

# STUDIES IN SULPHONES. PART I. SCHIFF'S BASES OF 4'-NITRO-4'-AMINODIPHENYLSULPHONE AND THEIR REDUCTION PRODUCTS \*

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Twenty-four Schiff's bases of 4-nitro-4'-amino-, and 4 : 4'-diamino-diphenylsulphones are described.

In the development of antibacterial chemotherapy during the past decade much attention has been paid to the study of substituted sulphanilamides but no systematic attempts have been made to develop the drugs of the sulphone type. The discovery of the high anti-treptococcal activity, though accompanied with high toxicity, of 4 : 4'-diaminodiphenylsulphone (Buttle *et al.*, *Lancet*, 1937, *i*, 1331) and its possible use in the treatment of tuberculosis and leprosy (Raiziss *et al.*, *J. Amer. Chem. Soc.*, 1939, **61**, 2763; Smith *et al.*, *J. Pharm. Expt. Ther.*, 1942, **74**, 163; Roblin *et al.*, *J. Amer. Chem. Soc.*, 1941, **63**, 1930) led to the synthesis of Promin (*cf.* Jain *et al.*, *Science & Culture*, 1945-46, **11**, 568), Diasone (Bauer, *J. Amer. Chem. Soc.*, 1939, **61**, 617) and Promizole (Bambas, *ibid.*, 1945, **67**, 668).

Analogous to the Schiff's bases of sulphanilamide (Goissedet *et al.*, *Compt. rend. soc. Biol.*, 1936, **121**, 1092; Gray *et al.*, *Biochem. J.*, 1937, **31**, 724) which have been shown to possess good therapeutic property with the added advantage of low toxicity, it was thought of interest to make a systematic study of the Schiff's bases of 4-nitro-4'-amino- and 4 : 4'-diaminodiphenylsulphones in anticipation of their possessing low toxicity.

Condensation of 4-nitro-4'-aminodiphenylsulphone with (i) benzaldehyde, (ii) *o*-methoxy-, (iii) *p*-methoxy-, (iv) *o*-hydroxy-, (v) *m*-nitro-, (vi) *p*-dimethyl-amino-, (vii) *p*-diethylamino-, (viii) 3 : 4-methylenedioxy-benzaldehydes, (ix) 3 : 4-methylenedioxy-6-nitrobenzaldehyde, (x) 2-hydroxynaphthaldehyde, (xi) cinnamic aldehyde and (xii) furfuraldehyde gave the twelve odd numbered nitro-Schiff's bases respectively, having the general formula (A) (vide Table I below).

Compounds (I), (III), (V), (VII), (XV) and (XIX) on reduction with sodium hydrosulphite gave (II), (IV), (VI), (VIII), (XVI) and (XX) respectively, of the general formula (B) (vide Table I). These six amino-Schiff's bases were also prepared by the action of the corresponding aldehydes on 4 : 4'-diaminodiphenylsulphone. The nitro-Schiff's bases (IX), (XI), (XIII), (XVII), (XXI) and (XXIII) decomposed on reduction into 4 : 4'-diaminodiphenylsulphone and the respective aldehyde; the corresponding even-numbered amino-Schiff's bases were, however, prepared from 4 : 4'-diaminodiphenylsulphone by the direct action of the respective aldehyde.

Except in the case of cinnamic aldehyde, which gave [XXII, (C<sub>6</sub>H<sub>5</sub>CH=CH-CH=N.C<sub>6</sub>H<sub>4</sub>)<sub>2</sub>.SO<sub>2</sub>], in no other case could two molecules of the aldehyde be condensed with 4 : 4'-diaminodiphenylsulphone.

Buttle *et al.* (*Biochem. J.*, 1938, **32**, 1101) have prepared (II), (VI) (XII), (XVI) and (XXI) from 4 : 4'-diaminodiphenylsulphone and reported them to be less toxic than the parent sulphone.

## EXPERIMENTAL

All the compounds and their analytical data are tabulated below.

The odd-numbered nitro-Schiff's bases from 4-nitro-4'-aminodiphenylsulphone, with the exception of (IX), were prepared by the general procedure described for

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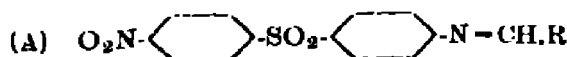
(I). Product (IX) was prepared either by the dry fusion of the reactants or by conducting the reaction in alcohol in the presence of zinc chloride.

Out of the twelve even-numbered amino-Schiff's bases (II), (IV), (VI), (VIII) (XVI) and (XX) were prepared by the general procedure described for (II) by the reduction of the corresponding nitro compound. The remaining amino-Schiff's bases were prepared by the condensation of 4 : 4'-diaminodiphenylsulphone with the corresponding aldehyde either by fusion or in the presence of alcohol.

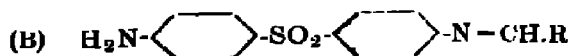
4-Nitro-4'-benzylideneaminodiphenylsulphone (I).—4-Nitro-4'-aminodiphenylsulphone (2.8 g) and benzaldehyde (1.5 g.) in absolute alcohol (15 c.c.) were refluxed for 1 hour when the product separated. This was filtered out, washed with hot alcohol and crystallised from pyridine, m.p. 184°, yield 3.6 g.

4-Amino-4'-benzylideneaminodiphenylsulphone (II).—To a suspension of compound (I, 1 g.) in alcohol (5 c.c.) boiling under reflux, sodium hydrosulphite (3 g.) suspended in water (10 c.c.) was gradually added during 1 hour when a clear solution resulted. This was neutralised with 5% sodium hydroxide solution and the precipitated product was collected, washed with water and crystallised from dilute acetic acid, m.p. 231°, yield 0.6 g.

TABLE I



R stands for the respective aldehyde less -CHO.



No.	Formula of Schiff's base.	M.p.	% Nitrogen		% Sulphur	
			Found.	Calc.	Found.	Calc.
I.	$C_{19}H_{14}O_4N_2S$	184°	7.55	7.65	8.56	8.74
II.	$C_{19}H_{14}O_2N_2S$	231	8.14	8.83	—	—
III.	$C_{20}H_{16}O_2N_2S$	192	7.07	7.00	7.97	8.08
IV.	$C_{20}H_{16}O_2N_2S$	199	7.40	7.65	—	—
V.	$C_{20}H_{16}O_2N_2S$	203	6.94	7.00	—	—
VI.	$C_{20}H_{16}O_2N_2S$	227	7.78	7.65	—	—
VII.	$C_{19}H_{14}O_2N_2S$	226	7.42	7.83	—	—
VIII.	$C_{19}H_{14}O_2N_2S$	172	8.08	7.99	—	—
IX.	$C_{19}H_{14}O_2N_2S$	210	10.00	10.22	—	—
X.	$C_{19}H_{14}O_2N_2S$	243	11.10	11.02	—	—
XI.	$C_{21}H_{18}O_2N_2S$	122	10.13	10.27	7.74	7.82
XII.	$C_{21}H_{18}O_2N_2S$	249	11.05	11.10	—	—
XIII.	$C_{23}H_{22}O_2N_2S$	213	9.52	9.81	—	—
XIV.	$C_{23}H_{22}O_2N_2S$	222	10.49	10.32	—	—
XV.	$C_{20}H_{16}O_2N_2S$	215	6.77	6.83	7.99	7.80
XVI.	$C_{20}H_{16}O_2N_2S$	230	7.37	7.37	—	—
XVII.	$C_{20}H_{16}O_2N_2S$	240	9.35	9.23	7.19	7.03
XVIII.	$C_{20}H_{16}O_2N_2S$	241	10.10	9.98	—	—
XIX.	$C_{23}H_{22}O_2N_2S$	234	6.81	6.45	7.22	7.41
XX.	$C_{23}H_{22}O_2N_2S$	238	7.21	7.00	—	—
XXI.	$C_{21}H_{18}O_2N_2S$	194	7.02	7.14	—	—
XXII.	$C_{20}H_{16}O_2N_2S$	244	5.85	5.88	—	—
XXIII.	$C_{17}H_{12}O_2N_2S$	150	7.68	7.88	9.20	9.00
XXIV.	$C_{17}H_{12}O_2N_2S$	153	8.55	8.80	—	—