with cold water gave a solid residue. The crude mixture was recrystallized from methanol, and yielded a pure sample, m.p. 112–113°. The I.R. gave a sharp peak at 5.70 μ indicative of ester. Yield was 38% of theory.

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New Compounds: Synthesis of Some Phosphorus–Nitrogen Compounds for Pharmacological Study I

By A. ABOU-MOUSTAFA, M. KHALIFA, and H. EL MANGOWRI

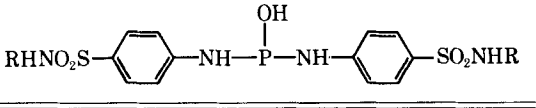
The synthesis of some phosphorus–nitrogen compounds *via* the condensation of phosphorus trichloride with a number of sulfa drugs is described. With sulfacetamide, sulfathiazole, and sulfadimidine three molecules of the sulfa compound condensed with one molecule of the acid (sulfamethazine) chloride although the molecular ratio of the reactants was 2 of the former to 1 of the latter. On the other hand, with sulfanilamide and sulfapyridine the condensation took place according to the ratio mentioned earlier.

THE INTEREST in the synthesis of phosphorus–nitrogen compounds arises from the fact that some of these compounds are of potential medicinal value. Cates *et al.* in a series of publications (1–5) reported the synthesis of nearly 60 such compounds and those containing substituted *p*-toluidine and 2-aminopyridine moieties were prepared for evaluation as antineoplastic agents. Likewise, it has been reported that the *N*-arylsulfonylphosphinimide derivatives synthesized by Oyamada have tumor inhibiting activity against mammary carcinoma (6).

The present investigation, however, is concerned with the synthesis of some phosphorus compounds *via* the condensation of phosphorus trichloride with a number of sulfonamides since these latter drugs are of considerable therapeutic value.[1]

Several attempts were made to condense sulfanilamide with phosphorus trichloride. Condensation in reagent dioxane according to the method of Cates (1, 4) proved to be unsatisfactory due to the immediate formation of an insoluble addition complex which did not dissolve even when the reflux was continued for several hours. The addition product afforded the starting sulfa compound after being worked up. The use of other nonpolar solvents such as carbon tetrachloride (6–8), absolute ether (2–4, 9), and dry benzene (2, 9) which were used by other investigators proved unsuitable because sulfanilamide itself is insoluble in these solvents and it was recovered unchanged from the reaction mixture. Accordingly, attention was directed to the use of polar solvents. Audrieth and

TABLE I—*N*-SUBSTITUTED DERIVATIVES OF PHOSPHORODIAMIDOUS ACID



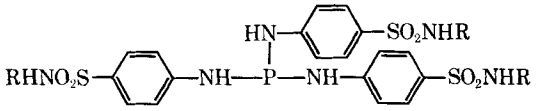
R	Solvent of Crystallization[a]	M.p.,[b] °C.	Formula	Anal.,[c] % N Calcd.	N Found	S Calcd.	S Found	P Calcd.	P Found
H	A	178–180 230 dec.	$C_{12}H_{15}N_4O_5PS_2$	14.35	13.90	16.42	16.50	7.93	7.94
2-Pyridyl	B	195–200 250 dec.	$C_{22}H_{21}N_6O_5PS_2$	15.44	15.07	11.78	11.35	...	...

[a] A, aqueous alcohol; B, absolute alcohol. [b] Liquid crystal. Melting points were performed by the capillary tube method and are uncorrected. [c] Analyses performed by Janssen Pharmaceutica, Beerse, Belgium.

Received February 27, 1967, from the Pharmaceutical Chemistry Department, Faculty of Pharmacy, Riyadh University, Riyadh, Saudi Arabia.
Accepted for publication May 10, 1967.
The authors express their appreciation to Dr. A. A. Khowaiter, Riyadh University, for research facilities which made this investigation possible and to Professor Y. M. Abou-Zeid, Cairo University, for his interest.

[1] The products at present are under preliminary screening for possible antineoplastic action or any useful pharmacological activity.

TABLE II—*N*-SUBSTITUTED DERIVATIVES OF PHOSPHORUS TRIAMIDE



R	Solvent of Crystallization[a]	M.p., °C.	Formula	Anal.,[c] % N Calcd.	N Found	S Calcd.	S Found	P Calcd.	P Found
Acetyl	C	278–280 dec.	$C_{24}H_{27}N_6O_9PS_3$	12.53	11.97	14.34	14.35	...	...
2-Thiazolyl	B	208–210[b] 260 dec.	$C_{27}H_{24}N_9O_6PS_6$	15.87	14.93	24.23	25.17	3.89	3.91
4,6-Dimethyl-2-pyrimidinyl	B	248–250[b] 270 dec.	$C_{36}H_{39}N_{12}O_6PS_3$	19.48	19.78	11.14	11.68	3.58	3.50

[a] B, absolute alcohol; C, aqueous acetic acid. [b] Liquid crystal. Melting points were performed by the capillary tube method and are uncorrected. [c] Analyses performed by Janssen Pharmaceutica, Beerse, Belgium.

Toy (8) in their work on the preparation of *N*-substituted derivatives of phenyl esters of amido and diamido phosphoric acid reported the use of pyridine–chloroform and the same mixture was later used by Cates (1). In the present investigation the pyridine–chloroform mixture (2:1) was successfully used in all the condensations.

That the phosphorus atom in the synthesized compounds is linked to the N^4 of the sulfa drug was shown qualitatively by the failure of all the condensation products to diazotize and by their solubility in dilute alkali and insolubility in dilute mineral acids.

EXPERIMENTAL

The condensation was carried out according to the following general procedure.

Phosphorus trichloride (0.01 mole), dissolved in pyridine–chloroform (25 ml.), was gradually added to the sulfa compound (0.02 mole). The mixture was refluxed for 24 hr. with all except sulfanilamide in which case refluxing for 12 hr. was sufficient. Then the solvent was distilled *in vacuo*, and the yellowish brown viscous residue was suspended in dilute hydrochloric acid, filtered, and washed with water until the washings gave a negative chloride test with silver nitrate T.S. The product, after being dried, was crystallized from the appropriate solvent. (See Tables I and II.)

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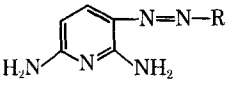
New Compounds: Synthesis of Some Sulfazopyridine Derivatives for Pharmacological Study

By H. Y. ABOU-ELENEIN, M. KHALIFA, and Y. M. ABOU-ZEID

The synthesis of some sulfazopyridine derivatives is described.

SINCE THE discovery of sulfamidochrysoidine[1] (1), a large number of sulfamoyl phenylazo dyes was made and their chemotherapeutic action was studied against various bacterial infections. In recent years combinations of sulfonamides and azo dyes are widely used as urinary disinfectants. The authors now report the synthesis of some azo dyes containing a sulfonamido moiety together with a diaminopyridyl moiety (I).

Received February 6, 1967, from the Faculty of Pharmacy, Cairo University, Cairo, United Arab Republic.
Accepted for publication May 4, 1967.
The products at present are under preliminary screening for possible antimicrobial action or any useful pharmacological activity.
[1] Prontosil.



I

Derivatives having the above general formula were synthesized by coupling diazotized sulfonamides with 2,6-diaminopyridine hydrochloride. Attempts to prepare 2,6-diaminopyridine by amination of pyridine with sodamide in the presence of solvents were unsuccessful; in the absence of solvents, a 20% yield was obtained. Two methods were applied for diazotizing the sulfa compounds: (*a*) the standard procedure and (*b*) the alternate one, which consists of dissolving the sulfonamide in sodium hydroxide first. The diazotized sulfa compound