20-dione in 15 ml. of methanol. Almost immediately, crystals began to form. After allowing the mixture to stand overnight, the precipitate was collected with suction; yield 0.8 g., m.p. 230–232°. The analytical sample, crystallized once more from aqueous methanol, melted at 231.4–232.6°, $[\alpha]_D$ +31.2° (acetone), reported[4a] m.p. 236–238°.

Anal. Calcd. for $C_{21}H_{34}O_3$: C, 75.40; H, 10.25. Found: C, 75.32; H, 10.15.

This compound was not identical with that obtained by refluxing I (R = H) with sodium borohydride overnight, for the infrared spectrum disclosed that a carbonyl group in a six-membered ring was still present in the former.

The 3,20-diacetate melted at 156.2–157.0°, $[\alpha]_D$ +69.3° (acetone).

There was no hydroxyl peak present in the infrared spectrum and no m.p. depression was obtained on admixture with an authentic sample[8]; reported[4a] m.p. 160.5–161.0°.

Anal. Calcd. for $C_{25}H_{38}O_5$: C, 71.74; H, 9.15. Found: C, 72.05; H, 9.37.

Pregnan-3α,17α,20β-triol-11-one (II, R = OH).—When pregnan-3α,17α-diol-11,20-dione (I, R = OH) was allowed to react at room temperature overnight with sodium borohydride in aqueous methanol, no crystals formed and only pregnan-3α,11β,17α,20β-tetrol was isolated in good yield. If the reaction was halted at the end of three hours by the addition of water and extraction with chloroform, it was possible to obtain a 55% yield of pregnan-3α,17α,20β-triol-11-one, m.p. 218–220°, after recrystallization of the chloroform residue from aqueous methanol. The analytical sample, crystallized once more, had a m.p. of 219.0–220.6°, $[\alpha]_D$ +36.0 (acetone), reported[4b] m.p. 220°, $[\alpha]_D$ +38°.

Anal. Calcd. for $C_{21}H_{34}O_4$: C, 71.95; H, 9.79. Found: C, 72.07; H, 10.01.

The infrared spectrum indicated the presence of a carbonyl group in a six-membered ring.

The 3,20-diacetate had a m.p. of 245.0–246.2°, $[\alpha]_D$ +72.7° (acetone) and did not depress the m.p. of an authentic sample[8]; reported[4b] m.p. 249–250°.

Anal. Calcd. for $C_{25}H_{38}O_6$: C, 69.09; H, 8.81. Found: C, 68.98; H, 8.99.

Oxidation of Pregnan-3α,11β,20β-triol 3,20-Diacetate (V, R = H).—To a solution of 1.0 g. of V (R = H) in 10 ml. of acetone was added a solution of 635 mg. of N-bromoacetamide in 2 ml. of water and the mixture was placed in a refrigerator at 5° for 1 hour. The excess oxidizing agent was destroyed by the addition of 1 g. of sodium sulfite in 5 ml. of water; then excess water was added to precipitate the product completely; yield 0.95 g. of III (R = H), m.p. 159–160°. One crystallization from methanol raised the m.p. to 160.4–161.0°, $[\alpha]_D$ +69.3° (acetone).

This product gave no m.p. depression on admixture with pregnan-3α,20β-diol-11-one 3,20-diacetate obtained above, and the infrared spectra were identical.

Anal. Calcd. for $C_{25}H_{38}O_5$: C, 71.74; H, 9.15. Found: C, 71.43; H, 9.44.

Oxidation of Pregnan-3α,11β,17α,20β-tetrol 3,20-Diacetate (V, R = OH).—In an analogous fashion, 1.0 g. of V (R = OH) was oxidized to the corresponding 11-ketone III (R = OH) with N-bromoacetamide; yield 0.89 g., m.p. 235–238°. One crystallization from methanol raised the m.p. to 245.2–246.2°, $[\alpha]_D$ +72.1° (acetone).

This product gave no m.p. depression on admixture with pregnan-3α,17α,20β-triol-11-one 3,20-diacetate obtained above, and the infrared spectra were identical.

Anal. Calcd. for $C_{25}H_{38}O_6$: C, 69.09; H, 8.81. Found: C, 68.84; H, 9.00.

(8) Kindly supplied by Dr. L. H. Sarett.

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Complexes of Boron Trifluoride with Amides

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Systems of boron trifluoride with formamide, acetamide and dimethylformamide have been investigated. Each of the amides was found to add one mole of boron trifluoride; however, only the complex with dimethylformamide was sufficiently stable and non-reactive to allow purification. The lower reactivity and higher thermal stability of this particular complex is attributed to the greater basic strength of the nitrogen and to the absence of a hydrogen atom on the nitrogen.

Experimental

Reagents.—Matheson tank boron trifluoride was subjected to a series of bulb-to-bulb vacuum distillations and was found to be spectroscopically free of silicon tetrafluoride.

Du Pont "stabilized" tetrahydrofuran was refluxed over sodium hydroxide for 24 hours and distilled. The distillate was refluxed over lithium aluminum hydride for seven hours and was again distilled. $BF_3O(CH_2)_4$ was prepared by passing boron trifluoride into tetrahydrofuran at 0° until there was no further take-up of the gas. The crude etherate was distilled collecting the fraction boiling at 58° and 1.2 mm.

Paragon "99%" formamide was triply distilled at 4 mm. pressure. The distillate however retained a slight odor of hydrogen cyanide. Eastman Kodak actamide was distilled and the fraction boiling at 221–223° and atmospheric pressure was recrystallized from chloroform. The water in du Pont "Technical" dimethylformamide was removed by azeotropic distillation with benzene and then the amide was distilled. The fraction boiling at 152° and atmospheric pressure was collected.

Dimethylformamide–Boron Trifluoride.—Nine-hundredths of a mole of dimethylformamide was dissolved in 20 g. of tetrahydrofuran, and this was slowly added to a stirred solution of 0.1 mole of boron trifluoride–tetrahydrofuran etherate in 10 g. of tetrahydrofuran at 0°. After the addition was complete, most of the solvent was removed at reduced pressure. The solid material then was recrystallized from tetrahydrofuran. Fluorine was determined by the lead chlorofluoride method after the complex had been decomposed by base.[2]

Anal. Calcd. for $C_3H_7ONBF_3$: C, 25.57; H, 5.01; F, 40.45. Found: C, 25.54; H, 5.29; F, 39.81, 39.46, 39.98.

Dimethylformamide boron trifluoride melts at 58–59° (uncor.) and distils at 100° and 0.1 mm. Samples purified by vacuum distillation had sharper melting points than those purified by recrystallization from tetrahydrofuran or ethanol. The carbonyl band of the amide at 5.9 μ was not shifted in the infrared spectrum of the complex. The complex was immediately decomposed by water. The specific conductance of a 0.01 *M* solution, 30 millimhos, did not change significantly with time. Moreover, addition of nitron acetate to a fresh solution gave an immediate and large precipitation of nitron fluoborate. In contrast to its reactivity toward water, the complex was quite stable toward boiling ethanol. A half-gram sample of the compound was dissolved in 75 cc. of ethanol and the solution was refluxed for three days, after which time the complex was almost completely recovered. The stability of this complex of a tertiary amine toward heat and alcohols could well be due to the absence of a hydrogen atom on the nitrogen atom, disallowing dehydrohalogenation.

Formamide and Acetamide Complexes.—Attempted preparations of the addition compounds of formamide and acetamide with boron trifluoride in solution failed to produce crystalline material; only oils were obtained. To establish the stoichiometry of the reactions, boron trifluoride was added to a weighed sample of the amide in a vacuum system. When no further decrease in the pressure of the system took place, the reaction tube was evacuated and weighed.

	Formamide		Acetamide	
Amide, mmoles	6.68	3.62	6.84	6.89
BF_3, mmoles	6.80	3.57	6.72	6.92
Mole fr. BF_3/amide	1.018	0.986	0.985	1.001

The results clearly indicate the existence of one-to-one

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(2) J. I. Hoffman and G. E. F. Lundell, *Bur. Stand. J. Res.*, **3**, 581 (1929).

complexes of the amides with boron trifluoride. This is in agreement with the work of Bowlus and Nieuwland on acetamide.[3]

No method was devised for the purification of the complexes. The reaction products were very hygroscopic and were immediately decomposed by water. Tetrahydrofuran and ethanol reacted rapidly with the complexes, yielding precipitates of ammonium fluoborate.

The compounds did not possess sufficient thermal stability to allow high vacuum distillation or sublimation. The complex with formamide decomposed on warming in vacuum, with evolution of carbon monoxide and hydrogen cyanide, which gases were identified by their infrared spectra. Ammonium fluoborate was one of the solid reaction products, but since the solid reaction product was very soluble in water no boron nitride was considered to be formed.

Anal. Calcd. for NH_4BF_4: HBF_4, 83.44. Found: HBF_4, 83.89.

The complex of acetamide with boron trifluoride began to decompose in vacuum at about 90°, with liberation of a small amount of acetic acid. At 130–140° and 0.1 mm. a yellow viscous oil distilled over. Efforts to purify and characterize this oil were not successful. The boron present in the oil was in the form of a fluoborate salt.

(3) H. Bowlus and J. A. Nieuwland, THIS JOURNAL, **53**, 3835 (1931).

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Some Amides of Piperazines

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Since 1,4-bis-(benzenesulfonyl)-piperazine[1] exhibited marked activity in inhibiting growth of tubercle bacillus in serum, twelve new amides of piperazines were synthesized for testing against this organism. These compounds were prepared by modifications of the method of Pollard and Adelson.[2] Anhydrous piperazines were used; anhydrous sodium carbonate was added; and propanol-2 or benzene was employed as a reaction solvent instead of ether. Data concerning these compounds are given in Table I.

TABLE I

DATA CONCERNING SOME AMIDES OF PIPERAZINES

Compound, piperazine	Crystallized from	Yield, % purified product	M.p., °C. (cor.)	Nitrogen, % Calcd.	Found
1-(*p*-Chlorobenzoyl)-4-phenyl	Methanol	29.2	119–121	9.32	9.24
1-(*o*-Chlorobenzoyl)-4-phenyl	Methanol	22.5	109–111	9.32	9.17
1-(*m*-Nitrobenzenesulfonyl)-4-phenyl	Formamide	43.2	153–154	12.10	12.29
1-(*p*-Bromobenzenesulfonyl)-4-phenyl	Methanol	38.6	180–182	7.35	7.35
1,4-Bis-(*p*-chlorobenzoyl)	Propanol-2	36.0	238.8–239.8	7.71	7.75
1,4-Bis-(*p*-toluenesulfonyl)	Boiling dioxane	42.0	295.3–296.3	7.11	7.09
1,4-Bis-(*o*-chlorobenzoyl)	Methanol	22.9	214–215.5	7.71	7.71
1,4-Bis-(*m*-nitrobenzenesulfonyl)	Formamide	34.4	262–264	12.28	12.14
1,4-Bis-(*p*-chlorobenzoyl)-2,5-dimethyl	Chlorobenzene	38.2	288–289	7.16	6.93
1,4-Bis-(*o*-chlorobenzoyl)-2,5-dimethyl	Formamide	48.2	296–298	7.16	7.15
1,4-Bis-(*m*-nitrobenzenesulfonyl)-2,5-dimethyl	Formamide	48.5	249–250	11.57	11.25
1,4-Bis-(*p*-bromobenzenesulfonyl)-2,5-dimethyl	Formamide	51.5	262–263	5.07	5.21

These new amides were ineffective against tubercle bacillus.

The authors express their sincere appreciation for the *in vitro* tuberculostatic testing of these compounds. The tests were performed in the laboratory of Dr. Guy P. Youmans, Department of Bacteriology, Northwestern University Medical School, and made available by arrangement with Parke, Davis and Company.

(1) M. E. Smith and C. B. Pollard, THIS JOURNAL, **63**, 630 (1941).
(2) C. B. Pollard and D. E. Adelson, *ibid.*, **56**, 150 (1934).

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Homologs of Some Steroid Hormones

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In connection with other work in progress in these laboratories, some homologs of testosterone and one homolog of ethinyltestosterone were prepared. These new steroids in which the hydroxyl is at C_{25} instead of C_{17} possess no androgenic activity. These compounds were synthesized from 25-ketonorcholesteryl acetate (I), a by-product of the oxidation of cholesteryl acetate dibromide.[1]

25-Hydroxy-Δ^4-norcholestene-3-one (IX) was obtained using a procedure similar to that described for the synthesis of testosterone.[2] 25-Ketonorcholesteryl acetate (I) was reduced to the diol monoacetate (II); this was then benzoylated and the resulting 3-acetate-25-benzoate partially hydrolyzed to give 25-benzoxynorcholesterol (V). Oxidation by a modification of the method of Oppenauer[3] followed by hydrolysis produced the ketone (IX).

25-Ethinyl-Δ^4-norcholestene-25-ol-3-one (X) was prepared by the ethynation of I with potassium acetylide to give the 25-ethinyl derivative (VI) followed by Oppenauer oxidation. The reaction of ethylmagnesium iodide with I yielded 26-methyl-25-hydroxycholesterol (VII). Both VII and 25-hydroxycholesterol[4] were oxidized to XI and XII, respectively. A derivative of IX, 25-chloro-Δ^4-norcholestene-3-one (XV), was also prepared in which the hydroxyl at C_{25} was replaced with chlorine.

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(2) L. Ruzicka, A. Wettstein and H. Kägi, *ibid.*, **18**, 1478 (1935).
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