TABLE IV

ESTERS OF *p*-NITROBENZENESULFONIC ACID

Starting material	Solvent	Yield, %	M. p., °C.	Formula	Sulfur analyses, % Calcd.	Found
o-Phenylphenol	Alcohol	93	110–111	$C_{18}H_{13}O_5NS$	9.03	9.01
m-Phenylphenol	Methanol	31	97–98	$C_{18}H_{13}O_5NS$	9.03	8.84
p-Phenylphenol	Alcohol	92	148.5–149.5	$C_{18}H_{13}O_5NS$	9.03	9.19

ported are for crude products. Crystallizations from the solvents indicated in the tables yielded small, colorless crystals in each instance.

That these esters may serve as satisfactory derivatives for the phenylphenols is indicated by the following experiment. One gram of *p*-phenylphenol was treated in the usual manner with *o*-nitrobenzenesulfonyl chloride and the corresponding ester was obtained in 96% yield. After two crystallizations from alcohol the derivative melted between 138 and 139°, as had been found for the product prepared on a larger scale and carefully purified.

The *m*-phenylphenol used in this work was supplied by the Dow Chemical Company. This kindness is gratefully acknowledged.

Summary

1. Some new sulfonic acid esters of the phenylphenols have been prepared and their properties reported.

2. Most of the esters will serve as satisfactory derivatives for the identification of these phenols.

PULLMAN, WASH. RECEIVED DECEMBER 13, 1937

[CONTRIBUTION NO. 41 FROM THE DEPARTMENT OF CHEMISTRY OF THE POLYTECHNIC INSTITUTE OF BROOKLYN]

Syntheses in the Pyrazine Series. I. The Curtius and Hofmann Degradation of Pyrazine-2,5-dicarboxylic Acid[1]

BY PAUL E. SPOERRI AND A. ERICKSON

The wide use of pyridium as a urinary antiseptic has resulted in the preparation of many related compounds and in an investigation of their bacteriological properties. These compounds usually differ from pyridium by the introduction of functional groups in the pyridine or benzene ring. The present investigation has as its ultimate goal the preparation of a dye of a similar structure in the pyrazine series with the hope that this may have superior bactericidal properties.

As a starting point certain diaminopyrazines such as the 2,5- or the 2,6-diamino compounds which might be coupled with diazonium salt were needed.

The immediate object of this experimental study has therefore been to investigate possible methods of preparing aminopyrazines.

The usual reduction methods of preparing primary amines are evidently not applicable to pyrazine. Attempts to nitrate the pyrazine ring have been unsuccessful apparently due to the stability of the pyrazine nucleus. Further, the pyrazine ring is quite easily reduced which eliminates the possibility of employing methods which involve the reduction of other substituent groups (*e. g.*, NO, NHOH, CN).

The possibility of employing the reaction of ammonia on a halogen substituted pyrazine in the presence of a suitable condensing agent is not very hopeful since the halogen compounds are reported to be extremely unstable, liberating halogen upon mere standing.

The introduction of the amino group directly by the use of sodamide has been suggested. Some work in this direction is reported in the literature. Tschitschibabin and Shukina[2] have investigated the action of sodamide on 2,5-dimethylpyrazine in xylene. They were able to isolate among other products a small quantity of 3-amino-2,5-dimethylpyrazine. The yield, however, is poor and the product not entirely satisfactory for coupling reactions. Bergstrom and Ogg[3] found that potassium amide in liquid ammonia solution attacks pyrazine but were unable to isolate any definite product.

(1) Paper read at the Rochester meeting of the A. C. S., *Division of Organic Chemistry*, September 9, 1937.

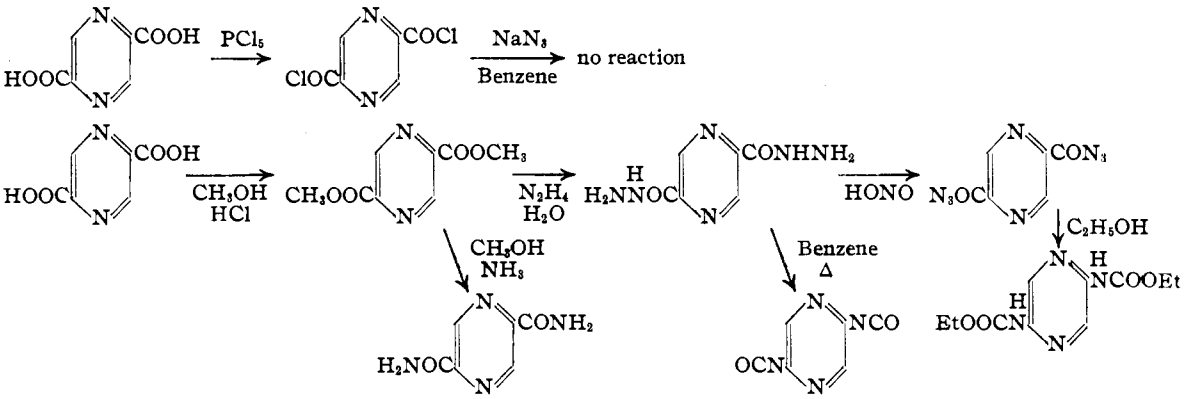
(2) Tschitschibabin and Shukina, *C. A.*, **25**, 2728 (1931); *J. Russ. Phys.-Chem. Soc.*, **62**, 1189–99 (1930).

(3) Bergstrom and Ogg, THIS JOURNAL, **53**, 249–250 (1931).

Most of the earlier work on pyrazine compounds involved identification by the preparation first of the various double salts characteristic of organic bases and second the corresponding carboxylic acids by oxidation of side-chains.

In view of the fact that information on the acids was available it appeared desirable to investigate the possibility of applying the Curtius and Hofmann rearrangement reactions for the conversion of the carboxyl into the amino group.

Three methods were employed in the attempt to carry out this conversion, the modified Curtius, the standard Curtius and the Hofmann reactions, as illustrated in the following diagram



In the Curtius reactions all the steps took place smoothly with good yields with the exception of the final reaction. Both the urethan and the isocyanate proved to be stable toward hydrolytic agents. The urethan could not be converted into the amine by fuming hydrochloric acid in a bomb tube or by concd. potassium hydroxide. The isocyanate was stable toward fuming hydrochloric acid and potassium hydroxide.

In attempting the Hofmann degradation the amide was found to be stable toward both hypochlorous and hypobromous acids.

Experimental

Preparation of Diacid Chloride of Pyrazine-2,5-dicarboxylic Acid.—Two-tenths gram of dicarboxylic acid was heated with 0.5 g. of phosphorus pentachloride in an oil-bath at 110–115° for one hour. The reaction mixture liquefied when heated. On cooling, yellow needle-like crystals form. The phosphorus oxychloride was distilled off *in vacuo* on a water-bath and the residue dried *in vacuo*. The crude acid chloride was purified by sublimation; m. p. 143–144°.

Anal. Calcd. for $C_6H_2O_2N_2Cl_2$: C, 35.12; H, 0.98; N, 13.66. Found: C, 35.20, 35.10; H, 1.25, 1.26; N, 13.38.

Action of Sodium Azide on Acid Chloride.—To a solution of 0.3 g. of acid chloride in 15 cc. of dry benzene, 0.55 g. of sodium azide was added. The reaction mixture was heated on a water-bath at 80° for one hour. Two cc. of the benzene solution was evaporated to dryness *in vacuo*. The solid residue melted at 143–144° (unconverted acid chloride).

Preparation of Dimethyl Ester of Pyrazine-2,5-dicarboxylic Acid.—One hundred cc. of absolute methanol was saturated with dry hydrogen chloride gas. Three grams of dicarboxylic acid was added and refluxed on a water-bath for twenty minutes while passing through a stream of dry hydrogen chloride. The acid dissolves after a few minutes. After standing overnight, the reaction mixture was concentrated *in vacuo*, chilled, filtered and the ester washed with ether and dried *in vacuo*. The ester can be purified by recrystallization from methanol: yield 2.88 g.; m. p. 168–169° (sealed cap).

Anal. Calcd. for $C_8H_8O_4N_2$: C, 48.98; H, 4.08; N, 14.29. Found: C, 49.18, 49.04; H, 4.24, 4.08; N, 14.13, 14.35.

Preparation of Dihydrazide of Pyrazine-2,5-dicarboxylic Acid.—One gram of the dimethyl ester was dissolved in 20 cc. of methanol and to the hot solution was added 15 cc. of hydrazine hydrate (42% soln.). The hydrazide precipitated almost immediately as a yellow flaky solid. The mixture was refluxed for one-half hour on a water-bath. After standing overnight, the hydrazide was filtered off, digested in a large volume of 95% alcohol, filtered, washed with ether, and dried *in vacuo*; yield 0.97 g.; m. p. 270°.

Anal. Calcd. for $C_6H_8N_6O_2$: C, 36.73; H, 4.08; N, 42.86. Found: C, 36.94, 37.06; H, 4.38, 4.20; N, 42.37.

Preparation of Diazide of Pyrazine-2,5-dicarboxylic Acid.—Two grams of sodium nitrite was dissolved in 15 cc. of water; 0.97 g. of the hydrazide was suspended in this solution and the mixture cooled in an ice-bath. Ten cc. of 5 *N* hydrochloric acid was added dropwise while the reaction mixture was kept at 0–5°. A white flocculent precipitate formed immediately. The mixture was allowed to stand in an ice-bath for five minutes, and then the azide was filtered off, washed thoroughly with ice water, and dried *in vacuo* over potassium hydroxide and sulfuric acid; yield 0.98 g. The dried material decomposes violently at 133–134°.

Anal. Calcd. for $C_6H_2O_2N_8$: C, 33.03; H, 0.92. Found: C, 33.35, 33.48; H, 1.33, 1.38.

Preparation of Diurethan of Pyrazine-2,5-dicarboxylic Acid.—Seventy-seven hundredths gram of the dried azide was suspended in 200 cc. of absolute ethanol and warmed gradually in a water-bath to boiling. It was then refluxed for one hour during which time the azide dissolved. The mixture was evaporated *in vacuo* to a small volume, cooled, filtered, and dried *in vacuo*; yield 0.70 g.; m. p. above 270°. The crude product was purified by digesting in a large volume of absolute ethanol, filtering, washing with ether and drying *in vacuo*.

Anal. Calcd. for $C_{10}H_{14}O_4N_4$: C, 47.24; H, 5.51; N, 22.05. Found: C, 47.20, 47.37; H, 5.80, 5.89; N, 22.29, 22.76.

A series of experiments attempting to hydrolyze the urethan included the following methods

(1) Urethan + fuming hydrochloric acid in bomb tube at 110° for four hours
(2) Urethan + fuming hydrochloric acid in bomb tube at 150° for fifteen hours
(3) Urethan + fuming hydrochloric acid in bomb tube at 210° for fifteen hours
(4) Urethan + alcoholic potassium hydroxide, refluxed on water-bath for two hours
(5) Urethan + concd. sulfuric acid
(6) Urethan + solid potassium hydroxide, fused and steam distilled

Preparation of Diisocyanate of Pyrazine-2,5-dicarboxylic Acid.—Seven-tenths gram of dried azide was suspended in 250 cc. of dry benzene and warmed on a water-bath to boiling. After refluxing for two hours, the mixture was concentrated *in vacuo*, cooled and filtered. The yellow amorphous isocyanate was washed with ether and dried *in vacuo*; yield 0.48 g.; m. p. 250°. A sample for analysis was digested in a large volume of dry benzene, filtered, washed twice with ether and dried *in vacuo*.

Anal. Calcd. for $C_6H_2O_2N_2$: C, 44.44; H, 1.24. Found: C, 44.15, 44.06; H, 1.89, 1.70.

Preparation of Diamide of Pyrazine-2,5-dicarboxylic Acid.—One gram of dimethyl ester was dissolved in 50 cc. of hot absolute methanol and refluxed for one-half hour while passing through a stream of ammonia. The reaction mixture was chilled in an ice-bath, saturated with ammonia, and allowed to stand overnight. The mixture was concentrated *in vacuo* on a water-bath, chilled, and the white amorphous amide filtered off and dried *in vacuo*; yield 0.75 g.; m. p. above 270°.

Anal. Calcd. for $C_6H_6O_2N_4$: C, 43.37; H, 3.61 Found: C, 43.75, 44.00; H, 3.95, 3.73.

Summary

In an attempt to apply the Curtius and Hofmann rearrangements to the pyrazine series, the intermediate products characteristic of these series of reactions have been isolated in pure form.

Starting with the known pyrazine-2,5-dicarboxylic acid, the following new derivatives have been prepared and described: (1) dimethyl ester, (2) dihydrazide, (3) diazide, (4) diurethan, (5) diisocyanate, (6) diamide, (7) diacid chloride.

BROOKLYN, N. Y. RECEIVED DECEMBER 4, 1937

[A COMMUNICATION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

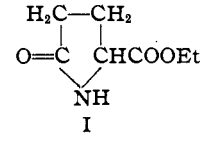
The Selective Hydrogenation of Substituted Amides

BY JOHN C. SAUER AND HOMER ADKINS

Hydrogen under 100 to 300 atm. reacts with amides in dioxane at 200–260° under the influence of copper–chromium oxide to give amines.[1] Alkenes, ketones, aldehydes, cyanides, oximes, furanoid and pyridinoid nuclei react with hydrogen under much less drastic conditions so that among the unsaturated groups probably only benzenoid and pyrroloid nuclei and perhaps carbalkoxy groups will remain unchanged during the hydrogenation of an amide. The study reported herewith is primarily concerned with the behavior toward hydrogen of several compounds which are amido or carbethoxy pyrrolidones, piperidones, or quinolones. The objective of the investigation has been to ascertain the relationship of structure to the relative reactivity with hydrogen of the amide and ester groups concerned. The results are summarized in Table I.

(1) Wojcik and Adkins, THIS JOURNAL, **56**, 2419 (1934); Paden and Adkins, *ibid.*, **58**, 2487 (1936).

Pyrrolidones.—5-Carbethoxypyrrolidone-2, I, was hydrogenated rapidly, the ester group being converted in 93% yield to a carbinol group, II, without any reaction occurring at the amide group.



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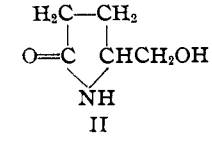
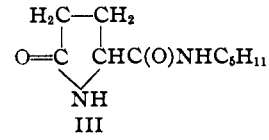
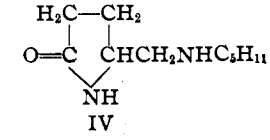


II

In a similar fashion the side chain amide group in 5-amylcarbamylpyrrolidone-2, III, was hydrogenated in preference to the lactam group in the ring, the chief product in 68% yield being 5-amylaminomethylenepyrrolidone-2, IV. The minor



III



IV