tion behavior of a monomer into a "reactivity" term Q, correlated with the degree of conjugation, and a "polarity" factor e. Experimental data are summarized in Tables I, II and III.

TABLE I

STYRENE (M_1)–PENTACHLOROSTYRENE (M_2) SYSTEM

Monomer composition Mole fraction M_2	Polymer composition % Cl	Mole fraction M_2
0.070	8.4	0.054
.159	15.2	.105
.274	24.8	.192
.428	31.1	.261
.654	42.2	.420
.842	48.6	.541
1.000	64.0	.999

$r_1 = 1.31 \pm 0.2$ $r_2 = 0.10 \pm 0.02$

TABLE II

METHYL METHACRYLATE (M_1)–PENTACHLOROSTYRENE (M_2) SYSTEM

Monomer composition Mole fraction M_2	Polymer composition % Cl	Mole fraction M_2
0.2	8.6	0.051
.4	21.7	.156
.6	33.9	.289
.8	49.7	.553
.9	56.0	.715
1.0	63.9	.994

$r_1 = 4.0 \pm 0.4$ $r_2 = 0.35 \pm 0.05$

TABLE III

Monomer	Q	e
Styrene	1.0	−1.0
Methyl methacrylate	0.64	0.0
Pentachlorostyrene	0.2	+0.25

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Heterocyclic Basic Compounds. XII. 7-Bromo- and 7-Iodo-quinolines[1]

BY A. E. CONROY,[2] HARRY S. MOSHER[3] AND FRANK C. WHITMORE[4]

Various workers[5-8] have synthesized N-substituted 4-amino-7-halogen quinolines, certain of which possess considerable antimalarial activity. Outstanding among these is 4-(7-chloro-4-quinolylamino)-2-diethylaminomethylphenol,[9] SN 10,751.[10] The present note describes the synthesis of the 7-bromo- (SN 13,167) and the 7-iodo- (SN 13,168) analogs, which were obtained by coupling, according to Burckhalter, *et al.*,[9] 4-amino-2-diethylaminomethylphenol and the appropriate 4-chloro-7-haloquinoline. The 4-chloro-7-haloquinolines were prepared by the method of Price and Roberts[7] starting with the *m*-haloaniline and ethoxymethylenemalonic ester. The intermediate 4-hydroxy-7-haloquinolines and 4-chloro-7-haloquinolines have also been prepared by Surrey and Hammer[6] by another method. The melting points reported by these authors do not agree in certain cases with those found in this work.

Experimental[11]

3-Carbethoxy-4-hydroxy-7-bromoquinoline.—The intermediate ethyl α-carbethoxy-β-*m*-bromoanilinoacrylate was obtained in 40% yield (45 g.) by allowing a mixture of 50 g. of *m*-bromoaniline[12] and 63 g. of ethoxymethylenemalonic ester[13] to stand overnight. The resulting solid mass was twice recrystallized from a 1:1 solution of ether and ligroin; white needles, m. p. 70–71°. This material, 40 g., was cyclized by refluxing in diphenyl ether according to Price and Roberts.[7] After recrystallization from diphenyl ether, followed by thorough washing with diethyl ether, there was obtained a 44% yield (15 g.) of 3-carbethoxy-4-hydroxy-7-bromoquinoline as a white powder, m. p. 307–309°.

Anal. Calcd. for $C_{12}H_{10}O_3NBr$: C, 48.65; H, 3.38. Found: C, 48.74; H, 3.54.

3-Carbethoxy-4-hydroxy-7-iodoquinoline.—The intermediate ethyl α-carbethoxy-β-*m*-iodoanilinoacrylate was obtained in 43% yield (78 g.) by allowing a mixture of 90 g. of *m*-iodoaniline[12] and 89 g. of ethoxymethylenemalonic ester to stand overnight. The resulting solid mass was recrystallized once from acetone and once from a 1:1 solution of ether and ligroin; white needles, m. p. 92–93°. The product, 70 g., was cyclized and purified as in the above case. There was obtained a 45% yield (28 g.) of 3-carbethoxy-4-hydroxy-7-iodoquinoline as a white powder, m. p. 302–304°.

Anal. Calcd. for $C_{12}H_{10}O_3NI$: C, 42.00; H, 2.92. Found: C, 42.44; H, 3.17.

4-Hydroxy-7-bromoquinoline.—The intermediate 4-hydroxy-7-bromoquinoline-3-carboxylic acid was obtained in 70% yield (8 g.) by the hydrolysis of 13 g. of the 3-carbethoxy-4-hydroxy-7-bromoquinoline with 5% sodium hydroxide solution according to the method of Price and Roberts[7]; light yellow powder, m. p. 266° dec. The decarboxylation of 7 g. of this material was carried out by heating at 300° until the evolution of carbon dioxide ceased. The resulting crystalline cake was recrystallized from 95% ethanol giving 4 g. (68%) of 4-hydroxy-7-bromoquinoline as light tan crystals, m. p. 289–291° (lit.[6] 279–281°).

Anal. Calcd. for C_9H_6ONBr: C, 48.20; H, 2.68. Found: C, 48.01; H, 2.76.

4-Hydroxy-7-iodoquinoline.—The intermediate 4-hydroxy-7-iodoquinoline-3-carboxylic acid was obtained in 66% yield (15 g.) by the hydrolysis of 25 g. of the 3-carbethoxy-4-hydroxy-7-iodoquinoline with 5% sodium hydroxide solution; light grey powder, m. p. 263° dec. The

(1) Taken in part from a thesis submitted by Edward A. Conroy to The Pennsylvania State College in partial fulfillment of the requirements for the Ph.D. degree.

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(5) Andersag, Breitner and Jung, U. S. Patent 2,333,970, *C. A.*, **38**, 3771 (1941); German Patent 683,692, *Chem. Zentr.*, **110**, II, 2446 (1939).

(6) Surrey and Hammer, THIS JOURNAL, **68**, 115 (1946).

(7) Price and Roberts, *ibid.*, **68**, 1206 (1946).

(8) Burckhalter, *et al.*, U. S. Patent 2,419,199, *C. A.*, **41**, 4815 (1947).

(9) Burckhalter, *et al.*, presented before the Medicinal Section of the American Chemical Society, April 9, 1946.

(10) The Survey Number, designated SN, serves to identify a drug in the Monograph "A Survey of Antimalarial Drugs, 1941–1945," F. Y. Wiselogle, editor, Edwards Brothers, Ann Arbor, Mich., 1946.

(11) All melting points are uncorrected. Analyses by Arlington Laboratories, Fairfax, Virginia.

(12) Winans, THIS JOURNAL, **61**, 3564 (1939).

(13) Fuson, Parham and Reed, *J. Org. Chem.*, **11**, 194 (1946)

decarboxylation of 13 g. of this material was carried out by heating at 330° until the evolution of carbon dioxide ceased. The resulting crude 4-hydroxy-7-iodoquinoline was recrystallized from 50% ethanol; 6 g. (54%) of light yellow powder, m. p. 306–308° (lit.[6] 346–348°).

Anal. Calcd. for C_9H_6ONI: C, 39.85; H, 2.22. Found: C, 40.31; H, 2.55.

4-Chloro-7-bromoquinoline.—Three grams of the 4-hydroxy-7-bromoquinoline was converted to 4-chloro-7-bromoquinoline by treatment with phosphorus oxychloride essentially as described by Surrey and Hammer.[6] After recrystallization from 95% ethanol there was obtained a 61% yield (2.0 g.) of the 4-chloro-7-bromoquinoline as white crystals, m. p. 105–106° (lit.[6] 100.5–101.5°).

Anal. Calcd. for C_9H_5NClBr: C, 44.50; H, 2.06. Found: C, 44.76; H, 2.35.

4-Chloro-7-iodoquinoline.—This was obtained in an analogous manner from 4 g. of 4-hydroxy-7-iodoquinoline. Recrystallization from 75% ethanol gave a 35% yield (1.5 g.) of light yellow crystals, m. p. 101–102° (lit.[5] 101°; lit.[6] 95.5–97°).

4-(7-Bromo-4-quinolylamino)-2-diethylaminomethylphenol.—The hydrolysis of 35.4 g. of 2-diethylaminomethyl-4-acetylaminophenol[14] was accomplished by refluxing for two hours with 300 ml. of 6 *N* hydrochloric acid. The *p*H of the solution was adjusted to approximately 3 with 105 ml. of a 40% sodium hydroxide solution. To 250 ml. of this solution was added 22 g. of 4-chloro-7-bromoquinoline and the reaction mixture was refluxed for three and one-half hours according to the method of Burckhalter and co-workers.[8,15] The viscous oil which separated was removed, dissolved in methanol, and reprecipitated by dilution with dilute ammonia solution. The product, after twice recrystallizing from a 1:1 solution of 95% ethanol and acetone, was obtained in 55% yield (20 g.) as a light yellow powder, m. p. 206–208° dec.

Anal. Calcd. for $C_{20}H_{22}ON_3Br$: C, 60.00; H, 5.50. Found: C, 59.96; H, 5.73.

4-(7-Iodo-4-quinolylamino)-2-diethylaminomethylphenol.—This was prepared and purified in a similar manner from 16 g. of 4-chloro-7-iodoquinoline; 49% yield (12 g.), light yellow powder, m. p. 196–198° dec.

Anal. Calcd. for $C_{20}H_{22}ON_3I$: C, 53.70; H, 4.92. Found: C, 54.18; H, 5.16.

Acknowledgment.—The authors are indebted to Parke, Davis and Company, Detroit, Michigan, for financial assistance.

(14) Supplied by Parke, Davis and Company.
(15) Burckhalter, *et al.*, THIS JOURNAL, **70**, 1363 (1948).

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N-(Hydroxylethylmethylaminoethyl)-phenothiazine SC 1923: a New Antihistaminic

BY JOHN W. CUSIC

Many derivatives of phenothiazine have recently been made and studied for their anti-histaminic properties.

The 8-chlorotheophyllin salt of N-(dimethylaminoethyl)-phenothiazine was made by the author and tried clinically by Gay and Carliner.[1] Halpern[2] has reported extensively on several phenothiazines and recently N-pyrrolidylethylphenothiazine has been reported by Hunter, *et al.*[3]

(1) Gay, *etc.*, *Bull. Johns Hopkins Hosp.*, **83**, 356 (1948).
(2) Halpern, *Compt. rend. soc. biol.*, **140**, 361, 363 (1946).
(3) Hunter, *et al.*, THIS JOURNAL, **70**, 3100 (1948).

N-(Hydroxylethylmethylaminoethyl)-phenothiazine (SC 1923) has been prepared by the reaction of N-methylethanolamine with N-(β-chloroethylphenothiazine).[4] Its hydrochloride melted at 185–186°. *Anal.* Calcd. for $C_{17}H_{21}N_2SOCl$; S, 9.52. Found: S, 9.62. The methobromide melted at 154–155°. *Anal.* Calcd. for $C_{18}H_{23}N_2SOBr$; Br, 20.21; S, 8.11. Found: Br, 20.24; S, 8.02.

When tested by Dr. Homer Freese of our Pharmacology Department according to the histamine spray technic of Loew[5] SC 1923 had an $ED_{50} = 0.43 \pm 0.15$ mg./kg. as compared to an ED_{50} of 0.66 ± 0.13 mg./kg. for β-dimethylaminoethylbenzhydryl ether.

Its effect on the mammalian capillary bed has been studied by Haley.[6]

(4) Gilman, THIS JOURNAL, **66**, 888 (1944).
(5) Loew, *etc.*, *J. Pharm. and Exper. Therap.*, **83**, 120 (1945).
(6) Haley and Harris, *ibid.*, **95**, 293 (1949).

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Non-exchange of Sulfur between Carbon Disulfide and Hydrogen Sulfide in Benzene Solution

BY DAVID L. DOUGLAS, ROBERT A. COOLEY AND DON M. YOST

The recent communication of Edwards, *et al.*,[1] in which they mention a study of the exchange of $S^{=35}$ in aqueous solution with carbon disulfide as a separate phase, prompts us to report some work done in this laboratory in 1941. We undertook the investigation of the exchange of S^{35} between H_2S^{35} and carbon disulfide in benzene solution. Our experiments, detailed in Table I, showed that no exchange greater than the experimental error (1%) occurs between carbon disulfide and hydrogen sulfide in benzene solution after ninety-five hours at 120°.

TABLE I

THE NON-EXCHANGE BETWEEN CARBON DISULFIDE AND HYDROGEN SULFIDE IN BENZENE SOLUTION[2]

Temp., °C.	Time of exchange, hr.	Concns. of reactants, moles/liter × 10^3 H_2S	CS_2	Observed activity, counts/min. H_2S	CS_2	% exchange, max.
97	1	4.2	108	411 ± 3	0 ± 1	0.3
120	95	4.2	108	178 ± 1	0 ± 2	.8
120	95	4.2	108	181 ± 1	0 ± 1	.3

Experimental.—The source of the active sulfur and the counting technique are described in a previous paper.[3] A CS_2–C_6H_6 solution was made up by weighing out reagent grade carbon disulfide and mixing it with reagent benzene in a volumetric flask. The H_2S^{35}–C_6H_6 solution was prepared and analyzed by standard methods.

In a typical experiment 1 ml. of each of the two solutions were pipetted into a glass bulb of 5–10 ml. capacity. This was immediately immersed in liquid air and sealed off. The bulb was then placed in boiling water or a thermostated oven for a measured period of time. On completion of the run the hydrogen sulfide was trapped in 1 *N* sodium hydroxide and precipitated as silver sulfide. The carbon disulfide in the benzene was separated as potassium xanthate and precipitated as copper xanthate. The

(1) R. R. Edwards, F. Nesbitt and A. K. Solomon, THIS JOURNAL, **70**, 1670 (1948).
(2) Ph.D. Thesis, R. A. Cooley, 1941, Cal. Tech.
(3) R. A. Cooley and D. M. Yost, THIS JOURNAL, **62**, 2474 (1940).