

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 C₉H₆ONI: 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 C₉H₆NCIBr: 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-quinolyamino)-2-diethylaminomethylphenol.—The hydrolysis of 35.4 g. of 2-diethylaminomethyl-4-acetylamino-phenol¹⁴ 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-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 C₂₀H₂₂ON₃Br: C, 60.00; H, 5.50. Found: C, 59.96; H, 5.73.

4-(7-Iodo-4-quinolyamino)-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 C₂₀H₂₂ON₃I: C, 53.70; H, 4.92. Found: C, 54.18; H, 5.16.

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(14) Supplied by Parke, Davis and Company.

(15) Burckhalter, *et al.*, *THIS JOURNAL*, **70**, 1363 (1948).

DEPARTMENT OF CHEMISTRY
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N-(Hydroxyethylmethylaminoethyl)-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 Halpern² has reported extensively on several phenothiazines and recently N-pyrrolidylethylphenothiazine has been reported by Hunter, *et al.*³

(1) Gay, *et al.*, *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-(Hydroxyethylmethylaminoethyl)-phenothiazine (SC 1923) has been prepared by the reaction of N-methyl-ethanolamine with N-(β-chloroethylphenothiazine).⁴ Its hydrochloride melted at 185–186°. *Anal.* Calcd. for C₁₇H₂₁N₃SOCl; S, 9.52. Found: S, 9.62. The methobromide melted at 154–155°. *Anal.* Calcd. for C₁₈H₂₃N₃SOBr; 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 Loew⁵ SC 1923 had an ED₅₀ = 0.43 ± 0.15 mg./kg. as compared to an ED₅₀ of 0.66 ± 0.13 mg./kg. for β-dimethylaminoethylbenzhydrol ether.

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

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

(5) Loew, *et al.*, *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 S³⁵ between H₂S³⁵ 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 SOLUTION²

| Temp., °C. | Time of ex- change, hr. | Concns. of reactants, moles/liter × 10 ³ | | Observed activity, counts/min. | | % ex- change, max. |
|------------|-------------------------------|---|-----------------|-----------------------------------|-----------------|-----------------------------|
| | | H ₂ S | CS ₂ | H ₂ S | CS ₂ | |
| 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 CS₂-C₆H₆ solution was made up by weighing out reagent grade carbon disulfide and mixing it with reagent benzene in a volumetric flask. The H₂S³⁵-C₆H₆ 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).

