_3NAsO_3$: As, 21.02. Found: As, 20.82.

(8) J. D. Capps and C. S. Hamilton, *ibid.*, **60**, 2105 (1938).

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1-Acetylcyclohexanol

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The recently reported scheme of Billimoria and Maclagen[1] for the introduction of the cortisone side chain into simple alicyclic ring systems prompts the early publication of our work in this same direction. The method described by these investigators involves, as an intermediate, 1-acetylcyclohexanol (III) which was obtained from 1-hydroxycyclohexanecarboxylic acid by reaction with methyllithium.

The synthetic procedure for the introduction of the side chain which was conceived by us is quite similar to that of Billimoria and Maclagen[1] and like their method involves 1-acetylcyclohexanol (III) as a key intermediate; however, the synthesis from cyclohexanone by our procedure involves only two reactions. In this way we have obtained 1-acetylcyclohexanol from 1-ethynylcyclohexanol (II) in

(1) J. D. Billimoria and N. F. Maclagen, *Nature*, **167**, 81 (1951).