

TABLE I

Serial No.	Name	M.P./°C.	Nitrogen percentage	
			Found	Required
14	4-Sulphanilamido acetophenone*	189-90	9.4	9.7
15	<i>ω</i> -Sulphanilamido acetophenone	176-77 dec.	9.5	9.7
	<i>ω</i> -Sulphanilamido acetophenone hydrochloride	200-02 dec.
16	<i>ω</i> -(N ⁴ , Acetylsulphanilamido) acetophenone	151-52 dec.
	<i>ω</i> -Sulphanilamido acetophenone	169	8.1	8.2
	<i>ω</i> -Sulphanilamido, <i>α</i> -acetophenone hydrochloride	189 dec., sintg. 185
	<i>ω</i> -(N ⁴ , Acetyl sulphanilamido) acetophenone	2021-04 dec.
17	N ⁴ -Acetyl sulphanilamido guanidine	117-18 dec.	25.4	25.9
18	3, N ⁴ -Acetyl sulphanilamido, 1 : 2 : 4 - triazole	210 dec.	25.1	24.9
19	5-Sulphanilamido benzotriazole	135-37	24.0	24.2
20	5-Sulphanilamido indazole	243-44 dec.	19.2	19.4
	5-(N ⁴ , Acetyl sulphanilamido) indazole	262 dec.
21	7-Sulphanilamido indazole	249-50 dec.	19.3	19.4
22	1-Sulphanilyl indole	159 dec.	10.1	10.3
	1-(N ⁴ , Acetyl sulphanilyl) indole	146-47	9.0	9.0
23	3-Sulphanilamido indotriazine	200-01 dec.	24.2	24.7
	3-(N ⁴ , Acetyl sulphanilamido) indotriazine	261-62 dec.
36	<i>m</i> -Hydroxy benzylidene sulphanilamide ..	138	10.3	10.1
37	<i>o</i> -Nitrobenzylidene sulphanilamide	indef.	13.5	13.8
38	<i>o</i> -Nitrobenzylidene sulphathiazole	indef.	14.0	14.4
39	<i>m</i> -Nitrobenzylidene sulphathiazole	220-22 dec.	13.9	14.4

* Literature⁹ gives the melting point 208°C.

The amino bodies were condensed severally with crystallised acetyl sulphanilyl chloride in pyridine medium and the resulting N⁴-acetyl sulphanilamide derivatives subjected to the hydrolytic action of hot dilute hydrochloric acid, with one exception, namely, No. 22, which was obtained by hydrolysis of its N⁴-acetyl derivative with hot dilute (10 parts of 10 per cent. sodium hydroxide. Except in the case of the N⁴-acetyl derivatives of guanidine (No. 17) and triazole (No. 18), where the attempts to isolate the final compounds were not met with success, hydrolysis to the sulphonamides proceeded smoothly.

Examination of the Schiff's bases derived from the sulphonamides, as also those of the sulphones, has disclosed that while most of them are as active as the parent compounds themselves, at least in experimental streptococcal infections, a few of them were remarkably much less toxic.^{5, 11} These compounds are chemically rather unstable and their activity is conceived^{5, 6, 12} to be due to their cleavage into the original sulphonamides, on oral administration. While this mechanism of action holds for most members of this group, there are a few instances for which this explanation would not appear

acceptable without further modification. Thus, for example, *p*-hydroxy benzylidene sulphanilamide^{7, 8} is said to be more active than sulphanilamide itself. Again, the high activities claimed for the N⁴-*p*, nitrobenzylidene sulphonamides^{9, 10, 11} are noteworthy. It is also of interest that both *o*-nitrobenzylidene and *m*-hydroxy benzylidene sulphapyridines^{8, 9, 11} should be rated superior to sulphapyridine or sulphanilamide against streptococci, but inferior to sulphapyridine against pneumococci. The results with the sulphapyridine derivatives are remarkable: while a decreased activity towards the pneumococcus is conceivable, it is difficult to understand how sulphapyridine, if it is the active agent, could give an *increased* activity against streptococci, when administered as compounds which liberate it in the body. However, if these results are true, the only explanation that could be advanced would be that the "aldehyde half" of the molecule or its derivative elaborated *in vivo* exerts a modifying action on the chemotherapeutic efficacy of the "active half". The Schiff's bases (Nos. 36-39) shown in the table, besides a few others already reported in literature, were therefore prepared in order to investigate in some detail the mechanism of action of Schiff's bases derived from the sulphonamides.

The compounds reported herein are being investigated as to their usefulness in experimental bacterial infections with particular reference to plague in mice at this Institute.

Experimental

The synthesis of the final sulphonamides having been effected according to the customary procedures, the experimental details have been omitted.

3-Amino indotriazine.—A mixture of aminoguanidine carbonate (2.74 gm.) and isatin (2.94 gm., 1 mol.) in glacial acetic acid (100, c.c.) was gently refluxed for one half hour, diluted with water and basified with excess of ammonia. The 3-amino indotriazine recrystallised from alcohol as yellow needles, melting at 195-96°; yield-4.5 gm. (Found: N, 37.3; C₉H₇N₅ requires N, 37.8 %.)

The *Schiff's bases* (Nos. 36-39) were prepared by boiling together alcoholic solutions of molecular proportions of the appropriate aldehyde and the sulphonamide until crystal-separation occurred. The reaction mixture was cooled, the separated solid filtered and washed free of any traces of unreacted initial compounds by means of alcohol. These could not be recrystallised from solvents owing to their instability; they consisted of pale plates.

Except Nos. 17 and 18, the sulphonamides (Nos. 14-16, 19-23) were all recrystallised from alcohol; Nos 17 and 18 were obtained from water, all of

them (Nos. 14–22) were obtained as characteristic colourless needles, the exception being No. 18 which formed colourless prisms. The indotriazine derivative consisted of yellow needles.

The yields of all the compounds were good.

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Summary

With the object of ascertaining the relative antibacterial merits of sulphonamides derived, among a few others, chiefly from heterocyclic ring systems, a series of N¹-substituted sulphonamides containing the triazole, benzotriazole, indazole, indole, and indotriazine rings have been synthesised. Additional compounds reported are the sulphonamide derivatives of acetophenone and guanidine.

A few Schiff's bases derived from the sulphonamides have also been prepared for their possible therapeutic usefulness and for a study of the mode of action of the sulphonamido Schiff's bases in general.

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