

contained in a 500-ml. flask equipped with a motor stirrer, a dropping funnel and a reflux condenser closed with a calcium chloride tube was added dropwise a solution of 6.8 g. (0.05 mole) of sulfuryl chloride in 50 ml. of chloroform (15 min.). The color of the solution gradually changed during the addition of the sulfuryl chloride from a deep red to a light amber. After stirring at room temperature for 45 minutes the solution was allowed to stand overnight (red color returned), and then refluxed 1.5 hours. The solvent was removed by distillation leaving a pink solid which was dissolved in 35 ml. of boiling methanol. The solution was digested with Norit A, filtered hot, diluted with water and cooled. Filtration yielded 8.3 g. (85.3%) of white 1-chloro-4-hydroxydibenzofuran melting over the range of 85–105°. Purification was effected by fractional recrystallization from carbon tetrachloride. A total of 1.5 g. (11.8%) of pure product was obtained which melted at 154–155°. The infrared spectrum showed an absorption band at 3.0 μ , characteristic of the hydroxyl group.

Anal. Calcd. for $C_{12}H_7ClO_2$: Cl, 16.2. Found: Cl, 16.2, 16.2.

This compound was considered to be 1-chloro-4-hydroxydibenzofuran as bromination of 4-hydroxydibenzofuran has been shown to give 1-bromo-4-hydroxydibenzofuran.⁶

1,3-Dichloro-4-hydroxydibenzofuran.—A solution of 8.6 ml. (0.10 mole) of sulfuryl chloride in 50 ml. of chloroform was added dropwise over a period of 30 minutes to a stirred solution of 9.2 g. (0.05 mole) of 4-hydroxydibenzofuran in 200 ml. of chloroform. The solution was stirred at room temperature for 3 hours, then refluxed for 1.5 hours (until there was no further evidence of hydrogen chloride evolution). After the solvent was removed by distillation, the remaining gray residue was taken up in the minimum amount of refluxing carbon tetrachloride (250 ml.), and the resulting solution was digested with Norit A, filtered hot and allowed to cool slowly. The copious precipitate of white needles was filtered off yielding 6.6 g. (52.0%) of product melting at 158–159.5°. One recrystallization from carbon tetrachloride gave 4.6 g. (36.2%) of pure 1,3-dichloro-4-hydroxydibenzofuran, m.p. 160–161°. The infrared spectrum showed an absorption band at 3.15 μ , characteristic of the hydroxyl group.

Anal. Calcd. for $C_{12}H_6Cl_2O_2$: Cl, 27.8. Found: Cl, 27.5, 27.8.

Similar chlorination of the 1-chloro-4-hydroxydibenzofuran gave a 92.0% yield of 1,3-dichloro-4-hydroxydibenzofuran, m.p. 160–161°. A mixed m.p. of the two products showed no depression.

This compound was considered to be 1,3-dichloro-4-hydroxydibenzofuran since nitration of 1-bromo-4-methoxydibenzofuran has been shown to yield 1-bromo-3-nitro-4-methoxydibenzofuran.⁷

4-Hydroxyphenoxathiin.—4-Phenoxathiinylithium⁸ was prepared by adding 0.1 mole of *n*-butyllithium⁹ in 72 ml. of ether to a stirred suspension of 20.0 g. (0.1 mole) of phenoxathiin in 50 ml. of ether. After stirring and refluxing for 24 hours, the mixture was cooled in an ice-salt-bath. One-tenth mole of *n*-butylmagnesium bromide in ether was then added at such a rate that the temperature did not rise above -2° . The resulting mixture was stirred and cooled for one hour, then oxygen was swept over the surface until a Color Test I¹⁰ was negative (12 hours). Hydrolysis was carried out with iced 6 *N* hydrochloric acid. The acid layer was extracted well with ether and the resulting combined ether layer was extracted with 5% sodium hydroxide until an acidified sample gave no precipitate. Acidification of the combined alkaline solution and filtration gave 10.1 g. (46.7%) of light tan product melting over the range of 85–91°. Repeated recrystallizations from methanol and petroleum ether (b.p. 77–115°) raised the melting point to 98–99° and gave a final pure yield of 3.5 g. (15.5%).

Anal. Calcd. for $C_{12}H_8O_2S$: S, 14.83. Found: S, 14.75, 14.97.

(6) H. Gilman and P. R. Van Ess, *THIS JOURNAL*, **61**, 1365 (1939).

(7) H. Gilman, P. T. Parker, J. C. Bailie and G. E. Brown, *ibid.*, **61**, 2836 (1939).

(8) H. Gilman, M. W. Van Ess, H. B. Willis and C. G. Stuckwisch, *ibid.*, **62**, 2606 (1940).

(9) H. Gilman, J. A. Beel, C. G. Brannen, M. W. Bullock, G. E. Dunn and L. S. Miller, *ibid.*, **71**, 1499 (1949).

(10) H. Gilman and F. Schulze, *ibid.*, **47**, 2002 (1925).

1-Hydroxythianthrene.—1-Thianthrenyllithium¹¹ was prepared by adding 0.11 mole of *n*-butyllithium⁹ in 92 ml. of ether to a stirred suspension of 21.6 g. (0.1 mole) of thianthrene in 50 ml. of ether. After stirring and refluxing for 22 hours, the mixture was cooled in an ice-salt-bath. One-tenth mole of *n*-butylmagnesium bromide in ether was added at such a rate that the temperature did not rise above -2° , and the resulting mixture was cooled and stirred for one hour. While maintaining the internal temperature below -2° , oxygen was swept over the surface of the reaction mixture until Color Test I¹⁰ became negative (11 hours). The mixture was hydrolyzed with iced hydrochloric acid, the layers were separated, the acid layer was washed well with ether and the combined ether layer was extracted with 5% sodium hydroxide until no precipitate appeared when a test portion was acidified. Acidification of the combined alkaline layer and filtration gave 5.0 g. (21.6%) of 1-hydroxythianthrene melting over the range of 74–82°. Repeated recrystallizations from petroleum ether (b.p. 77–115°) raised the melting point to 117–118°.

Anal. Calcd. for $C_{12}H_8OS_2$: S, 27.60. Found: S, 27.62, 27.71.

Removal of the solvent from the reaction mixture ether layer yielded 6.8 g. of unreacted thianthrene (31.5% recovery) melting at 151–153°. Based on the unrecovered thianthrene, the crude yield of 1-hydroxythianthrene was 31.5% and the pure yield was 2.5%.

Acknowledgment.—The authors are grateful to Dr. Velmer A. Fassel and Mr. Marvin Margoshes and to the Ames Laboratory for the infrared absorption measurements.

(11) H. Gilman and C. G. Stuckwisch, *ibid.*, **65**, 1461 (1943).

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Some Derivatives of 2-Amino-3-bromotetrahydropyran

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During the course of investigation of the preparation of nucleotide-like compounds a number of derivatives of 2-amino-3-bromotetrahydropyran were prepared.

Dihydropyran was quantitatively converted to 2,3-dibromotetrahydropyran (I), according to the direction of Paul.² Treatment of I with silver cyanate resulted in a 92% yield of 3-bromo-2-tetrahydropyranyl isocyanate (II). The action of aqueous ammonia on II gave the corresponding urea III; the disubstituted urea, 1,3-bis-(3-bromo-2-tetrahydropyranyl)-urea (IV), could be obtained by the hydrolysis of II, whereas the reaction of II with absolute ethyl alcohol afforded the urethan V. Furthermore, when II reacted with ethyl glycinate, ethyl 3-bromo-2-tetrahydropyranylhydantoate (VI) was obtained, but attempts at ring closure to the corresponding hydantoin by means of 25% hydrochloric acid were unsuccessful.

Efforts to prepare similar derivatives of 3-bromo-2-tetrahydropyranyl isothiocyanate met with failure. The reaction of 2,3-dibromotetrahydropyran with silver thiocyanate gave upon distillation a liquid boiling at 107–110° (2 mm.) (VII). The conclusion that VII was the thiocyanate rather than the isothiocyanate was based on observations that the compound did not yield the substituted thiourea

(1) Parke, Davis and Co., Detroit 32, Michigan.

(2) R. Paul, *Compt. rend.*, **198**, 375 (1934).

when treated with ammonia, and that treatment with dilute acid resulted in the liberation of hydrogen cyanide. After three weeks of standing in a refrigerator at 5°, VII deposited crystals which upon purification proved to be bis-(3-bromo-2-tetrahydropyran-2-yl) ether. It should be noted that this compound had been previously obtained as a hydrolysis product of I by Paul.³ Further attempts to prepare 3-bromo-2-tetrahydropyran-2-yl isothiocyanate by the action of phosphorus pentasulfide on II were to no avail. When an intimate mixture of II and phosphorus pentasulfide was heated gently, a vigorous exothermic reaction set in at 60° which resulted in the formation of intractable tars.

The reaction of 2,3-dibromotetrahydropyran and *o*-bromoaniline gave N-(3-bromo-2-tetrahydropyran-2-yl)-*o*-bromoaniline (VIII), in good yield.

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Experimental

3-Bromo-2-tetrahydropyran-2-yl Isocyanate (II).—In a one-l. three-necked flask provided with a condenser, calcium chloride tube and Hershberg stirrer, were placed 170 g. (0.69 mole) of 2,3-dibromotetrahydropyran² and 300 ml. of dry, thiophene-free benzene. To this, in small portions, 103 g. (0.69 mole) of silver cyanate was added over a period of two hours, after which the silver bromide was removed by filtration through a Celite pad. Removal of the solvent *in vacuo* left a dark brown residue. Vacuum distillation of the latter yielded 121 g. (85% yield) of 3-bromo-2-tetrahydropyran-2-yl isocyanate boiling at 100–102° at 2 mm.

Anal. Calcd. for C₆H₈BrNO₂: N, 6.80. Found: N, 6.70.

(3-Bromo-2-tetrahydropyran-2-yl)-urea (III).—To 4.12 g. (0.020 mole) of II was added to 50 ml. of concentrated ammonium hydroxide solution. The mixture was stirred at room temperature for ten minutes, whereupon large crystals precipitated. Filtration of the product followed by recrystallization from ethyl alcohol yielded 4.26 g. of III, melting at 147–148°, yield 95%.

Anal. Calcd. for C₆H₁₁BrN₂O₂: N, 12.10. Found: N, 11.99.

1,3-Bis-(3-bromo-2-tetrahydropyran-2-yl)-urea (IV).—In a 50-ml. erlenmeyer flask was placed 4.12 g. (0.020 mole) of II. To this was added 25 ml. of water, and the mixture was boiled until the carbon dioxide evolution had ceased. This required approximately ten minutes. Filtration of the solid yielded 3.74 g. of product, m.p. 149–150° dec., yield 97%.

Anal. Calcd. for C₁₁H₁₈Br₂N₂O₂: N, 7.26. Found: N, 7.30.

3-Bromo-2-tetrahydropyran-2-yl Carbamate (V).—A mixture of 5.0 g. (0.0242 mole) of II and 20 ml. of 99.95% ethyl alcohol was refluxed for five minutes with careful exclusion of moisture. Refrigeration of the homogeneous solution for 48 hours failed to form crystals. The excess solvent was removed *in vacuo*, and 5 ml. of water was added to the residual sirup. Scratching induced crystallization of V. Recrystallization from ethanol gave 5.1 g. of V, m.p. 98–99°, yield 84%.

Anal. Calcd. for C₈H₁₄BrNO₃: N, 5.69. Found: N, 5.52.

Ethyl (3-Bromo-2-tetrahydropyran-2-yl)-1-hydantoate (VI).—To 4.12 g. (0.020 mole) of II was added, with efficient cooling, 2.06 g. (0.020 mole) of freshly prepared ethyl glycinate. A solid formed immediately, which after recrystallization from acetone melted at 128–130°. The yield was 5.2 g., or 84%.

(3) R. Paul, *Bull. soc. chim. France*, [5] 1, 1397 (1934).

Anal. Calcd. for C₁₀H₁₇BrN₂O₄: N, 9.06. Found: N, 8.70.

Attempted Preparation of 3-Bromotetrahydropyran-2-yl Isothiocyanate.—A mixture of 103 g. (0.445 mole) of 2,3-dibromotetrahydropyran and 300 ml. of dry, thiophene-free benzene was placed in a one-l. three-necked flask, provided with a condenser and calcium chloride tube and a Hershberg stirrer. To this was added in very small portions over a two-hour period 74 g. (0.445 mole) of dry silver thiocyanate. Upon completion of the addition the mixture was gently refluxed for two more hours, after which the precipitated silver bromide was removed by filtration. Vacuum distillation of the solvent left a residue, which distilled off at 107–110° (2 mm.) and had a strong odor, typical of a thiocyanate. The yield was 56 g. or 47% of theoretical. In view of the fact that the compound decomposed rapidly at room temperature, it was not submitted for analysis. Storage in the absence of light at 5° resulted in the deposition of crystals which, when recrystallized from ethyl alcohol, melted at 108–109° and possessed the correct analysis for di-(3-bromotetrahydro-2-pyran-2-yl) ether. Paul reports a m.p. of 110° for this compound.³

Anal. Calcd. for C₁₀H₁₆Br₂O₃: C, 34.91; H, 4.69; Br, 46.45. Found: C, 34.88; H, 4.91; Br, 46.66.

N-(3-Bromo-2-tetrahydropyran-2-yl)-*o*-bromoaniline (VIII).—A mixture of 71 g. (0.29 mole) of 2,3-dibromotetrahydropyran in 250 ml. of dry benzene was cooled to 5° in an ice-bath. To this was added slowly 100 g. (0.58 mole) of *o*-bromoaniline. Upon completion of the addition the mixture was gently warmed, and a vigorous reaction set in which had to be controlled by external cooling. After 20 minutes the precipitated *o*-bromoaniline hydrobromide was removed by filtration and the filtrate was stripped of solvent *in vacuo*. The solid residue weighed 78 g. and melted at 89–92°. An analytical sample, recrystallized three times from ethyl alcohol, melted at 93–95°. The yield of crude material was 79%.

Anal. Calcd. for C₁₁H₁₃Br₂NO: N, 4.18. Found: N, 3.96.

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3-Bromotropolone Hydrobromide, a Product Obtained from the Bromination of 1,2-Cycloheptanedione¹

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The synthesis of 3-bromotropolone (III), involving the bromination-dehydrobromination of 1,2-cycloheptanedione (I), has been described by Cook, *et al.*,² and by Nozoe, *et al.*³ The reaction of I in acetic acid with two moles of bromine at 0°² followed by heating on a steam-bath resulted in the formation of a dense crystalline solid, melting point not given, which it was said did not possess tropolone-like properties, and which was inadequately characterized as 3,7-dibromo-3-cyclohepten-1,2-dione (IV).⁴ When warmed with aqueous methanol, 3-bromotropolone (III) was obtained, or when boiled in 6 *N* sodium hydroxide the corresponding sodium salt was obtained.

(1) Presented before the Division of Organic Chemistry, 126th National Meeting of the American Chemical Society, New York, N. Y., September 12–17, 1954.

(2) J. W. Cook, A. R. Gibb, R. A. Raphael and A. R. Somerville, *Chemistry and Industry*, 427 (1950); *J. Chem. Soc.*, 503 (1951).

(3) T. Nozoe, S. Seto, Y. Kitahara, M. Kunori and Y. Nakayama, *Proc. Japan Acad.*, 26, 38 (1950).

(4) The only characterization of this product by Cook, *et al.*,² was a bromine analysis which was 3.0% lower than that required by C₇H₈Br₂O₂. It was pointed out that the product could be recrystallized rapidly from acetic acid, but an accurate analysis could not be obtained owing to its instability.