decarboxylation of 13 g. of this material was carried out by heating at  $330^{\circ}$  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.  $306-308^{\circ}$  (lit.<sup>6</sup>  $346-348^{\circ}$ ).

Anal. Caled. for C<sub>9</sub>H<sub>6</sub>ONI: 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.<sup>6</sup> After recrystallization from 95% ethanol there was obtained a 61% yield (2.0 g.) of the 4-chloro-7-bromoquino-line as white crystals, m. p.  $105-106^{\circ}$  (lit.<sup>6</sup>  $100.5-101.5^{\circ}$ ).

Anal. Calcd. for C<sub>9</sub>H<sub>b</sub>NClBr: 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.  $101-102^{\circ}$  (lit.<sup>5</sup>  $101^{\circ}$ ; lit.<sup>6</sup>  $95.5-97^{\circ}$ ).

4-(7-Bromo-4-quinolylamino)-2-diethylaminomethylphenol.—The hydrolysis of 35.4 g. of 2-diethylaminomethyl-4-acetylaminophenol<sup>14</sup> was accomplished by refluxing for two hours with 300 ml. of 6 N hydrochloric acid. The pH 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-7bromoquinoline and the reaction mixture was refluxed for three and one-half hours according to the method of Burckhalter and co-workers.<sup>8,15</sup> 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).

DEPARTMENT OF CHEMISTRY

SCHOOL OF CHEMISTRY AND PHYSICS

THE PENNSYLVANIA STATE COLLEGE

STATE COLLEGE, PENNSYLVANIA RECEIVED MAY 5, 1949

# 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.<sup>1</sup> Halpern<sup>2</sup> has reported extensively on several phenothiazines and recently N-pyrrolidylethylphenothiazine has been reported by Hunter, *et al.*<sup>3</sup> N-(Hydroxylethylmethylaminoethyl)-phenothiazine (SC 1923) has been prepared by the reaction of N-methylethanolamine with N-( $\beta$ -chloroethylphenothiazine).<sup>4</sup> Its hydrochloride melted at 185–186°. *Anal.* Calcd. for C<sub>17</sub>-H<sub>21</sub>N<sub>2</sub>SOC1; S, 9.52. Found: S, 9.62. The methobromide melted at 154–155°. *Anal.* Calcd. for C<sub>18</sub>H<sub>23</sub>N<sub>2</sub>-SOBr; Br, 20.21; S, 8.11. Found: Br, 20.24; S, 8.02. When tested by Dr. Homer Freese of our Pharmacology Deportment coversing to the histoming array taching of

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

Its effect on the mammalian capillary bed has been studied by Haley.<sup>6</sup>

(4) Gilman, THIS JOURNAL, 66, 888 (1944).

(5) Loew, elc., J. Pharm. and Exper. Therap., 83, 120 (1945).

(6) Haley and Harris, ibid., 95, 293 (1949).

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RECEIVED MAY 14, 1949

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.*,<sup>1</sup> 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 1

THE NON-EXCHANGE BETWEEN CARBON DISULFIDE AND Hydrogen Sulfide in Benzene Solution<sup>2</sup>

	Time of Concns. of ex- reactants,			Observed	% ex-	
°C.	change, lır.	nioles/li H2 <b>S</b>	$ ext{ter} \stackrel{ imes}{\times} \frac{10^3}{ ext{CS}_2}$	$\mathbf{H}_2 \mathbf{S}$	/min. CS2	change, max.
97	1	4.2	108	411 = 3	$0 \neq 1$	0.3
120	95	4.2	108	$178 \pm 1$	$0 \neq 2$	.8
120	95	4.2	108	$181 \pm 1$	$0 \neq 1$	. 3

**Experimental.**—The source of the active sulfur and the counting technique are described in a previous paper.<sup>8</sup> 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 Nsodium 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.

<sup>(1)</sup> Gay, eic., Bull. Johns Hopkins Hosp., 83, 356 (1948).

<sup>(2)</sup> Halpern, Compi. rend. soc. biol., 140, 361, 363 (1946).

<sup>(3)</sup> Hunter, et al., THIS JOURNAL, 70, 3100 (1948).

<sup>(3)</sup> R. A. Cooley and D. M. Yost, THIS JOURNAL, 62, 2474 (1940).

(4) E. S. Johnson, THIS JOURNAL, 28, 1209 (1906).

(5) Harding and Doran, *ibid.*, 29, 1476 (1907).

CALIFORNIA INSTITUTE OF TECHNOLOGY

PASADENA 4, CALIF. RECEIVED APRIL 30, 1949

# The Exchange between Br<sub>2</sub><sup>\*</sup> and HgBr<sub>2</sub> in Carbon Disulfide Solution

# By David L. Douglas, Robert A. Cooley and Don M. Yost

The exchange of bromine atoms between bromine and various inorganic bromides has been previously reported.<sup>1-3</sup> In view of the lack of published quantitative data and because of the general usefulness of the reaction in preparing samples of pure radioactive bromine, we are reporting some work done in this Laboratory in 1941. A study was made of the exchange of  $Br^{82}$  atoms between  $Br_2^*$  and HgBr<sub>2</sub> in carbon disulfide solution. The results of six experiments showed that the exchange is complete within at least two and onehalf minutes at somewhat less than 0°. Table I contains the details of the experiments and results.

#### TABLE I

## Exchange of Bromine between Mercuric Bromide and Bromine in Carbon Disulfide at $0^{\circ 4}$

Re- ac- tion	Concentra- tions in moles/liter		Measured	activity	Frac- tion of Br <sub>2</sub> actu- ally meas-	Ex-
sec.	Br <sub>2</sub>	HgBr2	Bra	HgBr <sub>2</sub>	ured	%
245	6.82	1.67	1136 = 10	$274 \pm 2$	1.00	99 <b>±</b> 2
266	6.82	1.67	992 = 8	362 🛥 3	0.854	$121 \pm 2$
324	1.34	1.67	82 = 1	252 = 6	.406	$100 \pm 3$
290	1.34	1.67	$130 \pm 1$	250 = 5	.650	100 = 3
245	6.26	1.67	$3066 \pm 18$	$1160 \pm 7$	.666	96 = 1
157	6.26	1.67	$2863 \Rightarrow 16$	$1318 \pm 9$	.593	$102 \pm 1$

**Experimental.**—Radioactive bromine was prepared in the usual manner by irradiating *n*-butyl bromide with neutrons from a Rn-Be source. A solution of the active bromine in reagent carbon disulfide was prepared and analyzed by standard methods. The mercuric bromide solution was prepared by weighing out the pure solid into a known volume of carbon disulfide. The actual exchange reaction and separation were car-

The actual exchange reaction and separation were carried out as follows: 5 ml. of the solutions of  $Br_2^*$  and HgBr<sub>2</sub>, cooled to 0°, were pipetted into a 250-ml. distilling flask which was surrounded by an ice-bath. As soon as the solutions were mixed thoroughly the bromine and carbon disulfide were distilled off in a vacuum and collected in a trap at  $-78^\circ$ . The time elapsed from the moment of mixing to the completion of the distillation is recorded in

(3) R. Muxart, Compt. rend., 224, 1107 (1947).

column 1 of Table I. Clearly the temperature dropped below  $0^{\circ}$  during this time; however, no attempt was made to measure this drop.

The bromine was reduced and precipitated as silver bromide. The mercuric bromide residue in the flask was dissolved in nitric acid and the bromine precipitated as silver bromide. The activities of the precipitates were measured by counting techniques. Determination of the fraction of the bromine which was actually trapped was accomplished by analyzing the silver bromide precipitate.

The activities were corrected for time of measurement and background—the short lived activity being allowed to decrease to a negligible value before use. The "% exchange" was calculated thus

$$\% \text{ exchange } = \frac{\text{Activity from } \text{HgBr}_2}{\text{Fraction of } \text{Br}_2 \text{ measured}} > 100$$

Mole fraction  $Br_2$  in  $HgBr_2-Br_2 \times Sum$  of activities

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CALIFORNIA INSTITUTE OF TECHNOLOGY

PASADENA 4, CALIFORNIA RECEIVED APRIL 30, 1949

## p-Chloro- $\alpha$ -(trichloromethyl)-benzyl Alcohol and a Chlorination Apparatus

### BY EDWARD M. FRY

At the time the insecticidal value of 1,1,1-trichloro-2,2-bis-(p-chlorophenyl)-ethane became evident very little was known of its toxicology and as part of a program aimed at evaluating these properties a synthesis designed to utilize isotopic carbon at the point of attachment of the two chlorophenyl rings was undertaken. However, rapid and widespread use of DDT soon revealed its low toxicity with respect to humans and the project was discontinued, the synthesis being halted at pchloro- $\alpha$ -(trichloromethyl)-benzyl alcohol. Carbon dioxide containing isotopic carbon was not used in this investigation and as none of the intermediate compounds are new, nor were any new or improved synthetic procedures used, the work is of interest only with respect to the method used with brief mention of experimental conditions. The scheme is as follows



Carbon dioxide generated from barium carbonate reacted in a threefold excess of 1 N Grignard reagent to give the acid. The acid chloride in benzene solution reacted with cold ethereal diazomethane, then in the cold with dry hydrogen chloride to give  $p,\alpha$ -dichloroacetophenone. The ketone in an equal volume of trichloroacetic acid on treatment with chlorine for two days at 120–125° gave  $p,\alpha,\alpha,\alpha$ -tetrachloroacetophenone which, on reduction with a small excess of 3 N aluminum isopropoxide in isopropyl alcohol, gave the alcohol.

<sup>(1)</sup> J. N. Wilson and R. G. Dickinson, THIS JOURNAL, 61, 3519 (1939).

<sup>(2)</sup> Kolthoff and O'Brien, J. Chem. Phys., 7, 401 (1939).

<sup>(4)</sup> R. A. Cooley, Ph.D. Thesis, Cal. Tech., 1941.