The preparation of a number of analogous addition compounds was attempted with several amines and hydroxy compounds. Usually a solid formed on mixing equimolecular amounts of the materials at room temperature, but sometimes chilling was required. Recrystallization was effected by cooling a solution of the addition compound in ether or petroleum ether.

A typical example of the preparation of these compounds is as follows. A solution of 10 g. of dicyclohexylamine in 10 ml. of petroleum ether was mixed with 5 g. of cyclohexanol in 10 ml. of petroleum ether. The clear solution was strongly chilled to deposit crystals which were filtered out, washed with petroleum ether and dried in air; m. p. 47–48°. *Anal.* Calcd. for $(C_6H_{11})_2NH \cdot C_6H_{11}OH$: N, 4.99. Found: N, 4.87.

The table gives data on a number of these materials. Several recrystallized products melted below room temperature, but the existence of a compound is shown by the analysis of the melt.

The only known reference[1] on this subject is an article by Fougue, who described the formation of a hydrate (m. p. 23°) and an alcoholate (m. p. 28°) of dicyclohexylamine, but who did not discover the apparent generality of this behavior. It is, furthermore, quite surprising that these materials were not found earlier in view of the large amount of work done on reactions of cyclohexanol with ammonia and of cyclohexanone and hydrogen with ammonia, where conditions for isolation of an addition compound must have been at least as favorable as in this case.

(1) Fougue, *Compt. rend.*, **166**, 394 (1918).

TABLE I

AMINE–ALCOHOL ADDITION COMPOUNDS

Amine	Alcohol	M. p., °C.	Nitrogen, % Calcd.	Found
Dicyclohexyl-	Cyclohexanol	47–48	4.99	4.87
Dicyclohexyl-	2-Me-cyclohexanol	59–60	4.74	4.65
Dicyclohexyl-	1,2-Cyclohexanediol	64–66	4.72	4.72
Dicyclohexyl-	1,3-Cyclohexanediol	64–66	4.72	4.72
Dicyclohexyl-	1,4-Cyclohexanediol	90–91	4.72	4.59
Dicyclohexyl-	*o*-Cyclohexylcyclohexanol	43–45	3.86	3.61
Dicyclohexyl-	*p-t*-Butylcyclohexanol	75–76	4.15	4.12
Dicyclohexyl-	β-Phenethyl alcohol	Below	4.62	4.27
Dicyclohexyl-	1,3-Butanediol	room	5.16	5.10
Dicyclohexyl-	Benzyl alcohol	temp.	4.84	4.72
Dibenzyl-	Cyclohexanol	Below	4.72	4.63
Piperidine	1,3-Cyclohexanediol	room	6.96	6.78
Cyclohexyl-	Cyclohexanol	temp.	7.04	6.84

RESEARCH LABORATORIES
THE GOODYEAR TIRE & RUBBER COMPANY
AKRON, OHIO

RECEIVED OCTOBER 30, 1939

COMMUNICATIONS TO THE EDITOR

STEROLS. LXXXI. CONVERSION OF SARSASAPOGENIN TO PREGNANEDIOL-3(α),20(α)

Sir:

In studying the reaction of sarsasapogenin with acetic anhydride at 200° we have obtained a product in good yield (after alkaline hydrolysis) of the composition $C_{27}H_{44}O_3$, m. p. 171–173°, which we are tentatively designating as pseudosarsasapogenin. *Anal.* Calcd. for $C_{27}H_{44}O_3$: C, 77.8; H, 10.6. Found: C, 77.8; H, 10.6. Pseudosarsasapogenin upon mild oxidation with chromic anhydride in acetic acid gives a good yield of an unsaturated diketone, m. p. 201–203°. *Anal.* Calcd. for $C_{21}H_{30}O_2$: C, 80.2; H, 9.6. Found: C, 80.1; H, 9.6. This diketone upon reduction with sodium and ethanol gave a product, m. p. 236–239°, which gave no depression with an authentic sample of pregnanediol-3(α),20(α), m. p. 237–239°. *Anal.* Calcd. for $C_{21}H_{36}O_2$: C, 78.8; H, 11.3. Found: C, 78.7; H, 11.3. Acetylation of this reduction product with hot acetic anhydride gave an acetate of m. p. 177–179° which gave no depression with an authentic sample of the diacetate of pregnanediol-3(α),20(α) m. p. 177–179°. *Anal.* Calcd. for $C_{25}H_{40}O_4$: C, 74.2; H, 10.0. Found: C, 74.2; H, 10.0.

The ready availability of sarsasapogenin makes it now one of the most suitable sources of hormones such as progesterone, testosterone and desoxycorticosterone. The details of the work concerning the preparation and reactions of pseudosarsasapogenin, and its conversion to the above hormones will be published in a forthcoming issue of THIS JOURNAL.

We wish to thank Parke, Davis and Company for their generous help and assistance in the various phases of this work.

SCHOOL OF CHEMISTRY AND PHYSICS
THE PENNSYLVANIA STATE COLLEGE
STATE COLLEGE, PENNA. RUSSELL E. MARKER
EWALD ROHRMANN

RECEIVED NOVEMBER 21, 1939

2-(*p*-AMINOBENZENESULFONAMIDO)-THIAZOLE: A NEW CHEMOTHERAPEUTIC AGENT

Sir:

Fosbinder and Walter [THIS JOURNAL, **61**, 2032 (1939)] reported the preparation of 2-(*p*-aminobenzenesulfonamido)-thiazole and stated that it had good activity in experimental streptococcic and pneumococcic infections in mice. Our own studies had already reached the point where promising pharmacologic and chemotherapeutic results (van Dyke, Rake, Greep, McKee, in press) warranted therapeutic trial of this drug and we assembled the following descriptive data for that purpose.

The 2-(*p*-aminobenzenesulfonamido)-thiazole prepared by us had the m. p. 197–197.5° (uncor.), 202.0–202.5° (cor.).

Its solubility in alcohol at 26° was 525 mg. per 100 cc. In water at 26° the solubility was about 60 mg. per 100 cc., giving *p*H 6.03, which is almost twice the solubility of sulfapyridine.

Our 2-(*p*-acetaminobenzenesulfonamido)-thiazole had m. p. 256–257° as reported by Fosbinder and Walter. **2-(*p*-Aminobenzenesulfonamido)-thiazole sodium salt** was prepared by a method essentially that described by Marshall [*Science*, **88**, 597 (1938)] for the sodium salt of sulfapyridine, m. p. 256.0–256.5° (uncor.) or 264.5–265.0° (cor.). *Anal.* Calcd. for $C_9H_8N_3O_2S_2Na$: Na, 8.30. Found: Na, 8.33. It was readily soluble in cold water. A 2% solution had a *p*H of 9.57.

2-(*p*-Aminobenzenesulfonamido)-thiazole hydrochloride was prepared by adding alcoholic hydrogen chloride to an alcoholic solution of the free base and adding ether; m. p. 193–197° (uncor.); solubility in water less than 2% with *p*H 1.28; loses hydrogen chloride on standing.

The potentiometric titration curves for the acidification of 2% solution of the sodium salts of 2(*p*-aminobenzenesulfonamido)-thiazole (Sulfathiazole), and sulfapyridine are submitted in Fig. 1. It will be seen that "Sulfathiazole" is more strongly acidic than sulfapyridine.

In addition to the 2-(*p*-aminobenzenesulfonamido)-4-methylthiazole of m. p. 237–238°, we prepared the next higher homolog, 2-(*p*-aminobenzenesulfonamido)-4-ethylthiazole, and found its melting point surprisingly lower, 149.5–150.5°.

Marshall's colorimetric method [*Science*, **88**, 85 (1938)] for the estimation of sulfapyridine has been found applicable to "Sulfathiazole." By this method, however, one cannot distinguish between sulfapyridine and "Sulfathiazole."

A good test has been found which distinguishes clearly between the two drugs. Thus, when a solution of the sodium salt of "Sulfathiazole" is treated with cupric sulfate solution, a characteristic purple precipitate is formed. With sulfapyridine an apple green precipitate is formed which gradually changes to greenish brown. This test has been used successfully on a few mg. of material. The precipitates have been characterized as follows: sulfapyridine, brown; calcd. for $(C_{11}H_{10}N_3O_2S)_2Cu$: Cu, 11.36. Found: Cu, 11.12. "Sulfathiazole," purple; calcd. for $(C_9H_8N_3O_2S_2)_2Cu$: Cu, 11.12. Found: Cu, 11.09.

Since these precipitates can be ashed and esti-

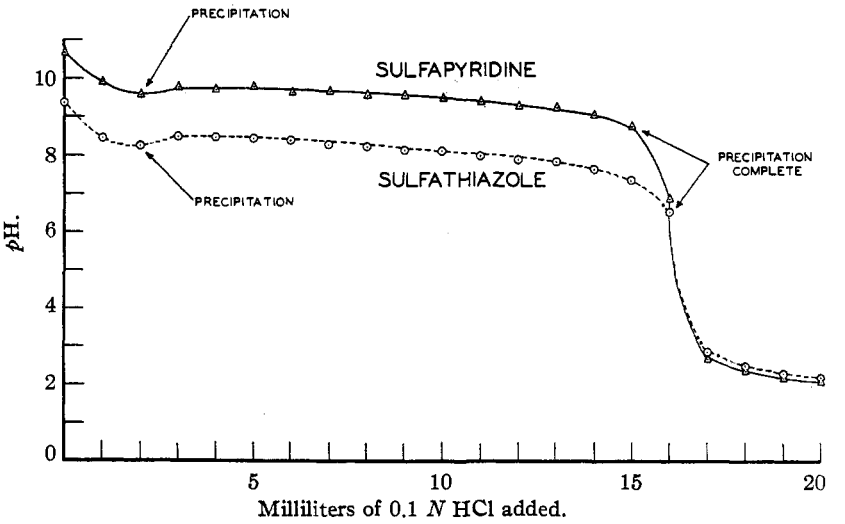

Fig. 1.—Potentiometric titrations of solutions of the sodium salts of sulfapyridine and sulfathiazole: 2% solution of sulfapyridine sodium salt, △; 2% solution of sulfathiazole sodium salt, ⊙.