CHEMOTHERAPY OF BACTERIAL INFECTIONS

Part XI. Synthesis of Some Derivatives of Diphenylsulphone

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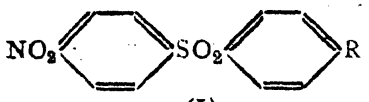
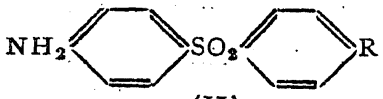
Compounds of the diphenylsulphone group are of interest from many points of view. Though not strictly belonging to the sulphanilamide group, 4:4'-diaminodiphenylsulphone and its derivatives show typical sulphanilamide activity, their bacteriostatic effect being reversed by *para* aminobenzoic acid. On the basis of the drug-diet experiments, Marshall, Litchfield and White[1] have found that 4:4'-diaminodiphenylsulphone is about ten times as effective as sulphanilamide in experimental streptococcal infections in mice; but the high degree of toxicity of this compound has prevented its use in practical therapy. Three derivatives of this compound, *viz.*, the disodium salt of the N, N'-didextrosesulphonate ('Promin'), the di-formaldehydesulphoxylate ('Diasone') and the diphosphorylated derivative, have been found to show definite protection against experimental tuberculosis in guinea pigs.[2] Promin has also been given a limited clinical trial in tuberculosis[3] and leprosy[4] and the results obtained appear to be somewhat encouraging and warrant further study. These led us to undertake a systematic study of the various derivatives of 4-aminodiphenylsulphone to try if compounds less toxic and more active could not be prepared.

In this paper we report the synthesis of the first series of compounds of types (I) and (II) wherein R is a hydrogen, chloro, bromo, iodo, hydroxy, cyano and substituted amino atoms or groupings. It is proposed to study



(I)



(II)

the effects of these groupings or atoms on the therapeutic activity and toxicity of the compounds.

To prepare compounds of type (I) attempts were made to synthesise the corresponding diphenylsulphide derivatives and then oxidise them to the sulphones. But the diazotisation of the easily accessible 4-nitro-4'-aminodiphenylsulphide was not smooth. On the other hand, 4-nitro-4'-aminodiphenylsulphone underwent diazotisation very smoothly and the diazo-group could be converted into a halogen atom and hydroxy group in good