TABLE I

$RSSCH_2CH_2NH_2 \cdot HCl$

R	M.p.; °C.	Yield, %	Recryst. solvent	Calcd., % C	H	N	S	Found, % C	H	N	S
n-Butyl	96–97	40.5	Ethanol	35.71	7.99	6.94	31.78	35.66	8.30	6.89	31.85
n-Hexyl	112–115	42.4	Carbon tetrachloride	41.80	8.77	6.10	27.90	41.68	9.01	5.57	27.84
n-Octyl	112–114	49.0	2-Propanol–acetonitrile	46.57	9.38	5.43	24.87	46.83	9.55	5.42	24.75
n-Decyl	111–112	68.4	Ethanol	50.90	9.87	4.90	22.43	50.52	9.81	5.41	22.43
Phenyl	137–138	63.2	Acetonitrile	43.32	5.46	6.32	28.92	42.84	5.47	6.44	29.26
Benzyl	150–151	50.9	2-Propanol	45.84	5.98	5.94	27.20	45.82	6.21	6.07	27.21

They found that in alkaline or strongly acidic solutions, at elevated temperatures especially, mixed disulfides disproportionate rapidly. Because of the possibility

$$2H_2NCH_2CH_2SSR \rightleftharpoons RSSR + H_2NCH_2CH_2SSCH_2CH_2NH_2$$

that the cystamine [bis(2-aminoethyl) disulfide] dihydrochloride isolated from each reaction mixture may have originated, not only by disproportionation of the mixed disulfide, but by the alkaline decomposition of 2-aminoethanethiosulfuric acid, the stability of the latter compound was determined under experimental conditions. The amino Bunte salt (1 equiv.) was stirred in a nitrogen atmosphere for 5 hr. with 1.75 equiv. of sodium hydroxide in methanol at 0°. Only a trace of sodium sulfite (<0.1% of theory) was formed indicating slight amino Bunte salt decomposition. The quantity was insufficient, however, to account for the amount of cystamine obtained in the mixed disulfide syntheses.

The extensive disproportionation of the unsymmetrical disulfides in the strongly alkaline reaction mixture necessitated rapid isolation at a low temperature. Recrystallization of the hydrochloride salts from water also induced disproportionation but the use of organic solvents seemed to avoid this difficulty.

The reaction of the selenium Bunte salt, 2-aminoethaneselenosulfuric acid, with a mercaptide under the conditions described here for the formation of unsymmetrical disulfides resulted in the synthesis of the selenosulfide. These results will be described in a separate communication.

Experimental[6]

2-Aminoethyl Alkyl (or Aryl) Disulfide Hydrochlorides.—To a solution of 3.0 g. (0.075 mole) of sodium hydroxide in 60 ml. of methanol, through which nitrogen was bubbled, was added 7.08 g. (0.045 mole) of 2-aminoethanethiosulfuric acid.[7] When solution was complete, the flask was immersed in an ice–water bath and the temperature was lowered to *ca.* 0°. The mercaptan (0.03 mole), previously distilled under nitrogen, was added to the solution, causing a slightly exothermic reaction and an almost immediate precipitation of sodium sulfite. After the addition of the mercaptan, aliquots of the mixture were centrifuged and the supernatant liquid was tested for the presence of unreacted mercaptan with sodium nitroprusside. When the test became weakly positive or negative, the time varying from 2 to 5 min. after the addition of the mercaptan, the reaction mixture was suction filtered through Whatman No. 50 filter paper. The cloudy filtrate, kept at 0–10°, was neutralized with ethanolic hydrogen chloride. The solid which formed, most of which was cystamine dihydrochloride, m.p. 210–215° dec., was removed by filtration and the filtrate was evaporated to dryness under reduced pressure at 50° using a rotary evaporator. The white, waxy residue was recrystallized several times to obtain an analytical sample.

Acknowledgment.—We wish to thank Dr. David P. Jacobus for helpful discussions concerning this work.

(6) Microanalyses were performed by Mr. Joseph Alicino, Metuchen, N. J. Melting points were determined on a Fisher-Johns melting point apparatus and are uncorrected.

(7) H. Bretschneider, *Monatsh.*, **81**, 372 (1950).

Preparation of N-Perchlorylpiperidine

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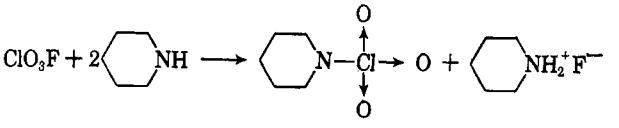
Perchloryl fluoride reacts with aqueous or anhydrous ammonia to produce a mixture of NH_4F and NH_4NHClO_3[1,2] from which salts of the unstable dibasic acid NH_2ClO_3 may be prepared by precipitation reactions in aqueous solution.

At the time of this work perchloryl fluoride was not known to form derivatives with amines other than ammonia. In general, perchloryl fluoride either reacts explosively with pure amines or produces complex mixtures of oxidation products. Reactions in aqueous or alcoholic solution are moderated but are characterized also by complex oxidation products of the organic base.[3]

In view of the above it was surprising to discover that aqueous piperidine will react with a fast flow of ClO_3F gas to form a light oily layer, identified as N-perchlorylpiperidine, on the surface of the aqueous solution. Piperidinium fluoride was found as a second product.

N-perchlorylpiperidine is the first known member of a new class of organic compounds and is the first liquid covalent perchlorylamide prepared to date.



Experimental

A rapidly stirred solution of 8.0 g. (0.094 mole) of piperidine in 250 ml. of water was treated with a fast flow of perchloryl fluoride gas (170 cc./min.) introduced through a fritted-glass dispersion tube below the surface of the solution. The aqueous solution clouded immediately and remained so during the 20-min. reaction time. The perchloryl fluoride flow was stopped, and the solution was purged with nitrogen for 10 min. The aqueous solution was extracted with ether and the ether extract was washed with three 50-ml. portions of 10% HCl. The ethereal solution was dried over magnesium sulfate and evaporated at room temperature under reduced pressure to give 5.2 g. (0.031 mole) of N-perchlorylpiperidine (66% yield based on the above equation).

N-perchlorylpiperidine is a *dangerously sensitive* material. It explodes on heating and on contact with anhydrous piperidine. A sample of the oil exploded with violence on storage in an outside bunker as a possible result of exposure to the heat of the sun or

(1) A. Engelbrecht and H. Atzwanger, *J. Inorg. Nucl. Chem.*, **2**, 348 (1956).

(2) H. C. Mandell and G. Barth-Wehrenalp, *ibid.*, **12**, 90 (1959).

(3) Unpublished observations at this laboratory.

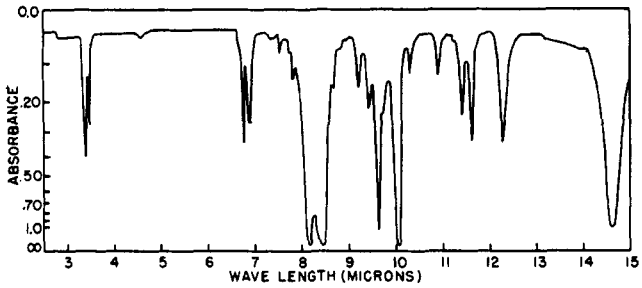


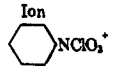
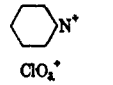
Fig. 1.—Infrared spectrum of liquid N-perchlorylpiperidine.

autocatalytic decomposition. Attempts to burn the pure compound during elemental analysis resulted in violent explosions and could only be carried out by first absorbing the compound on powdered alumina to desensitize it. Although the N-perchlorylpiperidine decomposes slowly at 25°, it may be stored indefinitely at −80°. The index of refraction ($n^{20}D$) of a freshly prepared sample is 1.4646.

Anal. Calcd. for $C_5H_{10}ClNO_3$: C, 35.8; H, 6.1; Cl, 21.2; N, 8.4; mol. wt., 167.6. Found: C, 37.4, 37.6; H, 8.8. 6.6; Cl, 21.2, 18.7; N, 9.1, 7.9; mol. wt., 169 (differential vapor pressure).

The above elemental analyses are only fair owing to instability of the compound; however, they do support the empirical formula. More positive evidence for the structure is provided by the mass cracking pattern of a freshly prepared sample (Table I). A

TABLE I

m/e	Ion	Relative intensity
167, 169		5.4/2.1
84		53.8
83, 85	ClO_4^+	11.1/4.4

complex pattern below m/e = 84 is similar to that observed for piperidine (API 618) and a relative intensity of 100 was assigned to mass peak 42.

The $-ClO_3$ group is bonded to the nitrogen as indicated by the infrared absorption spectrum and the absence of any N–H bond absorption at 2.7–3.0 μ. The major absorption peaks for the $-ClO_3$ group are found at 8.15, 8.42, and 14.63 μ. (See Fig. 1.)

The maximum yield to date of N-perchlorylpiperidine is 66% due to rapid hydrolysis of this compound by the basic solution in which it is formed. The hydrolysis products are being characterized now and will be reported on in a later publication.

Acknowledgment.—This work was supported by the U. S. Army Chemical Corps., Edgewood Arsenal. The authors are indebted to Miss Ruth Kossatz and Drs. H. Francis and J. Smith of these laboratories for their help in analyses, and to Dr. D. Rosenblatt of Edgewood Arsenal for his encouragement and helpful discussions during the course of the work.

Chloroethynyl Steroids. IV. The Synthesis of 16α-Fluoro-17α-chloroethynyl-4-androsten-17β-ol-3-one

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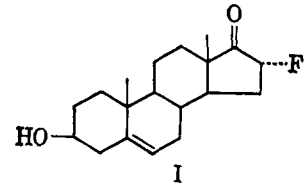
A possible rationale for the increased potency of the chloroethynylestrenones,[1] compared with the corresponding ethynylestrenones as inhibitors of pituitary gonadotrophin, is the acidification of the C-17β-ol owing to the inductive effect of the chlorine atom. It seemed possible that the substitution of additional electron-withdrawing groups around the C-17β-ol might lead to further increments in potency. In view of the ready availability of 16α-fluoro-5-androsten-3β-ol-17-one[2] (I) the synthesis of 16α-fluoro-17α-chloroethynyl-4-androsten-17β-ol-3-one (IV) appeared to provide an attractive test of this hypothesis.

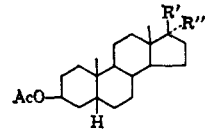
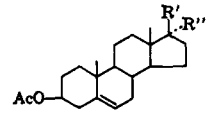
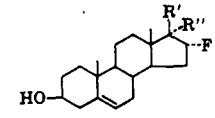
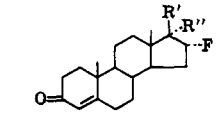


I

Chloroethynylation[3] of I afforded an approximately 2:3 mixture of II and III, which could be separated by crystallization. Jones[4] oxidation followed by acid-catalyzed isomerization of the Δ⁵-bond afforded the C-17 epimers, IV and V, of 16α-fluoro-17-chloroethynyl-4-androsten-17-ol-3-one.

The stereochemical assignments were made on the basis of rotation and the n.m.r. and infrared spectra of IV and V. Rotations[5] are summarized in Table I.

TABLE I

Compd.	[M]D R′ = OH; R″ = C≡CX	[M]D R′ = C≡CX; R″ = OH	Δ[M]D
	X = H −153°	X = H +97°	+250°
	X = H −357°	X = H −94°	+263°
	II, X = Cl −534°	III, X = Cl −136°	+398°
	IV, X = Cl + 17°	V, X = Cl +496°	+479°

The rotational evidence is satisfactory as far as the stereochemistry at C-17 is concerned, but does not exclude the possibility of epimerization of the C-16 fluorine during the chloroethynylation step. The later possibility appear rather remote since the mechanism of the epimerization would require formation of a Δ¹⁶-enolate which would resist chloroethynylation under the conditions of the reaction. Furthermore, long-range, spin–spin coupling between the protons at C-18 and fluorine at C-16β has been observed by Cross and Lan-

(1) J. H. Fried, T. S. Bry, A. E. Oberster, R. E. Beyler, T. B. Windholz, J. Hannah, L. H. Sarett, and S. L. Steelman, *J. Am. Chem. Soc.*, **83**, 4663 (1961).

(2) S. Nakanishi and E. Jensen, *J. Org. Chem.*, **27**, 702 (1962).

(3) H. G. Viehe, *Chem. Ber.*, **92**, 1950 (1959).

(4) C. Djerassi, R. R. Engle, and A. Bowers, *J. Org. Chem.*, **12**, 1547 (1956).

(5) T. Reichstein and C. Meystre, *Helv. Chim. Acta*, **22**, 728 (1939).