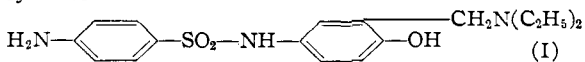


## NEW COMPOUNDS

 $\alpha$ -Diethylamino-4-sulfanilamido-*o*-cresol Hydrochloride

Because of the promising activity of both the sulfonamides<sup>1</sup> and the Mannich phenols<sup>2</sup> in malaria, a substance (I) which could be classified chemically both as a sulfonamide and a Mannich phenol was considered worthy of synthesis.



The proposed drug was found to be inactive in avian malaria by Dr. R. J. Porter, of the University of Michigan. It was also ineffective as an internal antiseptic in the tests by Dr. O. M. Gruhitz, of This Laboratory.

**Experimental.**—Hydrolysis of 23.6 g. (0.1 mole) of 4-acetamido- $\alpha$ -diethylamino-*o*-cresol was effected by treatment with 50 ml. of 20% hydrochloric acid at refluxing temperature.<sup>2</sup> The free base was liberated from solution by the addition of an excess of concentrated ammonia. To prevent decomposition of the 4-amino- $\alpha$ -diethylamino-*o*-cresol, the mixture was hurriedly extracted with ether. The combined extracts were washed with water, dried over magnesium sulfate and then treated with an acetone suspension of 23.3 g. (0.1 mole) of *p*-acetamidobenzene-sulfonyl chloride. The mixture was heated on a steam-bath until the volatile solvent had been removed. It was not possible at this stage to isolate a solid product, so the residue was heated under reflux for a half hour with 250 ml. of 5% hydrochloric acid. The pH was adjusted to about 5 through the addition of a concentrated solution of sodium hydroxide whereupon  $\alpha$ -diethylamino-4-sulfanilamido-*o*-cresol hydrochloride precipitated; yield 15 g. (39%); m. p. 234–236° (dec.). Recrystallized from boiling water containing boneblack and washed with acetone, the product became white; m. p. 236–237° (dec.).

*Anal.* Calcd. for  $C_{17}H_{22}N_2O_3S \cdot HCl$ : C, 52.91; H, 6.27. Found: C, 53.02; H, 6.45.

RESEARCH LABORATORIES  
PARKE, DAVIS & COMPANY  
DETROIT 32, MICHIGAN

J. H. BURCKHALTER<sup>2</sup>

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(1) Coggeshall, *J. Exp. Med.*, **71**, 13 (1939).

(2) Burckhalter, Tendick, Jones, E., Jones, P., Holcomb and Rawlins, *THIS JOURNAL*, **70**, 1363 (1948).

(3) Present address: Department of Pharmaceutical Chemistry, University of Kansas School of Pharmacy, Lawrence, Kansas.

Some New Substituted  $\beta$ -Nitrostyrenes<sup>1</sup>

In the course of other work several new substituted  $\beta$ -nitrostyrene derivatives have been prepared and characterized. These compounds were prepared essentially by the method outlined in Organic Syntheses<sup>2</sup> for the preparation of  $\beta$ -nitrostyrene in which the appropriate benzaldehyde was condensed with nitromethane. The compounds were characterized by melting point determination and nitrogen analysis. The nitrogen analyses were carried out using the Friedrich method as described by Clark<sup>3</sup> with slight modifications. The analyses and physical properties of these compounds are reported in Table I.

In addition, 3-chloro-5-nitrobenzaldehyde has not previously been reported; however, the corresponding ben-

(1) Taken from a thesis presented by Mary E. Carter to the Graduate School, University of Florida, in partial fulfillment of the requirements for the degree of Master of Science, September, 1949.

(2) D. E. Worrall, "Organic Syntheses," Col. Vol. I, J. Wiley and Sons, Inc., New York, N. Y., 1941, p. 413.

(3) E. P. Clark, "Semimicro Quantitative Organic Analysis," Academic Press, Inc., New York, N. Y., 1943, p. 37–43.

TABLE I

$\beta$ -Nitrostyrene	Formula	M. p., °C.	Nitrogen, %	
			Calcd.	Found
2,4-Dichloro-	$C_8H_5O_2Cl_2N$	110	6.42	6.38
3,4-Dichloro-	$C_8H_5O_2Cl_2N$	75	6.42	6.33
2-Chloro-5-nitro-	$C_8H_5O_4ClN_2$	142	12.25	12.21
3-Chloro-5-nitro	$C_8H_5O_4ClN_2$	126	12.25	12.30
2,3-Dimethoxy	$C_{10}H_{11}O_4N$	86.5	6.69	6.66

zoic acid has been reported by Blanksma.<sup>4</sup> This aldehyde was prepared by chlorination of *m*-nitro benzaldehyde in chloroform solution, using ferric chloride and iron as carrier. It was identified by qualitative elemental analysis and oxidation to the acid, this acid being identical with that reported by Blanksma.<sup>4</sup> It was subsequently converted to the  $\beta$ -nitrostyrene as reported above.

(4) Blanksma, *Chem. Zentr.*, **85**, I, 538 (1914).

DEPARTMENT OF CHEMISTRY  
UNIVERSITY OF FLORIDA  
GAINESVILLE, FLORIDA

GEORGE B. BUTLER  
MARY E. CARTER

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## Ephedrine-dibenzofuran-2-sulfonate

**Ephedrine-dibenzofuran-2-sulfonate.**—Ephedrine hydrochloride (6.05 g.) dissolved in 100 ml. of distilled water was added to a solution of 7.47 g. of dibenzofuran-2-sulfonic acid<sup>1</sup> in 100 ml. of distilled water at room temperature. An immediate turbidity which deepened in about five minutes to give a heavy white precipitate resulted. The precipitate was washed free of chlorides and dried under vacuum; yield 6.5 g., m. p. 196–198°. The compound is insoluble in water, ether, chloroform, benzene, dioxane, 10% sodium carbonate solution and dilute hydrochloric acid. It is slowly soluble in absolute ethanol.

*Anal.* Calcd. for  $C_{22}H_{22}NO_5S$ : N, 3.38; S, 7.75. Found: N, 3.37; S, 7.75.

The pharmacological properties of this compound will be reported elsewhere.

(1) Gilman, Smith and Oatfield, *THIS JOURNAL*, **56**, 1412 (1934).

SCHOOL OF PHARMACY

NORTH DAKOTA AGRICULTURAL COLLEGE

FARGO, NORTH DAKOTA

CLIFTON E. MILLER

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*p*-N-Dialkylaminoazobenzenesulfonamides<sup>1</sup>

Several *p*-N-dialkylaminoazobenzenesulfonamides have been described in the literature<sup>2</sup> under the erroneous general name of diazoaminosulfanilamides. Though they are reported to have slight chemotherapeutic action, their unusual structure prompted a brief study in this laboratory of several simple derivatives. The derivatives (Table I) were easily made, with the exception of Ia, by diazotization of sulfanilamide or sulfadiazine and coupling with the appropriate secondary amine according to the method of Elks and Hey.<sup>3</sup> Coupling with primary amines yielded unstable derivatives which sometimes decomposed violently.

The chemical properties of all derivatives were similar, though Ia was of more therapeutic interest because of its water solubility. They can best be considered as precursors of the diazonium salts of sulfanilamide or sulfa-

(1) This research was supported by a grant from the Carnegie Foundation and the Natural Science Research Fund of Vanderbilt University.

(2) Northey, "Sulfonamides and Allied Compounds," Monograph 106, p. 49, Reinhold Publishing Corp., New York, N. Y., 1948.

(3) Elks and Hey, *J. Chem. Soc.*, 441 (1943).