amorphous base from 1 g. of N-cholylpiperidine hydrochloride. After standing for 16 hr. the solution was diluted with water, neutralized with solid sodium bicarbonate solution, and extracted with ether. The dried solution was evaporated at reduced pressure and the residue further dried by addition of benzene and evaporation. Conversion to the hydrochloride and crystallization from methanol-ether gave 0.4 g. (35%) of pure salt, m.p. 269–270° dec., α_D +46° MeOH (*c* 2.55), λ^{Chf} 2.93, 4.1–4.2, 5.76 μ.

Anal. Calcd. for $C_{32}H_{56}O_5NCl$ (570.23): C, 67.38; H, 9.90. Found: C, 67.33; H, 9.87.

(b) **3-Acetate.**—The base from 1 g. of N-cholylpiperidine hydrochloride was treated in 10 cc. of dioxane with 4 cc. of pyridine and 6 cc. of acetic anhydride for 48 hr. at 20° and the product isolated as the hydrochloride, which was crystallized from methanol–ether; m.p. 249–252°, α_D +29° MeOH (*c* 2.56), λ^{Chf} 3.0, 4.2, 5.8 μ.

Anal. Calcd. for $C_{31}H_{54}O_4NCl$ (540.21): C, 68.92; H, 10.08. Found: C, 69.02; H, 10.30.

(c) **3-Veratrate.**—A solution of the cholylpiperidine from 0.85 g. of hydrochloride in 7 cc. of dioxane was treated with a solution in 4 cc. of dioxane and 3 cc. of pyridine with 2 g. of veratroyl chloride, prepared according to Kostanecki and Tambor[5] and crystallized from benzene–petroleum ether (m.p. 70–71°). After standing for 36 hr. in a refrigerator the mixture was worked up and the product crystallized as the hydrochloride from methanol–ether; m.p. 261° dec., α_D +43° MeOH (*c* 2.82), λ^{Chf} 2.96, 4.1–4.2, 5.9, 6.2 μ.

Anal. Calcd. for $C_{38}H_{60}O_6NCl$ (662.33): C, 68.91; H, 9.13. Found: C, 68.79; H, 9.54.

Cholic Acid Morpholide.—By the procedure given above, 2.15 g. of cholic acid hydrazide afforded 2.0 g. (82%) of crude product, m.p. 266–268°. Recrystallization from chloroform–methanol raised the m.p. to 273–275° dec., α_D +34° Py (*c* 1.92), λ^{Chf} 3.0, 6.1 μ.

Anal. Calcd. for $C_{28}H_{47}O_5N$ (477.67): C, 70.40; H, 9.92. Found: C, 70.44; H, 10.09.

N-Cholylmorpholine Hydrochloride.—This salt was obtained as the monohydrate in 46% yield by reduction of the above amide with lithium aluminum hydride and crystallization as hydrochloride; m.p. 289–290°, α_D −32° MeOH (*c* 2.20).

Anal. Calcd. for $C_{28}H_{50}O_4NCl \cdot H_2O$ (518.16): C, 64.90; H, 10.12. Found: C, 64.66, 65.07; H, 10.08, 10.37.

N-(3-Cathylcholyl)-morpholine hydrochloride melted at 235–238° dec., α_D +51° MeOH (*c* 0.36), λ^{Chf} 2.95, 4.3, 5.76 μ.

Anal. Calcd. for $C_{31}H_{54}O_6NCl$ (572.20): C, 65.06; H, 9.51. Found: C, 64.79; H, 9.35.

N,N-Dimethylcholylamine Hydrochloride.—N,N-Dimethylcholic acid amide was obtained by the general procedure described in 90% yield, m.p. 168–172° dec. (reported 170–171°,[6] 179°[3]), α_D +36° MeOH (*c* 2.56), λ^{Chf} 2.95, 6.12 μ. Reduction of 1.8 g. of amide with excess lithium aluminum hydride gave 1.53 g. (81%) of the amine hydrochloride, m.p. 280–281°, α_D +33° MeOH (*c* 2.24).

Anal. Calcd. for $C_{26}H_{48}O_3NCl$ (458.11): C, 68.18; H, 10.56. Found: C, 67.94; H, 10.43.

3-Cathyl-N,N-dimethylcholylamine hydrochloride melted at 242–243°, α_D +52° MeOH (*c* 1.76), λ^{Chf} 3.0, 4.2–4.4, 5.78 μ.

Anal. Calcd. for $C_{29}H_{52}O_5NCl$ (530.17): C, 65.69; H, 9.89. Found: C, 65.47; H, 9.89.

N,N-Diethylcholic Acid Amide.—The crude product, m.p. 115–120° (81% yield), separated very slowly from aqueous acetone to give very hygroscopic crystals of the monohydrate, m.p. 118–121°, α_D +35° MeOH (*c* 3.32), λ^{Chf} 2.95, 6.12 μ.

Anal. Calcd. for $C_{28}H_{49}O_4N \cdot H_2O$ (481.70): C, 69.81; H, 10.67. Found: C, 69.90; H, 10.27.

N,N-Diethylcholylamine hydrochloride, obtained in 51% yield by reduction of the crude amide (m.p. 115–120°), melted at 247–248°, α_D +33° MeOH (*c* 2.92).

Anal. Calcd. for $C_{28}H_{52}O_3NCl$ (486.17): C, 69.17; H, 10.78. Found: C, 69.24; H, 10.98.

(5) St. v. Kostanecki and J. Tambor, *Ber.*, **39**, 4022 (1906).

(6) P. Mylius, *Ber.*, **20**, 1968 (1887).

3-Cathyl-N,N-diethylcholylamine hydrochloride melted at 214–216°, α_D +47.5° MeOH (*c* 2.44), λ^{Chf} 3.0, 4.2, 5.76 μ.

Anal. Calcd. for $C_{31}H_{56}O_5NCl$ (558.23): C, 66.69; H, 10.11. Found: C, 66.97; H, 10.37.

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2-Hydroxy-4-aminobenzenephosphonic Acid, an Analog of *p*-Aminosalicylic Acid

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A series of phosphonic and phosphinic acids prepared in this Laboratory have been tested for antibacterial action *in vitro*.[1] Although a number of them have been found to possess some activity, only phosphanilic acid approached in potency such known antibacterial agents as sulfathiazole. The synthesis of compounds related to phosphanilic acid would appear desirable. We are reporting here the preparation of 2-hydroxy-4-aminobenzenephosphonic acid. This compound was of special interest because of its similarity to *p*-aminosalicylic acid (PAS), a well-known antitubercular agent.

The synthesis was accomplished starting with 2-methoxy-4-nitrobenzenephosphonic acid[2] which was demethylated to 2-hydroxy-4-nitrobenzenephosphonic acid; the latter was then reduced to the desired amino compound. The demethylation was performed by refluxing the methoxy compound in 40% hydrobromic acid for 28 hours. A shorter reflux time gave some unchanged starting material, while in more concentrated hydrobromic acid (48%) phosphorus was cleaved from the ring. 2-Hydroxy-4-nitrobenzenephosphonic acid was isolated from the hydrobromic acid solution and purified by recrystallization. The yields were somewhat low due to the solubility of the impure compound in both aqueous and organic solvents.

When an attempt was made to reduce 2-hydroxy-4-nitrobenzenephosphonic acid with Raney nickel and hydrogen at *p*H 6, we found that phosphorus was again cleaved from the ring; both *m*-aminophenol and phosphoric acid (as magnesium ammonium phosphate) were recovered from the filtrate. In contrast 2-methoxy-4-nitrobenzenephosphonic acid was readily reduced to the corresponding amino compound by the use of Raney nickel.

The reduction of the hydroxy compound was accomplished by the use of Adams platinum oxide catalyst and 10% hydrochloric acid as the solvent. Because of the poor yields in the isolation of the 2-hydroxy-4-nitrobenzenephosphonic acid, an attempt was made to reduce the hemi-potassium salt.[3] This salt, which is an intermediate in the isolation procedure, is much less soluble than the free acid. Unfortunately sufficient potassium bromide was occluded when this salt was isolated to dissolve the platinum oxide in acid solution and prevent reduction.

(1) J. D. Thayer, H. J. Magnuson and M. S. Gravatt, *Antibiotics & Chemotherapy*, **3**, 256 (1953).

(2) L. D. Freedman, H. Tauber, G. O. Doak and H. J. Magnuson, THIS JOURNAL, **75**, 1379 (1953).

(3) G. O. Doak and L. D. Freedman, *ibid.*, **73**, 5658 (1951).

Experimental

Melting points were taken as previously described.[3]

2-Hydroxy-4-nitrobenzenephosphonic Acid.—2-Methoxy-4-nitrobenzenephosphonic acid (15 g.) was refluxed for 28 hours in 75 ml. of 40% hydrobromic acid. The solvent was concentrated *in vacuo* to a volume of 5 ml. and cooled. Aqueous potassium hydroxide (50%) was added until the solution reached approximately *p*H 2 and the mixture was again cooled. The hemi-potassium salt of 2-hydroxy-4-nitrobenzenephosphonic acid precipitated and was removed by filtration. This salt was dissolved in 10% hydrochloric acid and the solution evaporated to dryness. The phosphonic acid was extracted from the residue with ether, and the ether solution evaporated to dryness. The resulting acid was finally recrystallized from 6 *N* hydrochloric acid. The yield of pale yellow crystals was 4 g., 29%, m.p. 202–204°.

Anal. Calcd. for $C_6H_6NO_6P$: N, 6.39; P, 14.14. Found: N, 6.37; P, 13.96.

2-Hydroxy-4-aminobenzenephosphonic.—The preceding compound (3.7 g.) was dissolved in 50 ml. of 10% hydrochloric acid and reduced with platinum oxide and hydrogen at 40 lb. pressure in a low-pressure catalytic hydrogenation apparatus. When the reduction was complete, the catalyst was removed and the filtrate was adjusted to *p*H 3.8 with sodium acetate. The desired amino acid slowly crystallized from solution. The crystals were washed with cold water and dried *in vacuo*. The yield was 2.13 g., 67%, m.p. 210–212°.

Anal. Calcd. for $C_6H_8NO_4P$: N, 7.41; P, 16.38. Found: N, 7.34; P, 16.00.

2-Methoxy-4-aminobenzenephosphonic Acid.—2-Methoxy-4-nitrobenzenephosphonic acid was suspended in water and sufficient sodium hydroxide added to dissolve the acid (the *p*H of the solution was 8). The nitro group was reduced with Raney nickel and hydrogen at 40 lb. pressure. The catalyst was removed and the free acid precipitated by acidifying the filtrate to *p*H 2. The compound was recrystallized from 10% hydrochloric acid containing a trace of sulfur dioxide to prevent oxidation of the amino group. The yield was 86%, m.p. 212–214°.

Anal. Calcd. for $C_7H_{10}NO_4P$: N, 6.90; P, 15.25. Found: N, 6.69; P, 14.94.

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Reactions of Di-*t*-butoxydiaminosilane[1]

BY P. D. GEORGE, L. H. SOMMER AND F. C. WHITMORE[2]

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The reactions of di-*t*-butoxydiaminosilane with water, alcohols, amines and carboxylic acids have been described[3] and the preparation of di-*t*-butoxy-bis-aminoalkoxysilanes through interaction of the diaminosilane with aminoalcohols has been reported.[4] Some extensions of this work have also been presented.[5] We now wish to describe the reactions of di-*t*-butoxydiaminosilane with a number of other reagents. The reactions of di-*t*-butoxydiaminosilane with acidic materials ranged all the way from: (1) simple intercondensation of amine groups to form organic polysilazanes, through (2) conversion of the amine groups to chloro substituents, and finally to (3) complete degradation to form *t*-butyl chloride, ammonium chloride and silicic acid. Upon being heated to about 200° in the presence of a little ammonium sulfate the diaminosilane underwent condensation with liberation of ammonia and was converted in high yield to a white crystalline cyclopolysilazane[3a] which we identified as the trimer, hexa-*t*-butoxycyclotrisilazane.[5] The diaminosilane reacted readily with a limited amount of hydrogen chloride to form di-*t*-butoxydichlorosilane in good yield. On the other hand the cyclic trimer gave with hydrogen chloride only a small amount of the dichlorosilane together with *t*-butyl chloride arising through cleavage of *t*-alkoxy groups from silicon. With hydrochloric acid the diaminosilane underwent incomplete degradation with the formation of *t*-butyl chloride, ammonium chloride and silicic acid.

The reactions of di-*t*-butoxydiaminosilane with ethylene chlorohydrin and ethylene cyanohydrin proceeded normally with evolution of ammonia and formation of the corresponding mixed orthosilicates bearing functional substituents in the alkyl groups. The compounds so obtained were di-*t*-butoxy-bis-(2-chloroethoxy)-silane and di-*t*-butoxy-bis-(2-cyanoethoxy)-silane.

Substantially no interaction of the diaminosilane occurred at 100° with ethylene oxide, nitromethane or acrylonitrile.

The infrared spectra of $(t\text{-BuO})_2Si(NH_2)_2$, $[(t\text{-BuO})_2SiNH]_3$, $(t\text{-BuO})_2Si(OCH_2CH_2Cl)_2$ and $(t\text{-BuO})_2Si(OCH_2CH_2CN)_2$ were determined and were found to be consistent with the structures presented. Absorption bands are tabulated in the Experimental part.

Experimental[6]

Materials.—The di-*t*-butoxydiaminosilane was obtained from the Minnesota Mining and Manufacturing Company and was redistilled before use, b.p. 96–97 at 32 mm., $n^{20}D$ 1.4193, d^{20} 0.9311.

Anal. Calcd. for $C_8H_{22}O_2N_2Si$: neut. equiv., 103; MR_D 55.68. Found: neut. equiv., 105; MR_D, 55.94.

The other reagents were high quality materials of commerce which were used without further purification.

Acidic Condensation.—In a 100-ml., round-bottom flask fitted with a reflux condenser was placed 20.0 g., 0.097 mole, of di-*t*-butoxydiaminosilane and 0.2 g. of ammonium sulfate. The reaction mixture was heated at 230° for one-half hour and ammonia was steadily evolved. Upon cooling the crude product solidified and was purified by recrystallization from a small quantity of acetone. There was obtained 14.4 g., 0.025 mole, 78% yield of white crystalline material m.p. 189–190° which was identified as hexa-*t*-butoxycyclotrisilazane, $[(t\text{-}C_4H_9O)_2SiNH]_3$.[7]

Anal. Calcd. for $C_{24}H_{57}N_3O_6Si_3$: N, 7.40; neut. equiv., 189; mol. wt., 568. Found: N, 7.34, 7.15; neut. equiv.,[8]

(1) Paper 36 in a series on organosilicon compounds. For paper 35 see THIS JOURNAL, **75**, 6337 (1953).

(2) Deceased.

(3) (a) C. S. Miner, Jr., L. A. Bryan, R. P. Holysz, Jr., and G. W. Pedlow, Jr., *Ind. Eng. Chem.*, **39**, 1368 (1947); (b) G. W. Pedlow, Jr., and C. S. Miner, Jr., U. S. Patents 2,566,363; 2,566,364; 2,566,365; 2,566,956 and 2,566,957, September 4, 1951.

(4) P. D. George, L. H. Sommer and F. C. Whitmore, THIS JOURNAL, **71**, 3254 (1949).

(5) E. Larsson and B. Smith, *Svensk Kem. Tid.*, **62**, 141 (1950).

(6) Calculated molecular refractions were obtained by use of bond refractions given by K. G. Denbigh, *Trans. Faraday Soc.*, **36**, 936 (1940), and by E. L. Warrick, THIS JOURNAL, **68**, 2455 (1946); similar results may be obtained by use of the method of R. O. Sauer, *ibid.*, **68**, 954 (1946).

(7) This material was obtained previously in the same manner and was identified as $[(t\text{-}C_4H_9O)_2SiNH]_3$.[4a] The cyclic trimer has also been obtained from the reaction of gaseous ammonia with di-*t*-butoxydichlorosilane in boiling carbon tetrachloride solution.[6]

(8) This value was obtained by allowing a 0.5-g. sample to stand overnight with 50 ml. of 0.1 *N* hydrochloric acid and then back-titrating to a methyl red end-point.