

STABLE ADRENALINE SOLUTION

VARIOUS attempts have been made to stabilise a 0.1 per cent. solution of adrenaline hydrochloride.^{1,2} Metabisulphite,^{3,4} ascorbic acid,^{5,6} glutathione,⁷ methylene blue,⁸ tryptophan,⁹ guanidine,¹⁰ one or other acid^{11,12,13,14} has been incorporated into its solution. This prevents the formation of a colour and/or a precipitate^{15,16} on storage. Preparation of an adrenaline solution in presence of an inert atmosphere, has no special advantage.¹⁷ The adjustment^{3,18} of pH of the final solution, and its maintenance undoubtedly increase¹ the keeping properties but does not secure stability on long storage in the tropics.

But as adrenaline used for therapeutical purpose, is a lævo-rotatory compound and as its other enantiomorphous forms are much less active in pressor action, a change in the rotatory power might also play a part in its inactivation on storage. Haddock¹⁹ noted that at pH 1.4 to 3.7 racemisation was negligible. But working in this direction it has, however, been noticed by us that an adrenaline solution undergoes a definite change in its rotatory power at room temperature (25-30° C.) under conditions even when no change in pH and colour, nor, any formation of precipitate due to adrenochrome^{15,16} has taken place. On ascertaining the strength of adrenaline in the solution by the Folin method no loss is being noticed whereas on assaying the same by the usual biological process on SPINAL cat, the solution is found to be much less potent in pressor activity. A similar phenomenon is being noticed with solutions from adrenaline salts of *d*-tartaric, *dl*-tartaric, *d*-camphoric, cinnamic and coumarin 3-carboxylic acids. In cases where, however, a solution has been obtained by dissolving adrenaline in presence of lævo-acid, such as L-malic, L-mandelic, L-camphoric and L-valeric acids, no such loss in pressor activity was noticed. The solution remains stable in other respects.

The solution would be much more stable particularly when prepared in presence of carbon-dioxide and stored in dark place.

The work is based on a pending patent application.

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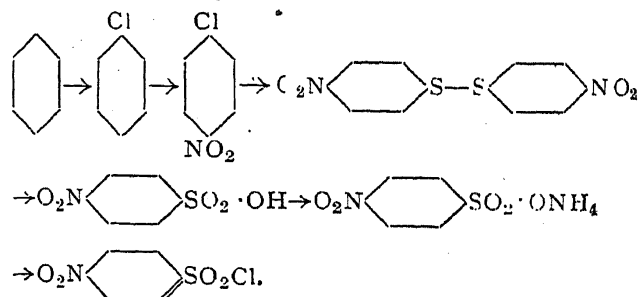
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SYNTHESIS OF SOME N-SUBSTITUTED
p-NITROBENZENESULPHONAMIDES¹

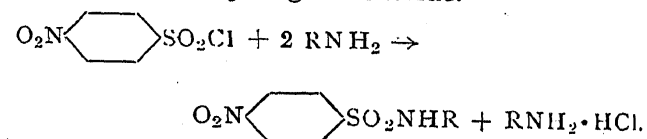
NUCLEAR disubstituted benzene compounds containing either a nitro or sulphonic acid group as one of the substituents, with the second substituent in the *p*-position, form an interesting group of related compounds from the standpoint of the Crum-Brown-Gibson Rule for aromatic substitution. It is well-known that the nitro group in nitrobenzene offers considerable steric hindrance to the introduction of a second substituent in the ring, especially in the case of the second substituent being an ortho-para directing group, the position taken by the second substituent being, of course, meta to the nitro group. The same remarks apply generally to the introduction of a second substituent in a compound like benzenesulphonamide.

The preparation, therefore, of a derivative like *p*-nitrobenzenesulphonamide, is of unusual interest as both the substituent groups are in mutually incompatible positions from the view-point of the rule quoted above. Hence, it is not surprising that the following indirect procedure has been adopted by workers in the field²⁻⁸ to obtain the apparently simple compound, *p*-nitrobenzenesulphochloride. This being a fundamental reagent in this work, it was prepared in good quantity, following generally the method of Bell.⁵



The present paper deals with the synthesis of eight N-substituted *p*-nitrobenzenesulphonamides, outlined in the table given below. Of these the last five have been reported for the first time.

The general method adopted for their preparation was the condensation of *p*-nitrobenzenesulphochloride in aqueous alcoholic solution with two molecular proportions of the appropriate amine in the cold, avoiding thereby any extraneous condensing agent for the elimination of hydrogen chloride.



The various amines as well as the whole series of intermediate products required for

Condensation of <i>p</i> -Nitrobenzenesulphochloride with	Product obtained	Yield %	M. P. in °C	Percentage of Nitrogen	
				Calc.	Found
Ammonia		93	176
Methylamine		86	107-107.5
Ethylamine		92	103
α -Naphthylamine		84	196-197	8.53	8.27
β -Naphthylamine		95	173-174	8.53	8.26
Methylaniline		97	127-128	9.59	9.47
Ethylaniline		80	158	9.15	9.11
Sulphanilamide		81	215	11.76	11.30

the preparation of *p*-nitrobenzenesulphochloride starting from benzene, were specially prepared and purified for this work by the usual or improved methods.

The nitrogen content of the compounds prepared was estimated by the Kjeldahl method using the modifications of Jodlbauer⁹ and Cope.¹⁰

The specific purpose for which the above nitro compounds were synthesised was to reduce them to the corresponding azo-bis compounds which will form the subject of the next communication in this series.

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1. This paper forms Part II of the author's M.Sc. Thesis entitled "Studies in the Synthesis of some substituted Benzenesulphonamides", recently submitted to the University of Madras. Part I has been published in *Curr. Sci.*, 1945, **14**, 46-47. 2. Blanksma, *Rec. trav. chim.*, 1900, **19**, 111. 3. —, *Ibid.*, 1901, **20**, 128. 4. Obermiller, *J. Prakt. Chem.*, 1914, **89**, 84. 5. Bell, *J. C. S.*, 1928, 2776. 6. Elgersma, *Rec. Trav. Chim.*, 1929, **48**, 753. 7. Demeny., *Ibid.*, 1929, **48**, 1146. 8. Barber, *J. C. S.*, 1943, 102. 9. Jodlbauer, *J. C. S.*, Abstracts, 1886, 834. 10. Cope, *J. Ind. Eng. Chem.*, 1916, **8**, 592. 11. I. G. Farbenindustrie, *A.-G. Brit., P.*, 1939, 500, 118.

PRELIMINARY NOTE ON THE POSSIBLE USE OF PENICILLIN TO REDUCE THE NUMBER OF BACTERIA IN FRESHLY PREPARED COW-POX VACCINE (AGAINST SMALL-POX)

It is a notoriously difficult task to reduce to a minimum the associated Bacteria (the chiefly occurring ones are fungus, staphylococci and streptococci—in some cases) in the vaccines prepared against small-pox from female buffalo calves—the animal that is now usually used in laboratories for preparing small-pox vaccine lymph. The usual method adopted for sterilising vaccine lymph is to suspend the finely powdered material obtained from the animals, in glycerine and store such glycerine-suspended lymph in ice box between 5° C. and 8° C., for long periods of time (8 months to a year). Bacterial counts are taken at various intervals and when the staphylococci are reduced to a minimum—by the slow antiseptic action of glycerine—the vaccine is issued for general use.

It was thought possible to use Penicillin along with glycerine, to reduce these associated bacteria to a minimum in a short time. A Flemming culture was obtained, one each, from Mr. M. J. Narasimhan, Director of Agriculture, and Dr. Ananthaswamy, Bacteriologist, Public Health Institute, for this purpose. Preliminary experiments show a very good inhibitory—lethal—action by Penicillin, in glyce-