were reversible. The results are summarized in Table III.

TABLE III

ISOTOPIC OXYGEN RATIO IN RESPIRATION WITH *Chlorella* AND YEAST

Respiring system	O_2 (O^{18} = 0.85%) present at start of expt., ml.	O_2 utilized in respiration, ml.	Per cent. O^{18} in O_2 at end of experiment	
			Obsd.	For no exchange
Chlorella cells in dark for 90 minutes	0.82	0.11	0.85	0.85
Yeast cells for 60 minutes	4.5	2.4	.84	.85

Here also there is no indication for an exchange reaction involving molecular oxygen.

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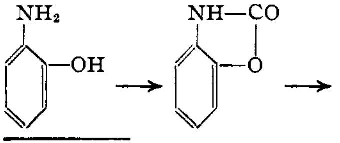
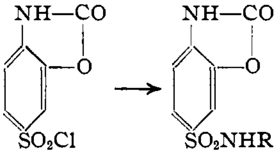
A Stable Derivative of 1-Amino-2-hydroxybenzene-4-sulfonamides

BY JOHN V. SCUDI AND R. P. BUHS

The urinary elimination of oxidation products of the sulfonamide drugs has been definitely established.[1,2] Certain oxidation products have been shown to be of importance in relation to the incidence of acetylsulfapyridine urolithiasis in experimental animals.[3] Since such oxidation products are of interest in connection with theories of the mode of action of these drugs, much attention has been devoted to 1-hydroxylaminobenzene-4-sulfonamide.[4] Another oxidation product which may have physiological significance is the 1-amino-2-hydroxybenzene-4-sulfonamide. The stable benzoxazolone analog of this compound has been prepared as follows





The method appears to be general for the preparation of benzoxazolone-5-sulfonamides.

The benzoxazolone-sulfonamide was administered in aqueous suspension by stomach tube to a series of mice infected with cultures of hemolytic streptococci. Subsequent examination of the urine showed that the oxazolone ring had not been cleaved in passage through the animal. The compound was not effective in protecting the infected mice.

Experimental

Benzoxazolone.—*o*-Hydroxyaniline in dry pyridine was treated with phosgene according to the method of von Meyer.[5] The benzoxazolone, crystallized from acidulated water, melted at 138–139°, cor. It was obtained in 50% yields. In our hands this method failed to give the yields previously reported.

Benzoxazolone-5-sulfonyl Chloride.—One-half mole of the benzoxazolone was added slowly with stirring to 2.5 mole of chlorosulfonic acid at 10–15°. The reaction mixture was stirred for fifteen minutes after all the benzoxazolone was added. The temperature was then raised to 60° and maintained at this temperature for two hours. The reaction mixture was poured onto ice. The product was removed by filtration and dissolved in ether. The ethereal solution was washed free of acid and dried with anhydrous sodium sulfate. The product was precipitated in good crystalline form by the addition of petroleum ether, m. p. 182–183° cor. The yields were 50 to 60%.

Anal. Calcd. for $C_7H_4O_4NSCl$: C, 35.96; H, 1.72. Found: C, 35.79, 35.66; H, 2.07, 2.08.

Benzoxazolone-5-sulfonamide.—9.0 g. of benzoxazolone-5-sulfonylchloride was added to 100 cc. of cold concentrated ammonium hydroxide, and the mixture was warmed to solution. On cooling the ammonium salt of the benzoxazolone-5-sulfonamide separated. This was removed by filtration and converted to the free sulfonamide by crystallization from 300 cc. of acidulated water. The product, melting at 269–270° (decompn.), was obtained in 60% yields.

Anal. Calcd. for $C_7H_6O_4N_2S$: C, 39.23; H, 2.82; N, 13.08. Found: C, 39.33; H, 3.02; N, 13.01, 12.91.

Benzoxazolone-5-sulfonanilide.—150 mg. of the benzoxazolone-5-sulfonyl chloride and 1 cc. of freshly distilled aniline in 3 cc. of dry dioxane were refluxed for fifteen minutes. The reaction mixture was cooled, acidified with hydrochloric acid and diluted to 10 cc. with water. The oil which separated crystallized on standing. The product, obtained in approximately 50% yields, melted at 215–216° cor. after crystallization from water.

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(1) J. V. Scudi, *Science*, **91**, 486 (1940).

(2) W. V. Thorpe and R. T. Williams, *Nature*, **146**, 686 (1940).

(3) J. V. Scudi and H. J. Robinson, *Am. J. Med. Sci.*, in press.

(4) For bibliography see A. C. Bratton, H. J. White and E. K. Marshall, Jr., *Proc. Soc. Exptl. Biol. Med.*, **42**, 847 (1939).

(5) E. von Meyer, *J. prakt. Chem.*, **92**, 256 (1915).

Anal. Calcd. for $C_{13}H_{10}O_4N_2S$: C, 53.77; H, 3.47; N, 9.65. Found: C, 53.52; H, 3.86; N, 9.75.

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Hydrogen Fluoride as a Condensing Agent. XIV. Alkylation Studies[1]

BY J. H. SIMONS AND G. C. BASSLER

As a condensing agent hydrogen fluoride is related to both the metallic halide and the acidic agents. It promotes reactions with alkyl halides, with olefins, and also with hydroxy compounds. For the metallic halide promoted reactions an alkyl halide–metallic halide complex may be postulated as the reactive intermediate. With the acidic agents a complex between the olefin and the acid can be postulated. With hydrogen fluoride the mechanism is obscure, but because of its relationships to the other types of agents, information obtained which aids in the interpretation of its reactions may be of general value. The following experiments were performed to obtain such information.

It seemed desirable to answer three questions concerning alkylations promoted by hydrogen fluoride. First, does hydrogen fluoride act by forming the alkyl fluoride, which then reacts and regenerates the hydrogen fluoride? It is known that hydrogen fluoride is readily removed from aliphatic compounds, *i. e.*, alkyl fluorides lose hydrogen fluoride readily to form olefins. It is also known that olefins, alkyl chlorides, and alcohols react with hydrogen fluoride under certain conditions to form fluorides. Second, what is the relative ease of reaction of olefins and alkyl fluorides with aromatic compounds in the presence of hydrogen fluoride? Third, what is the relative ease of reaction of alcohols and other alkyl halides? Three different sets of experiments were performed to answer these questions.

A sample of pure tertiary amyl fluoride was desired but it was found that this compound would not undergo distillation even at reduced pressure and at −12° without partial decomposition into the olefins and hydrogen fluoride. This was independent of whether the initial substance was prepared from tertiary amyl alcohol and aqueous hydrogen fluoride or the olefin and anhydrous hydrogen fluoride. A mixture of olefin and fluoride was made by adding to 200 cc. of amylenes (prepared by the dehydration of *t*-amyl alcohol) dry-ice and 17 g. of anhydrous hydrogen fluoride. Dry sodium carbonate was added in excess, and the mixture was filtered through a Büchner funnel packed with dry-ice. This procedure should produce a mixture of olefins and tertiary amyl fluoride.[2] Three reaction mixtures were prepared: (1) 60 cc. of amylenes, 21 g. of HF and 50 cc. of benzene; (2) 60 cc. of *t*-amyl fluoride and olefin mixture, 15 g. of HF, and 50 cc. of benzene; (3) 60 cc. of *t*-amyl fluoride and olefin mixture and 50 cc. of benzene. These were allowed to stand in ice for one hour and then an iced solution of sodium carbonate was added. The organic layers were removed, washed, and dried over potassium carbonate. From number 1 about 27 g. of high boiling material was obtained which consisted chiefly of polyalkylated benzene. From number two about 4 g. of high boiling material was obtained and of this it is estimated that perhaps half was aliphatic polymers. From number 3 less than 2 g. of high boiling residue was obtained which probably was chiefly aliphatic polymer.

The following substances were then used for reaction with toluene under similar conditions and for a time short of complete reaction for the most rapid reaction: (1) cyclohexene, (2) cyclohexyl fluoride, (3) cyclohexanol, (4) cyclohexyl chloride, (5) cyclohexyl bromide, and (6) cyclohexyl iodide; 1.5 moles of toluene was added to 3.2 to 3.3 moles of hydrogen fluoride and 0.33 mole of the cyclohexyl compound then added. The mixture was allowed to stand for two hours at room temperature and then the flask was again placed in ice and water carefully added. The organic materials were separated, neutralized, dried, and distilled. The yields of *p*-cyclohexyltoluene obtained were as follows: (1) 74%; (2) 75.6%; (3) 45%; (4) 8%; (5) 0%, and (6) 0%.

The above experiments were then repeated using the following aliphatic compounds in the same molar proportions: (1) octene-1, (2) a mixture made by adding hydrogen fluoride to octene-1 at low temperature (2-fluorooöctane apparently cannot be distilled without decomposition), (3) octanol-2, (4) 2-chlorooöctane, and (5) 2-bromooöctane. Yields of 2-*p*-octyltoluene were as follows: (1) 73%; (2) 13.5%, (3) 42%, (4) 0%, and (5) 0%. In number two a considerable residue was found which is probably aliphatic polymer.

These experiments strongly indicate that the aliphatic fluoride alone is not reactive but that the presence of hydrogen fluoride is also necessary. It also appears that an olefin reacts as readily or more readily than the fluoride. In the second series of experiments the yields are about the same but in the first and third the yield is less when the fluoride is used. This however, is complicated by the difficulties of obtaining the pure fluoride and the polymerization of the aliphatic compounds. The high yield obtained when the alcohol is used is interesting in view of the fact that water is a product of the reaction and remains to dilute the hydrogen fluoride. The decreasing yields as the atomic weight of the halide increases may be correlated in two ways. The reaction produces the hydrogen halide and the order of decreasing

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[1] For the previous paper of this series see Simons, Passino and Archer, THIS JOURNAL, **63**, 608 (1941).

[2] Grosse and Linn, *J. Org. Chem.*, **3**, 26 (1938).