

of the reference acid, a conclusion which is contrary to the observed facts.)

We suggest that the origin of this behavior is steric in nature—the observed weakening of the base occurring with the first member of the series in which the alkyl group of the base can interfere with the acid ( $H^+$  or  $BMe_3$ ). It is obvious that the point in the series at which the weakening is observed will depend upon the size of the reference acid. In the case of a large acid, such as trimethylboron, such interference occurs in a base having a shorter chain than in the case where the acid is the small proton. It would be expected that an even larger acid, *e. g.*, triethylboron or tri-*n*-propylboron, would lead to a shift of the irregularity to methylamine, or even to ammonia. This prediction is now being tested.

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#### THE RELATIONSHIP OF STRUCTURE TO ACTIVITY OF SULFANILAMIDE TYPE COMPOUNDS

Sir:

Kumler and Daniels<sup>1</sup> have suggested that the resonating form of the *p*-amino group with a separation of charge is a fundamental factor for the bacteriostatic activity of sulfanilamide type compounds. The experimental evidence for this suggestion is "that sulfanilamide has a higher (ultraviolet) extinction coefficient in base than in water."<sup>2</sup>

Because of the theoretical importance placed on this single observation, and since previous studies in this Laboratory<sup>3</sup> were not in agreement with it, we have repeated the work using a more suitable instrument (Beckman Spectrophotometer Model DU).<sup>4</sup> The data obtained for sulfanil-

TABLE I

#### ULTRAVIOLET SPECTRAL DATA ON SULFANILAMIDE

Form	Wave length of peak absorption, Å.	Extinction coefficient
Molecular (1 N NaCl)	2585	16,380 ± 49 <sup>a</sup>
Ionic (1 N NaOH)	2505	16,150 ± 48
Difference	80	230 ± 97
Per cent. difference		1.42 ± 0.6

<sup>a</sup> The limits of error are those encountered in quadruplicate determinations.

(1) Kumler and Daniels, *THIS JOURNAL*, **65**, 2190 (1943).

(2) Kumler and Strait, *ibid.*, **65**, 2349 (1943).

(3) E. J. Robinson and D. Richardson, personal communication.

(4) This instrument was made available to us through the courtesy of Dr. V. du Vigneaud and Dr. W. Summerson, Department of Biochemistry, Cornell University Medical School, New York, N. Y.

amide are recorded in Fig. 1 and Table I. The additive function  $-\log_{10}T$  was used in Fig. 1 to demonstrate the reliability of the method of correcting for solvent absorption.

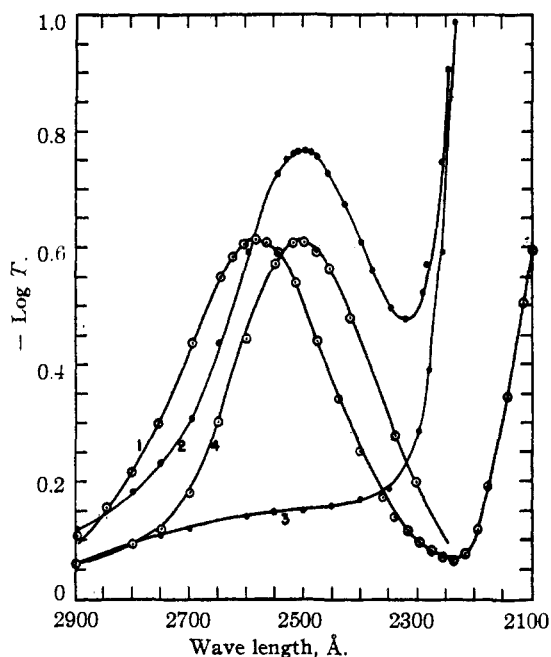


Fig. 1.— $\log_{10}$  of per cent. light transmitted by a 1-cm. sample of: 1,  $3.78 \times 10^{-5}$  M sulfanilamide in 1 N NaCl, 1 N NaCl blank; 2,  $3.78 \times 10^{-5}$  M sulfanilamide in 1 N NaOH, water blank; 3, 1 N NaOH, water blank; 4,  $3.78 \times 10^{-5}$  M sulfanilamide in 1 N NaOH, solid line obtained by subtracting curve 3 from 2, and points -O- from measurements with 1 N NaOH blank.

These results do not confirm those of Kumler and Strait, and there appears to be no adequate experimental basis for the assumption that the resonating form with a separation of charge contributes more in a sulfonamide ion. Moreover, the lack of correlation between the base constants and bacteriostatic activity of sulfanilamide type compounds in general<sup>5</sup> does not support the hypothesis that the base weakening resonance form is a fundamental factor for activity.

(5) Bell and Roblin, *THIS JOURNAL*, **64**, 2905 (1942).

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RECEIVED MARCH 15, 1944

#### SYNTHETIC THIOPHANE DERIVATIVES

Sir:

Karrer and Schmid<sup>1</sup> have recently described the synthesis of thiophanone-3 and of 2-methylthiophanone-3. Results essentially in agreement with those of the Swiss investigators have been obtained in this Laboratory.

(1) Karrer and Schmid, *Helv. Chim. Acta*, **27**, 116, 124 (1944).