

complete escape of the iodine from the insoluble organic material. Blanks were taken on the sodium iodide under the same conditions, and the small corrections deducted from the volumes of thiosulfate solution required to titrate the aliquots. The concentration of sulfenyl chloride was calculated from the corrected volume of thiosulfate. Titrations of known weights of the sulfenyl chloride by this procedure were quantitative, with a precision of about 1%. The concentration of styrene in the solution at any time was calculated from the measured concentration of the sulfenyl chloride, and the difference in initial concentrations of the two reactants. The concentration of sulfenyl chloride at infinite time served as a check on the initial concentrations, as well as on the quantitative nature of the reaction. The agreement was always within 1-2%. The specific reaction-rate constants were calculated from the familiar, second-

order expression

$$k = \frac{2.303}{t(a-b)} \times \log \frac{b(a-x)}{a(b-x)}$$

One run was attempted to carbon tetrachloride, purified by the procedure of Price,<sup>17</sup> at 25°, and using initial concentrations of 0.0152 and 0.0589 *M*, respectively, for sulfenyl chloride and styrene. Ten-ml. aliquots were titrated for I at intervals up to 8000 min. The precision of the titrations in this solvent were not as good as in the acetic acid runs, but the results were sufficiently accurate to show that the reaction had scarcely proceeded after 8000 minutes.

(17) C. C. Price, *THIS JOURNAL*, **58**, 1834 (1936).

LOS ANGELES, CALIFORNIA

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF SOUTHERN CALIFORNIA]

## Derivatives of Sulfenic Acids. XIV. 2,4-Dinitrobenzenesulfenium Ion

BY NORMAN KHARASCH, CHARLES M. BUSS<sup>1</sup> AND WILLIAM KING

RECEIVED JULY 7, 1953

Several lines of evidence support the conclusion that the interaction of 2,4-dinitrobenzenesulfenyl chloride and sulfuric acid involves the equilibrium:  $(\text{NO}_2)_2\text{C}_6\text{H}_3\text{SCl} + \text{H}_2\text{SO}_4 \rightleftharpoons [(\text{NO}_2)_2\text{C}_6\text{H}_3\text{S}]^+ + \text{HCl} + \text{HSO}_4^-$ .

In connection with an earlier study<sup>2</sup> of the reaction of 2,4-dinitrobenzenesulfenyl chloride, I, with aromatic systems under Friedel-Crafts conditions, it was noted that solutions of I in sulfuric acid are distinctly red. The purpose of the present study was to elucidate the nature of this color.

Because it was suspected that ionization of I—or of the intermediate sulfenic acid,  $(\text{NO}_2)_2\text{C}_6\text{H}_3\text{SOH}$ —was involved (see equation 1, below) the following data were obtained to determine whether such was indeed the case.

(a) The yellow, crystalline sulfenyl chloride dissolves in 96 or 100% acid to form stable bright red solutions.

(b) Solution of I in sulfuric acid is accompanied by evolution of hydrogen chloride, pointing to scission of the sulfur-chloride bond.

(c) The red color migrates to the cathode during electrolysis of solutions of I in 100% sulfuric acid.

(d) Addition of bisulfate ions (fused anhydrous potassium bisulfate) to solutions of I in 96% acid visibly repressed the red color; and this observation was corroborated by the effect of added bisulfate ions on the absorption spectrum of the solution (Fig. 1B). Similarly, addition of excess, dry hydrogen chloride to dilute solutions of I in concentrated sulfuric acid entirely repressed the development of the red color, giving an absorption characteristic of I, rather than of the solutions of I in absence of excess hydrogen chloride (compare Figs. 1A and 1C). As suspected, solutions of I in concentrated sulfuric acid do not obey Beer's law.

(e) Sulfuric acid solutions of I react rapidly with benzene, whereas reaction fails to occur in the absence of sulfuric acid or other Friedel-Crafts catalysts.<sup>2</sup> The expected product, 2,4-dinitrophenyl phenyl sulfide, was isolated in 30% yield—

(1) XIII, W. L. Orr and N. Kharasch, *THIS JOURNAL*, **75**, 8030 (1953).

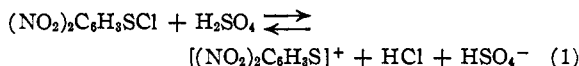
(2) C. M. Buess and N. Kharasch, *ibid.*, **72**, 3520 (1950).

the low yield being associated with difficulties attending isolation of the sulfide from concentrated sulfuric acid.

(f) Cryoscopic measurements of dilute solutions of I in sulfuric acid led to van't Hoff "i" factors between 1.6 and 2.6.

(g) The following related observations were also made. (1) While 2,4-dinitrobenzenesulfenyl bromide and thiocyanate also give the same characteristic color as do solutions of I in sulfuric acid, 2,4-dinitrobenzenesulfenamide does not give this color effect. 2,4-Dinitrochlorobenzene, bis-(2,4-dinitrophenyl) disulfide and 2,4-dinitrothiophenol also do not give colored solutions in sulfuric acid. (2) Addition of a variety of other basic substances (besides benzene, *cf.* item e, above) also discharge the red color of I in sulfuric acid solutions. (3) Solutions of I in dry ethylene chloride give typical red colors when treated with aluminum chloride or silver perchlorate. (4) 2-Nitrobenzenesulfenyl chloride (pale yellow) also gives a stable, distinct orange color when dissolved in concentrated sulfuric acid.

In view of the above observations, we believe that the major behavior involved when I dissolves in sulfuric acid may be expressed by equation 1.



The red color of the solution is ascribed to the positive ion, for which the name *2,4-dinitrobenzenesulfenium ion* is suggested. The reaction with benzene and other bases is to be expected, as are also the cathodic migration, the effects of added bisulfate ions and of hydrogen chloride, and the values found for the dissociation factors (eq. 1 requires a maximum of 3, assuming non-ionization of the HCl). The related color formation with aluminum chloride probably involves the interaction,  $\text{ArSCl} + \text{AlCl}_3 \rightleftharpoons \text{ArS}^+\text{AlCl}_4^-$  (Ar =

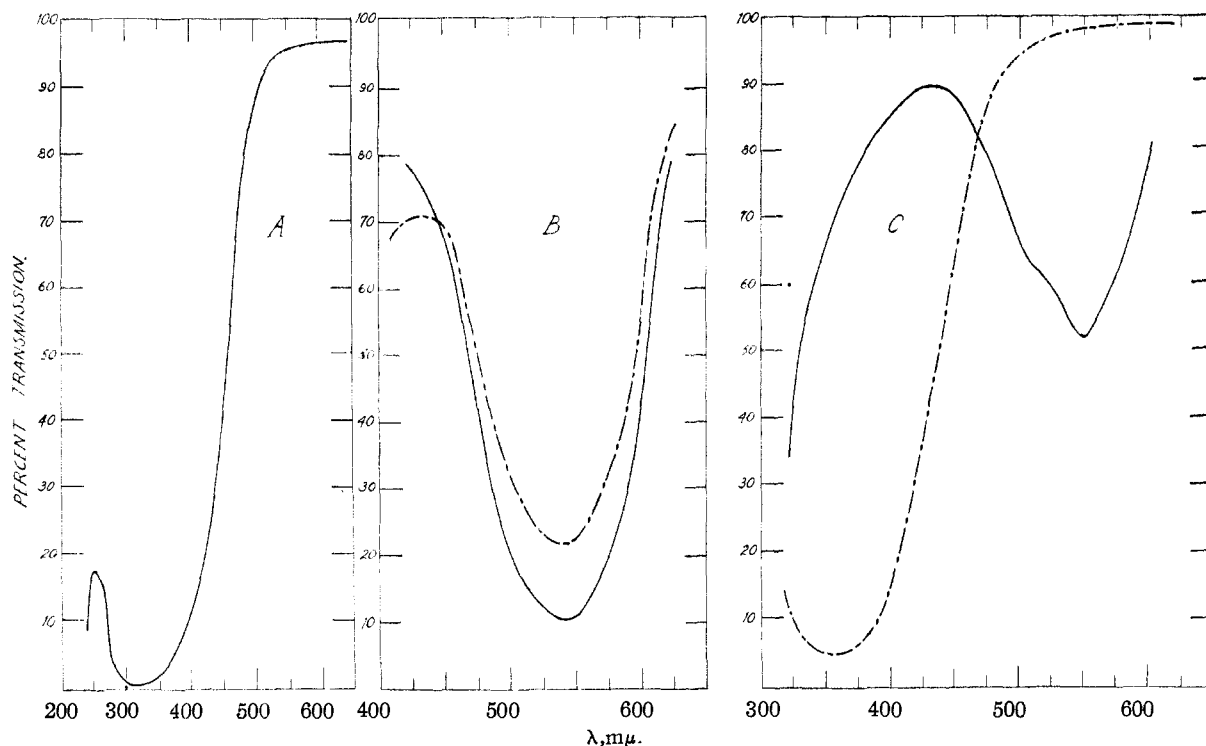
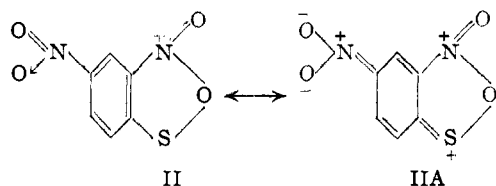


Fig. 1.—Absorption spectra: A, 2,4-dinitrobenzenesulfonyl chloride (I) in ethylene chloride ( $1.8 \times 10^{-4} M$ ); B, —, in I concentrated sulfuric acid,  $2.4 \times 10^{-4} M$ ; ----, same solution with added bisulfate; C, —, I in concentrated sulfuric acid,  $2.1 \times 10^{-6} M$ ; ----, same solution saturated with hydrogen chloride gas.

2,4-dinitrophenyl)—a conclusion which is supported by other studies in this Laboratory.<sup>3</sup>

In considering the full structure of 2,4-dinitrobenzenesulfonium ion, we would suggest that an interaction between oxygen and sulfur, as shown in II, is likely; and, of course, that such a structure represents only one of the possible resonance forms of this ion—other contributing forms being exemplified by IIA.



We should also note that it is known, from related work,<sup>4</sup> that I is readily hydrolyzed, and that the most-probable initial product of hydrolysis is 2,4-dinitrobenzenesulfenic acid. It is therefore possible that even in sulfuric acid solutions, the

(3) (a) For example, highly colored 1:1 complexes have been isolated in the case of  $p\text{-CH}_3\text{C}_6\text{H}_4\text{SCl} + \text{SbCl}_5$  (or  $\text{SbF}_5$ ) by D. L. Chamberlain (Ph.D. Dissertation, University of Southern California, 1953); and R. Swidler (Master's Thesis, University of Southern California, 1950) has demonstrated the reversible equilibrium



(b) The work on reaction with silver perchlorate was entirely preliminary, and product isolation was not completed to analytical stage. While it seems reasonable to suggest that the definite red color observed is associated with 2,4-dinitrobenzenesulfonyl perchlorate, secondary reactions do occur on warming the red solutions. These involve decomposition of the primary red product.

(4) N. Kharasch, T. C. Bruice and W. King, unpublished work.

hydrolytic reaction may precede ionization, and that the immediate precursor of the sulfenium ion is actually 2,4-dinitrobenzenesulfenic acid. Such a circumstance would not, however, alter the over-all interpretation suggested above.

It was also found that when solutions of I in concentrated sulfuric acid were decomposed by pouring on ice, that some undissociated I was isolated by extracting with carbon tetrachloride. This observation supports the other evidence, already cited, pointing to existence of undissociated I in the sulfuric acid solutions, and suggests the need to consider whether the red color may be associated with a form of the sulfonyl chloride in which the nitro group is protonated. Such a possibility seems very unlikely, however, because of: (a) the very low basicities of polynitro compounds,<sup>5</sup> (b) the lack of colors of solutions of other dinitro compounds (cf. *g*, above) in sulfuric acid, (c) the effects of added bisulfate ions and of hydrogen chloride on the colors of I in sulfuric acid, and (d) the lesser likelihood that a protonated form of I, rather than the ion II, would be the colored species.

The existence of solvated 2,4-dinitrobenzenesulfonium ion has, of course, much precedent in the extensive studies of carbonium ions in sulfuric acid solutions, as illustrated in the recent work of Newman and co-workers,<sup>6</sup> Burton, *et al.*,<sup>7</sup> and many earlier workers. Furthermore, aromatic ions as  $\text{ArS}^+$  have been postulated in earlier papers of this

(5) Cf., e.g., J. C. S. Brand, W. C. Horning and M. B. Thornley, *J. Chem. Soc.*, 1374 (1952).

(6) M. S. Newman, *Record Chem. Progr.*, 9, 1 (1948), and references there cited.

(7) H. Burton and G. W. H. Cheeseman, *J. Chem. Soc.*, 832 (1953), and references there cited.

series,<sup>8</sup> and by Suter and Archer,<sup>9</sup> as well as Foss.<sup>10</sup> The transitory existence of  $RS^+$  ( $R =$  simple alkyl), formed by impact of electrons with thiols and disulfides, has also been demonstrated recently.<sup>11</sup> It therefore seems likely that such ions may play a generally-significant role in the chemistry of sulfenic acids, the immediate derivatives of these acids, and allied bivalent sulfur compounds.

### Experimental

**General Observations on Solutions of 2,4-Dinitrobenzenesulfenyl Chloride (I) in Sulfuric Acid.**—Dilute solutions of I in sulfuric acid (5–10 mg. I/100 ml. J. T. Baker C.P., 96% acid) showed deep red, characteristic colors. The solutions were entirely clear, and remained unchanged for several days if protected from atmospheric moisture. The color was discharged rapidly by heating to ca. 200°, or by adding basic substances, such as water, ether, alcohols or unsaturated hydrocarbons. The observations of part g. of the discussion were made with small amounts of the pure reagents involved. The colors from 2,4-dinitrobenzenesulfenyl bromide and thiocyanate were visibly identical with those from I, but were not examined spectroscopically. The addition of anhydrous silver perchlorate to cold solutions of I in ethylene chloride gave bright red solutions which could be kept for extended periods at 0° (see also footnote 3a).

Evolution of hydrogen chloride from solutions of I in 96% or fuming acid was demonstrated by aspirating for 3 hr. (at ca. 25° and 30 mm.) and precipitating AgCl in a suitable trap. The weight of HCl evolved was never above 27% that expected for total HCl evolution on the basis of amount of I. Heating gave greater evolution of HCl, but caused also other complex changes.

**Migration of Color During Electrolysis.**—This was observed in a V-type cell, of 6-mm. tubing, fitted with platinum electrodes (made of thin strips), and a source of 24-volt direct current. The solvent was made from 30% fuming acid (1 vol.) and 96% acid (2 vol.), and 0.1 g. of I was dissolved in 50 ml. of this stock solution. The lower part of the cell was filled with the red solution, and this was overlaid (alternate drops to each side) with clear solvent acid. Sharp boundaries were obtained, and could be maintained for 10–12 hr., with current off. On charging the electrodes, however, the red color migrated to the cathode (ca. 2 cm. distance) within an hour. On reversing the current, the color traversed the cell in the opposite direction. If the entire cell was filled with the red solution, and electrolyzed for 90 min., the anode compartment cleared, but the cathode retained its deep color. Further electrolysis completely discharged the red color throughout the cell.

To avoid possible thermal migration, other electrolyses were conducted across a finely-fritted glass disk. Migration of the red color across the disk, against gravity, was again observed. Similar migration occurred in a cell containing a fritted disk set in a horizontal section between two vertical arms into which the electrodes dipped. To avoid mechanical disturbance, stirring was not used; but cooling was effected by immersing the cell in a large water reservoir. Acid of very near 100% composition (as determined by m.p.) was used in the latter cell for a number of the experiments.<sup>12</sup>

**Spectra.**—A model DU Beckman spectrophotometer, with 1-cm. quartz cells fitted with ground-glass stoppers (to prevent access of moisture or solvent loss), was used. Failure of Beer's law to hold for solutions of I in 96% acid was ob-

served by noting, at a given wave length, decided variations in calculated values of the extinction coefficient for solutions of a given concentration as well as 0.1 that concentration. The curves for a given solution of I could be duplicated satisfactorily after keeping the solution for several hours.

The solution for noting the effect of added bisulfate ions was made by heating fused, anhydrous potassium bisulfate with 96% acid until no more would dissolve, cooling to room temperature, and using this solution to prepare the desired solution of I. The "crossover" of the upper curve of Fig. 1B (solution with bisulfate ion added) with the lower curve at ca. 445  $m\mu$  is probably caused by the strong absorption by bisulfate ions below 450  $m\mu$ . Sulfuric acid containing hydrogen chloride was prepared by bubbling the dry gas into 96% acid, and using this solution to obtain the dotted curve of Fig. 1C.

The sulfenyl chloride I, m.p. 95–96°, used throughout this study was prepared by chlorinolysis of bis-(2,4-dinitrophenyl) disulfide,<sup>13</sup> and recrystallized from dry carbon tetrachloride.

The spectra of solutions of I plus aluminum chloride, in methylene chloride, were also studied; but the results were not reproducible—even though moisture was carefully excluded—for some secondary changes occur in these solutions. However, the general shape of the curve was similar to that for I in sulfuric acid, with strong absorption occurring between 400–500  $m\mu$ .

**Reaction of I, in Sulfuric Acid, with Benzene.**—A solution of 2.50 g. of I in 100 ml. of 96% sulfuric acid was cooled to 10° and stirred vigorously with 20 ml. benzene for several minutes, keeping the temperature below 15°. The organic layer was separated and evaporated to dryness. The residue was dissolved in a 4:1 (by volume) mixture of absolute ethanol and benzene, and charcoaled. The filtrate yielded 0.89 g. (30%) of 2,4-dinitrophenyl phenyl sulfide, m.p. 119–120°. Admixture with authentic sulfide (m.p. 120–120.5°) gave m.p. 119–120°; while admixture with ethyl 2,4-dinitrobenzenesulfenylate (m.p. 123–124°) gave m.p. 105–110°. The low yield of sulfide is most likely associated with the difficulty of extracting the product from the sulfuric acid—as shown by the similar low yields of recovery of the authentic sulfide from sulfuric acid solutions.

**Cryoscopic Measurements.**—These were made essentially as described by Newman and co-workers.<sup>14</sup> A check on the values was made by determining "i" values for benzoic acid (see Table I). In making the measurements, samples of the pure solutes were dried at 60° weighed and introduced into the cell, with stirring. Complete solubility of samples was confirmed by inspecting the homogeneity of the solutions in bright, transmitted light, in which even minute undissolved particles could be detected. The points of intersections of the time-temperature plot for the freezing mixture with that for the cooling liquid were taken as the freezing points. Determinations were repeated, after several hours, the values of  $\Delta\phi$ , above, being the average values. The freezing points of the solutions did not change (within the accuracy of the measurements) on standing in the cell for 24 hr.

TABLE I

F.p. of $H_2SO_4$ , °C.	$\Delta m$ , moles/kg. $H_2SO_4$	$\Delta\phi$ , °C.	"i"	Solute
8.9	0.0539	0.575	1.8	$C_6H_5COOH$
	.1859	2.348	2.1	$C_6H_5COOH$
8.8	.0205	0.264	2.1	I
	.0260	.252	1.6	I
9.0	.00411	.064	2.6	I
	.00552	.081	2.4	I
	.00419	.053	2.1	I
	.01440	.156	1.8	I

(13) N. Kharasch, G. I. Gleason and C. M. Buess, *THIS JOURNAL*, **73**, 1796 (1950).

(14) M. S. Newman, H. G. Kuivila and A. B. Garrett, *ibid.*, **67**, 704 (1945). The equation given in this reference was used to calculate "i" values. Recent refinements in the value of the cryoscopic constant of sulfuric acid [*cf. e.g.*, Gillespie, *J. Chem. Soc.*, 2473 (1950)], were not applied, since our values are not considered to be sufficiently accurate to warrant this. We estimate the values listed to be accurate to about 10%.

(8) N. Kharasch and S. J. Assony, *THIS JOURNAL*, **75**, 1081 (1953).

(9) C. M. Suter and S. Archer, *ibid.*, **74**, 4296 (1952); *cf.* also H. H. Samant and G. A. Brost, *ibid.*, **73**, 4175 (1951), for a related paper on other organosulfur ions in sulfuric acid solutions.

(10) O. Foss, *Acta Chem. Scand.*, **1**, 307 (1947).

(11) J. L. Franklin and H. E. Lumpkin, *THIS JOURNAL*, **74**, 1023 (1952).

(12) We are indebted to Drs. Robert Williams and K. J. Mysels for assistance in initial attempts to demonstrate conductivity differences between the pure solvent acid and solutions of I therein, using their sensitive, modified Jones conductance bridge. These initial experiments were not, however, conclusive, since the conductivity of the near 100% acid is high, and very sensitive to small changes in moisture content, as compared to the increase in conductivity expected from the small amounts of dissolved I which were used.

**Recovery of I from Solutions in Concentrated Sulfuric Acid.**—2,4-Dinitrobenzenesulfonyl chloride (I), 0.10 g., m.p. 96–97° was finely-ground and added to 20 ml. of 96% sulfuric acid. The mixture was let stand, and stirred occasionally, for one hr. This was filtered through a sintered-glass funnel, the filtrate poured on 50 g. of crushed ice, and

the latter mixture was extracted with 50 ml. of carbon tetrachloride. Evaporation of the solvent, from the extract, gave 5 mg. of unchanged I (m.p. and m.m.p. with authentic I, 95–96°).

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## NOTES

### 5-Thiol-7-hydroxy-1- $\gamma$ -triazolo [d]pyrimidine<sup>1,2</sup>

By CARL TABB BAHNER AND DOROTHY ELLIS BILANCIO

RECEIVED AUGUST 7, 1953

5-Thiol-7-amino-1- $\gamma$ -triazolo [d]pyrimidine has been reported to be a strong inhibitor of the growth of *Streptococcus faecalis* R.<sup>3</sup> but not of *Adenocarcinoma* 755.<sup>4</sup> The closely related compound having an hydroxy group in place of the 7-amino group has been prepared as described below. It produces a 65% reduction in the growth of *L. casei* at a concentration of 0.005 mg./ml.<sup>5</sup> The effect can be reversed by pteroylglutamic acid or adenine. The results of screening against various tumors are to be published elsewhere.

A solution of 7.0 g. of sodium nitrite in the minimum volume of water was added slowly to a solution of 15.0 g. of 2-thiol-4,5-diamino-6-hydroxypyrimidine<sup>6,7</sup> in one liter of 2 N H<sub>2</sub>SO<sub>4</sub> at 40°. Stirring was continued 15 minutes after all the sodium nitrite had been added. The solution was chilled for two hours and the solid product was recovered by filtration. It was suspended in boiling water and dissolved by addition of ammonia. The resulting solution was chilled and the crystals which formed were dissolved in boiling water. The hot solution was treated with activated charcoal, filtered hot, acidified with acetic acid and chilled. The crystals which formed were recrystallized from acetone; they then decomposed sharply at 265°. In sodium bicarbonate-buffered solution, the product reacted with iodine in the ratio of 4 atoms of iodine to 1 molecule of product. Grynberg<sup>8</sup> reported similar results with xanthine and guanine. However 8-azaguanine does not behave in the same way. Ultraviolet absorption data for this compound are shown in Table I. The sample for carbon and hydrogen analysis was dried at 110° and 0.1 mm. before analysis, but the analysis indicated the presence of one molecule of water. Roblin,<sup>9</sup> *et al.*, observed that the corresponding dihydroxy compound also was obtained as the monohydrate in spite of careful drying. *Anal.* Calcd. for C<sub>4</sub>H<sub>5</sub>N<sub>5</sub>O<sub>2</sub>S: C, 25.64; H, 2.69. Found: C, 25.85; H, 2.60.

(1) This research was supported in part by a grant from the Damon Runyan Memorial Fund for Cancer Research and in part by a research grant from the National Institutes of Health, U. S. Public Health Service.

(2) Presented in part at the Southeastern Regional Meeting of the American Chemical Society, Auburn, Ala., October 24, 1952.

(3) C. T. Bahner, H. A. Rutter, Jr., and J. R. Totter, *J. Tenn. Acad. Sci.*, **27**, 179 (1952).

(4) G. W. Kidder, V. C. Dewey, R. E. Parks, Jr., and G. L. Woodside, *Cancer Research*, **11**, 204 (1951).

(5) Gertrude Elion and George H. Hitchings, private communication.

(6) W. Traube, *Ann.*, **331**, 71 (1904).

(7) A. Albert, D. J. Brown and G. Cheeseman, *J. Chem. Soc.*, 474 (1951).

(8) M. Z. Grynberg, *Biochem. Z.*, **253**, 143 (1932).

(9) R. O. Roblin, Jr., J. O. Lampen, J. P. English, Q. P. Cole and J. R. Vaughan, Jr., *THIS JOURNAL*, **67**, 290 (1945).

TABLE I

#### ULTRAVIOLET ABSORPTION SPECTRA

pH	$\lambda_{max}$ .	$\lambda_{min}$ .
1	242	255
	270	278
	294	
6, 5	238	219
	288	253
10	232	252
	276	
11	277	250

We are indebted to Gertrude Elion and George H. Hitchings of the Wellcome Research Laboratories and Lee Bennett, Jr., of the Southern Research Institute for ultraviolet absorption data and to Galbraith Analytical Laboratories for carbon and hydrogen determination.

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### On Competition between the Clarke-Eschweiler and Pictet-Spengler Reactions

By RICHARD BALTZLY

RECEIVED JULY 28, 1953

Some years ago in these laboratories Dr. J. S. Buck and the author observed that the attempt to produce dimethylhomoveratrylamine from homoveratrylamine or N-methylhomoveratrylamine by the Clarke-Eschweiler reaction<sup>1</sup> gave mainly 2-methyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline. Similar results were obtained with N-benzylhomoveratrylamine<sup>2</sup> and an attempt to methylate  $\beta$ -(2,5-dimethoxyphenyl)-propylamine by this procedure afforded a compound that was not the corresponding dimethylamine and whose hydrochloride gave analyses consistent with the composition C<sub>13</sub>H<sub>20</sub>ClNO<sub>2</sub>.<sup>3</sup> In this latter case the authors were reluctant to ascribe to this substance the structure of a tetrahydroisoquinoline since there was no activating group in the parent phenethylamine para to the point of prospective ring closure.

More recently Castrillon<sup>4</sup> has reported the cycli-

(1) H. T. Clarke, H. B. Gillespie and S. Z. Weisshaus, *THIS JOURNAL*, **55**, 4571 (1933).

(2) J. S. Buck and R. Baltzly, *ibid.*, **64**, 2263 (1942).

(3) R. Baltzly and J. S. Buck, *ibid.*, **62**, 161 (1940).

(4) J. C. Castrillon, *ibid.*, **74**, 558 (1952).