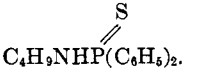
melting at 38–40° was obtained. Analytical data (Table I) confirmed the formula $C_4H_9NHP(C_6H_5)_2$.

The identity of the product was further established by splitting to *t*-butylamine hydrochloride and diphenylchlorophosphine by means of an ethereal solution of hydrogen chloride. The identity of these two substances was established by physical constants (melting point and mixed melting point, boiling point, and infrared spectra).

The NMR spectrum of the protons in the product agrees precisely with that expected for the structure $(CH_3)_3CNHP(C_6H_5)_2$.

This *N*-substituted aminodiphenylphosphine as well as several others prepared in this study was converted to the corresponding aminophosphine sulfide by reaction with an excess of sulfur in carbon disulfide in accordance with the following procedure:

To a continuously stirred solution of 1.3 g. (0.005 mole) of *N-t*-butylaminodiphenylphosphine in 25 ml. of dry carbon disulfide was added 0.3 g. (0.009 mole) of sulfur. The solution was warmed to about 35° and allowed to react for 10 hr., during which time the color changed from light brown to yellow and finally became almost colorless. On reduction of the volume of the reaction mixture through vacuum evaporation of most of the solvent, 1.2 g. (84%) of white prismatic crystals was obtained; m.p. 120.5–121.5°. Analytical data (Table I) confirmed the formula



$C_4H_9NH\overset{S}{P}(C_6H_5)_2$.

The aminophosphine was further characterized by conversion to the methyl iodide adduct $[(t\text{-}C_4H_9)NHP(CH_3)(C_6H_5)_2]I$ by reaction with a benzene solution of methyl iodide. The adduct was obtained as white needles melting at 198.5–200°. Analytical data are given in Table I.

Analytical data, yield data, and melting points for aminodiphenylphosphines and their sulfides prepared by procedures analogous to the above are summarized in Table I.

The preparation of *N*-diphenylaminodiphenylphosphine was carried out according to the following procedure: A solution of 1.7 g. (0.01 mole) diphenylamine in 10 ml. of dry (over calcium hydride) diethylene glycol dimethyl ether was added to a suspension of 0.8 g. of sodium hydride (54% dispersion in oil) in 25 ml. of the diglyme. After the theoretical amount of hydrogen (0.2 l.) had been evolved, 2.2 g. (0.01 mole) of diphenylchlorophosphine was added with stirring to the mixture. The temperature was raised to and held at 110° for 1.5 hr. The solid reaction product was filtered hot, washed with dry ethyl ether and weighed 0.6 g. (calculated weight of sodium chloride, 0.6 g.). The filtrate and ether washings were combined and the solvents removed under reduced pressure. The residue was recrystallized from ethanol. The resulting crystals weighed 0.8 g. (23%) and melted at 130–132°. The product was further characterized by alkaline hydrolysis to diphenylamine and diphenylphosphinic acid. Both of these substances were isolated and identified by melting point (including mixed melting point with known samples) and infrared spectra.

*Infrared spectra.* The infrared spectrum of each of the phosphorus-nitrogen derivatives obtained in this study was examined using a Perkin Elmer Model 21 spectrograph. The principal bands in each spectrum are listed in Table II.

### DISCUSSION

As indicated in Table II the infrared spectra of all the new compounds show the P—N bands in the 870–750 cm.$^{-1}$ region. This agrees well with the findings of Reist, Junga, and Baker with respect to diaminophosphine sulfides.[2d] The sulfides all showed an extra absorption band at approximately 715 cm$^{-1}$.

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## Some Halogenated 1,2,3-Benzotriazin-4(3H)ones

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*Received May 25, 1960*

In the course of routine screening, 1,2,3-benzotriazin-4(3H)one was found[1] to have sedative activity. In an attempt to prepare compounds exhibiting an enhancement of this activity, a number of benz-halogenated and 3-dialkylaminoalkyl analogs of the parent compound were prepared for pharmacological evaluation, not only as sedatives, but also for other types of activity as well.[2]

In line with this approach, since the completion of this work a note describing 4-substituted 1,2,3-benzotriazines as having "apresoline-like" adrenergic blocking activity has also appeared.[3]

Of the several methods referred to in the literature,[4] three seemed best suited for this work. The first of these (method A), involved cyclization *via* diazotization of an anthranilamide to the desired 1,2,3-benzotriazin-4(3H)one and was of the most general application.

The second procedure (method B) utilized the reaction of a dialkylaminoalkyl chloride with a benz-halogenated-1,2,3-benzotriazin-4(3H)one. The yields by this method, however, were generally lower than those obtained by method A.

A third, but even less successful approach (method C), involved the reaction of a dialkylaminoalkylamine with the diazotized methyl ester of an anthranilic acid.

The substituted anthranilamides were obtained by the action of ammonia, or dialkylaminoalkylamines, on the corresponding isatoic anhydrides, which in turn were prepared by reaction of the

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(1) We are indebted for this and for all other activity data to Dr. A. C. Osterberg and his associates, Experimental Therapeutics Research Section, Pearl River Laboratories.

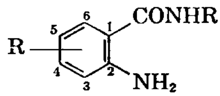
(2) For example, 7-chloro-3-amino-1,2,4-benzotriazine and its 1-oxide have been reported to have a high order of antiprotozoan activity against avian malaria by F. J. Wolf, K. Pfister, R. M. Wilson, Jr., and C. A. Robinson, *J. Am. Chem. Soc.*, **76**, 3551 (1954) and by F. J. Wolf, R. M. Wilson, Jr., K. Pfister, and M. Tishler, *J. Am. Chem. Soc.*, **76**, 4611 (1954).

(3) C. Grundmann and H. Ulrich, *J. Org. Chem.*, **24**, 272 (1959).

(4) E. Van Heyningen, *J. Am. Chem. Soc.*, **77**, 6562 (1955) and Refs. 1, 2, and 3 in that paper.

## TABLE I

### SUBSTITUTED ANTHRANILAMIDES

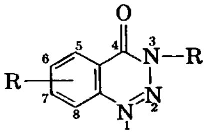


| R | R′ | Yield, % | M.P. | Formula | % Calcd. C | H | N | Cl | % Found C | H | N | Cl |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 4-Chloro | H | 32 | 180–181[a] | $C_7H_7ClN_2O$ | 49.3 | 4.14 | 16.4 | 20.8 | 49.2 | 4.14 | 16.6 | 20.9 |
| 4-Chloro | $(CH_3)_2$—N—$(CH_2)_3$ | 46 | 226–229[b] | $C_{12}H_{20}Cl_3N_3O$[b] | 43.9 | 6.12 | 12.8 | 32.4 | 43.9 | 6.13 | 12.6 | 32.5 |
| 4-Chloro | $(C_2H_5)_2$—N—$(CH_2)_3$ | 33 | 210–212[b] | $C_{14}H_{24}Cl_3N_3O$[b] | 47.1 | 6.78 | 11.8 | 29.8 | 46.8 | 7.01 | 12.0 | 29.6 |
| 5-Chloro | H | 51 | 170–171[c] | $C_7H_7ClN_2O$ | | | | | | | | |
| 5-Chloro | $(CH_3)_2$—N—$(CH_2)_3$ | 36 | 138–140[b] | $C_{12}H_{20}Cl_3N_3O$[b] | 43.9 | 6.12 | 12.8 | 32.4 | 43.7 | 6.45 | 12.7 | 30.7[d] |
| 5-Chloro | $(C_2H_5)_2$—N—$(CH_2)_3$ | 25 | 189–191[b] | $C_{14}H_{24}Cl_3N_3O$[b] | 47.1 | 6.78 | 11.8 | 29.8 | 46.9 | 6.84 | 12.0 | 29.8 |
| 3,5-Dichloro | H | 17[e] | 184–186[f] | $C_7H_6Cl_2N_2O$ | 41.0 | 2.95 | 13.7 | 34.6 | 41.5 | 2.96 | 13.8 | 34.5 |
| | | (59)[g] | 179–180 | | | | | | | | | |

[a] Reported m.p. 181°; L. B. Hunn, *J. Am. Chem. Soc.*, 45, 1027 (1923). [b] Melting point and analyses are of dihydrochlorides. [c] Reported m.p. 172°; Ref. 9. [d] Satisfactory chlorine analysis was not obtained. [e] Yield by isatoic anhydride method. [f] Reported m.p. 182.5°; Ref. 6. [g] Yield by method of Shiebley; Ref. 6.

## TABLE II

### SUBSTITUTED 1,2,3-BENZOTRIAZIN-4(3H)ONES



| Method | R | R′ | Yield, % | M.P., dec. | Formula | % Calcd. C | H | N | Cl | % Found C | H | N | Cl |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| A | 6-Chloro | H | 54 | 210–211 | $C_7H_4ClN_3O$ | 46.3 | 2.22 | 23.1 | 19.5 | 46.5 | 2.34 | 23.4 | 19.6 |
| A | 6-Chloro | $(CH_3)_2N$—$(CH_2)_3$ | 85 | 230–232[a] | $C_{12}H_{16}Cl_2N_4O$[a] | 47.6 | 5.32 | 18.5 | 23.4 | 47.8 | 5.39 | 18.8 | 23.6 |
| A | 6-Chloro | $(C_2H_5)_2N$—$(CH_2)_3$ | 82 | 185–186[a] | $C_{14}H_{20}Cl_2N_4O$[a] | 50.8 | 6.08 | 16.9 | 21.4 | 51.0 | 6.23 | 17.0 | 21.2 |
| A | 7-Chloro | H | 47 | 215–216[b] | $C_7H_4ClN_3O$ | 46.3 | 2.22 | 23.1 | 19.5 | 46.6 | 2.35 | 23.4 | 19.5 |
| A | 7-Chloro | $(CH_3)_2N$—$(CH_2)_3$ | 84 | 262–263[a] | $C_{12}H_{16}Cl_2N_4O$[a] | 47.6 | 5.32 | 18.5 | 23.4 | 47.8 | 5.41 | 18.2 | 23.4 |
| B | 7-Chloro | $(CH_3)_2N$—$(CH_2)_3$ | 57 | 269–270[a] | $C_{12}H_{16}Cl_2N_4O$[a] | 47.6 | 5.32 | 18.5 | 23.4 | 47.3 | 5.48 | 18.5 | 23.4 |
| A | 7-Chloro | $(C_2H_5)_2N$—$(CH_2)_3$ | 68 | 232–233[a] | $C_{14}H_{20}Cl_2N_4O$[a] | 50.8 | 6.08 | 16.9 | 21.4 | 50.5 | 6.07 | 16.6 | 21.3 |
| C | 7-Chloro | $(CH_3)_2N$—$(CH_2)_2$ | 47 | 267–270[a] | $C_{11}H_{14}Cl_2N_4O$[a] | 45.7 | 4.88 | 19.4 | 24.5 | 45.8 | 4.96 | 19.1 | 24.8 |
| A | 6,8-Dichloro | H | 78 | 195–196 | $C_8H_3Cl_2N_3O$ | 38.9 | 1.39 | 19.5 | 32.8 | 39.1 | 1.64 | 19.5 | 32.6 |

[a] M.p. and analyses are of hydrochlorides. [b] Reported m.p. 219–220°; Ref. 3.

appropriate anthranilic acid[5] with phosgene.[6] The physical data for the various anthranilamides and 1,2,3-benzotriazin-4(3H)ones prepared are listed in tables I and II, respectively. These compounds were found to be essentially devoid of biological activity[1] on pharmacological evaluation in experimental animals.

### EXPERIMENTAL[7]

The following examples are given to illustrate the methods used to prepare the compounds listed in Tables I and II. In general the experimental details varied very little from preparation to preparation.

*4-Chloroisatoic anhydride.* Phosgene was bubbled at room temperature through a solution of 85.8 g. (0.500 mole) of 4-chloroanthranilic acid[8] and 33.5 g. (0.316 mole) of sodium carbonate in 1750 ml. of water. The *p*H of the reaction mixture was maintained at 6–7 by a steady addition of an aqueous solution of 19.5 g. (0.184 mole) of sodium carbonate. After all of the carbonate was consumed, phosgene bubbling was continued until the *p*H dropped to about 2. The solid was filtered, washed with two 250-ml. portions of cold water, and air dried to yield 78.4 g. (79.5%) of white solid decomposing at 217°. A twice recrystallized sample from ethanol melted at 278–282° dec.

*Anal.* Calcd. for $C_8H_4ClNO_3$: C, 48.6; H, 2.01; Cl, 17.9; N, 7.09. Found: C, 48.7; H, 2.50; Cl, 18.2; N, 7.30.

The following two compounds were prepared by the above procedure.

*5-Chloroisatoic anhydride*[9] m.p. 278–281°; yield (87%).

*Anal.* Calcd. for $C_8H_4ClNO_3$: C, 48.6; H, 2.01; Cl, 17.9; N, 7.09. Found: C, 48.6; H, 2.23; Cl, 18.3; N, 7.33.

*3,5-Dichloroisatoic anhydride,* m.p. 251–253° dec.; lit.[9] m.p. 254–256°; yield (68%).

*4-Chloroanthranilamide.* A mixture of 12.0 g. (0.0608 mole) of 4-chloroisatoic anhydride and 304 ml. (0.608 mole) of 2*N* ammonium hydroxide was mechanically stirred for 4 hr. The solid was filtered and air-dried to yield 3.3 g. (32%) of crystalline, white product melting at 182–184°. An analytical sample was prepared by recrystallizing the crude twice from ethanol. The analytical data for this compound and the other substituted anthranilamides prepared similarly is given in Table I.

*7-Chloro-1,2,3-benzotriazin-4(3H)one* (Method A). To an ice-cold suspension of 3.12 g. (0.0183 mole) of 4-chloroanthranilamide in 20 ml. of water and 5.6 ml. of concd. hydrochloric acid was added a solution of 1.32 g. (0.0193 mole) of sodium nitrite in 10 ml. of water over 45 min. while maintaining the reaction temperature between 0–5°. The resultant orange mixture was treated with 7 ml. of 10*N* sodium hydroxide. The mixture changed to an orange solution, which was stirred for 10 min. and then acidified to *p*H 2 with concd. hydrochloric acid to give an orange solid which was filtered, washed with ice-water and air-dried; yield, 1.57 g. (47.3%), m.p. 179–181°. A sample recrystallized twice from ethanol afforded white needles melting at 215–216° dec.

The analytical data for this compound and the other analogous compounds is given in Table II. The dialkylaminoalkyl benzotriazinones, because of their amphoteric nature, were extracted from the reaction mixtures at neutral *p*H with chloroform.

*7-Chloro-3-(γ-dimethylamino)propyl-1,2,3-benzotriazin-4(3H)one* (Method B). To a solution of 0.75 g. (0.014 mole) of sodium methoxide in 50 ml. of anhydrous ethanol, was added 2.40 g. (0.0132 mole) of 7-chloro-1,2,3-benzotriazin-4(3H)one. After refluxing the mixture for 10 min., it was treated with 1.60 g. (0.0132 mole) of 3-dimethylaminopropyl chloride and then refluxed for 40 hr. The mixture was filtered hot, and the filtrate was concentrated *in vacuo* to a yellow sirup which solidified on cooling to a waxy solid melting at 43–46°. This solid was converted to the hydrochloride with ethanolic hydrochloric acid. The crystalline hydrochloride weighed 2.2 g. (57%) and melted at 256° dec.

*7-Chloro-3-(β-dimethylamino)ethyl-1,2,3-benzotriazin-4(3H)one* (Method C). A suspension of 7.0 g. (0.032 mole) of methyl-4-chloroanthranilate[8] hydrochloride in 35 ml. of water was treated gradually with a solution of 2.6 g. (0.038 mole) of sodium nitrite in 15 ml. of water at 0–5° over 20 min. The resultant diazonium salt solution was diluted to 350 ml. with ice water and then 5.0 g. (0.57 mole) of β-dimethylaminoethylamine was added over 10 min. The reaction mixture was stirred for 45 min. longer, and the resulting orange-yellow suspension was extracted thoroughly with ether. The pooled extracts were dried over anhydrous magnesium sulfate, and then concentrated *in vacuo* to a brown sirup. An alcoholic solution of this sirup in 15 ml. of solvent was treated with ethanolic hydrochloric acid and the precipitated hydrochloride was filtered and dried; yield, 4.4 g. (47%); m.p. 241–245° dec. The analytical sample was recrystallized from 95% ethanol, m.p. 267–270° dec.

*Acknowledgment.* We wish to express our appreciation to Mr. L. Brancone and his staff for the microanalytical results, to Dr. J. H. Clark and his staff for certain large scale preparations of intermediates, and to Mrs. J. L. Frederick for technical assistance on a part of this work.

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[5] The substituted anthranilic acids were either purchased from a commercial source or prepared by known methods.

[6] In the case of 3,5-dichloroanthranilamide the best method of preparation was found to be that of F. E. Shiebley, *J. Org. Chem.*, **3**, 414 (1938).

[7] All melting points are uncorrected.

[8] R. E. Lutz, G. Ashburn, J. A. Freek, R. H. Jordan, N. H. Leake, T. A. Martin, R. J. Rowlett, Jr., and J. W. Wilson, *J. Am. Chem. Soc.*, **68**, 1285 (1946).

[9] R. Dorsch, *J. prakt. Chem.*, [2] **33**, 45–51 (1886).

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## Synthesis of the Sulfur Analogs of Batyl and Chimyl Alcohols

D. David Lawson, Horace R. Getz,
and Donald A. Miller

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The occurrence of α-glyceryl ethers in the nonsaponifiable residues of oils from various marine animals[1,2] has been reported especially in those of the elasmobranch group. Recently batyl alcohol (I) has been isolated also from sources other

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[1] M. Tsujimoto and Y. Toyama, *Chem. Umschau Gebiete Fette, Öle, Wachse u. Harze*, **29**, 27 (1922); *Chem. Umschau Gebiete Fette, Öle, Wachse u. Harze*, **31**, 13, 135, 153 (1924); *Chem. Zentr.*, I, 878 (1922).

[2] I. M. Heilbron and W. M. Owens, *J. Chem. Soc.*, 942 (1928).