the residue was crystallized from methanol–water. Colorless prisms (328 mg.) were obtained, which softened to a bubbly mass at 165–175° and liquefied gradually until a meniscus formed at 205–208°, $[\alpha]^{24}D$ +12° (*c* 1.47, alc.). The infrared spectrum of the product in chloroform was identical with the spectrum of a sample of pseudogermine prepared by the procedure of Pelletier and Jacobs.[10]

Isomerization of Isogermine to Pseudogermine with Alcoholic Sodium Ethoxide.—Isogermine[8a] (200 mg.) was treated with alcoholic sodium ethoxide by the procedure described above. Crystallization of the crude reaction product from methanol–water gave pseudogermine (54 mg.), characterized by mixed melting point, rotation and infrared spectral comparison with an authentic sample.

Pseudogermine Acetonide.—Pseudogermine (700 mg.) was dissolved in a small volume of absolute alcohol by the addition of sufficient hydrochloric acid (1:1) to turn congo red. After addition of acetone (3 ml.), rubbing induced crystallization, and 615 mg., m.p. 280–283° dec., was obtained. Recrystallization from absolute alcohol gave pseudogermine acetonide hydrochloride in the form of colorless plates, m.p. 283–284° dec.

Anal. Calcd. for $C_{30}H_{47}O_8N \cdot HCl \cdot H_2O$: C, 59.63; H, 8.34. Found: C, 59.86; H, 8.44.

The hydrochloride (214 mg.) was dissolved in water (6 ml.) and the solution was made alkaline with 20% sodium carbonate solution and extracted with chloroform (six 10-ml. portions). The chloroform extract was washed with water (10 ml.), dried over sodium sulfate, and evaporated to dryness *in vacuo*. Crystallization from the same solvents gave translucent plates (71 mg.), m.p. 237–239° dec., $[\alpha]^{23}D$ +27° (*c* 1.51, alc.).

Anal. Calcd. for $C_{30}H_{47}O_8N$: C, 65.53; H, 8.62. Found: C, 65.46; H, 8.65.

Periodate Oxidation of Pseudogermine Acetonide Hydrochloride.—Pseudogermine acetonide hydrochloride (587 mg.) was oxidized with potassium periodate solution by the procedure described for the oxidation of germine acetonide hydrochloride. Crystallization of the crude product from acetone–ether yielded the aldehydo-γ-lactone (182 mg.) obtained earlier from germine acetonide hydrochloride. The identity of the two products was demonstrated by mixed m.p. and infrared spectral comparisons of the respective samples of aldehydo-γ-lactone and oxime.

Germine Tetraacetate.—A mixture of anhydrous germine (1 g.), acetic anhydride (20 ml.) and pyridine (20 ml.) was heated on the steam-bath for two hours. Evaporation of the excess reagents *in vacuo* at room temperature left an amorphous solid, which was dissolved in water (7 ml.). The solution was made alkaline with ammonia and extracted with chloroform (seven 25 ml. portions). The chloroform extract was washed with water (10 ml.), dried over sodium sulfate, and evaporated to dryness *in vacuo*. The residue crystallized from acetone; yield 938 mg., m.p. 248–251° dec. Two further recrystallizations from the same solvent afforded colorless prisms, m.p. 260–261° dec., $[\alpha]^{23}D$ −98° (*c* 1.57, py.).

Anal. Calcd. for $C_{27}H_{39}O_8N\ (COCH_3)_4$: C, 62.02; H, 7.59; acetyl, 25.40. Found: C, 61.77; H, 7.50; acetyl, 25.22.

The same product was obtained by room-temperature acetylation with acetic anhydride–pyridine[2a] and by heating with acetic anhydride alone for two hours.

Isogermine Tetraacetate.—Isogermine (400 mg.) was acetylated with acetic anhydride and pyridine as described above for germine. The crude product crystallized from ether–petroleum ether. Recrystallization from the same solvents afforded small needles (136 mg.), m.p. 222–226° dec., $[\alpha]^{24}D$ −80° (*c* 1.63, py.).

Anal. Calcd. for $C_{27}H_{39}O_8N(COCH_3)_4$: C, 62.02; H, 7.59; acetyl, 25.40. Found: C, 61.69; H, 7.49; acetyl, 25.85.

Pseudogermine Tetraacetate.—Pseudogermine (400 mg.) was acetylated with acetic anhydride and pyridine by the procedure described above for germine. The crude product crystallized from ether (U.S.P.)–petroleum ether. Recrystallization from the same solvents gave a micro-crystalline solid (140 mg.), m.p. 190–210°, $[\alpha]^{24}D$ −59° (*c* 1.70, py.).

Anal. Calcd. for $C_{27}H_{39}O_8N(COCH_3)_4 \cdot H_2O$: C, 60.41; H, 7.68; acetyl, 24.75. Found: C, 60.34; H, 7.29; acetyl, 24.44.

Dihydrogermine Pentaacetate.—Dihydrogermine[8b] (300 mg.) was acetylated with acetic anhydride and pyridine by the procedure described above for germine. The crude product crystallized from chloroform–ether. Two recrystallizations from acetone afforded clusters of prisms (191 mg.), m.p. 284–285° dec., $[\alpha]^{28}D$ −64° (*c* 1.41, py.).

Anal. Calcd. for $C_{27}H_{40}O_8N(COCH_3)_5$: C, 61.56; H, 7.68; acetyl, 29.82. Found: C, 61.51; H, 7.68; acetyl, 29.82.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE POLYTECHNIC INSTITUTE OF BROOKLYN]

The Decarboxylation of Pyrazinium Betaine Salts[1]

BY EUGENE V. HORT AND PAUL E. SPOERRI

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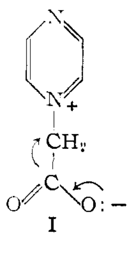
Betaine salts containing the pyrazinium nucleus decompose extremely readily with loss of carbon dioxide. The products of this decomposition with 2,5-dimethylpyrazine are 1-alkyl-2,5-dimethylpyrazinium salts.

In the course of a study on the quaternization of 2,5-dimethylpyrazine (DMP), the reaction with α-haloacids was found to proceed in an unusual manner. The expected betaine salts could not be isolated. Even at room temperature, carbon dioxide was evolved and only decarboxylated quaternary salts obtained. This ease of decarboxylation contrasts sharply with the stability normally exhibited by betaine salts. For example, 1-carboxymethylpyridinium bromide[2] and carboxymethyltrimethylammonium bromide[3] are reported to melt with decomposition at 200 and 233°, respectively.

It is possible to explain the unusual ease of decarboxylation of the pyrazinium compounds on the basis of resonance stabilization of the decarboxylation intermediate. The loss of carbon dioxide from a betaine molecule I leaves a negatively charged methylene group on the quaternary nitrogen II. This can be stabilized by a form III in which the negative charge is borne by the comparatively electronegative nitrogen atom.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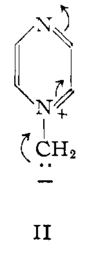
II


III

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[1] From the Ph.D. Thesis of E. V. Hort, June, 1950.

[2] M. Krüger, *J. prakt. Chem.*, [2] **43**, 280 (1891).

[3] H. Stoltzenberg, *Z. physiol. Chem.*, **92**, 471 (1914).

With the pyridinium analog, the negative charge must be borne by a carbon atom, and with the trimethylammonium analog no such resonance is possible.

The reaction of DMP with iodoacetic and bromoacetic acids alone or in various solvents gave 1,2,5-trimethylpyrazinium halides. Chloroacetic acid did not react at room temperature and gave carbon dioxide and tarry products at elevated temperatures. α-Bromopropionic acid gave 1-ethyl-2,5-dimethylpyrazinium bromide but only at an extremely slow rate at room temperature. The α-halobutyric acids and higher homologs were virtually unreactive. These reactions were all performed with an excess of DMP because it was observed that when excess bromoacetic acid was used the reaction quickly developed a deep red color. The reaction rate was much more rapid in polar than in non-polar solvents; acetic acid was particularly effective as a solvent.

Unsubstituted pyrazine reacted with bromoacetic acid and evolved carbon dioxide at a rate comparable to that obtained with DMP. However, a black material, not further identified, was obtained instead of the methyl quaternary salt. Quinoxaline, too, evolved carbon dioxide with bromoacetic acid and gave an unidentified tarry product.

Experimental

Materials.—The DMP used was first dried over barium oxide for several days and then distilled. The haloacids used were all dried *in vacuo* over phosphorus pentoxide.

Apparatus and Procedure.—A slow stream of nitrogen was used to sweep out a reaction and absorption train. After passing through a tube containing ascarite and then drierite the nitrogen bubbled through the contents of the reaction flask. The gases then passed through a drierite tube, a Fisher Absorption Bottle,[4] another drierite tube and a bubble counter. At intervals, the sweeping stream was stopped and the absorption bottle briefly removed from the train and weighed. When the train was used at higher than room temperature, a reflux condenser was employed with the reaction flask.

Reaction of DMP with Iodoacetic Acid.—A solution of 6.8 g. (0.0365 mole) of iodoacetic acid in 59 g. (0.56 mole) of DMP was allowed to react at room temperature in the absorption train. After 46.6 hours, 0.464 g. of carbon dioxide was evolved, indicating the reaction was 28.8% complete. The precipitate of pale yellow needles which had gradually formed did not adhere to the walls of the apparatus and was easily quantitatively transferred. The weight of precipitate, after washing with benzene and then acetone and drying, was 2.609 g. (0.0104 mole as the methyl iodide quaternary). This corresponds well to the 0.464 g. (0.0105 mole) of carbon dioxide collected. The precipitate melted with decomposition at 235° (reported 230° dec.[5]). An analytical sample was prepared by recrystallization from propanol.

Anal.[6] Calcd. for $C_7H_{11}N_2I$: C, 33.62; H, 4.43; N, 11.20. Found: C, 33.52; H, 4.37; N, 11.05.

Reaction of DMP with Bromoacetic Acid.—A solution of 8.34 g. (0.060 mole) of bromoacetic acid in 75 g. (0.695 mole) of DMP was allowed to react at room temperature in the absorption train. After 99.3 hours, 1.009 g. of carbon dioxide was evolved, indicating the reaction was 38.2% complete. The tan-white crystals which had started to form within an hour adhered to the walls of the flask and were not quantitatively transferred; yield 4.1 g. (33.6%), m.p. 222° dec. An analytical sample was recrystallized from butanol.

Anal. Calcd. for $C_7H_{11}N_2Br$: C, 41.39; H, 5.46; N, 13.80. Found: C, 41.29; H, 5.60; N, 14.01.

Comparison of Reaction Rates in Benzene and in Nitrobenzene.—A solution of 10.12 g. (0.0728 mole) of bromoacetic acid and 8.4 g. (0.0778 mole) of DMP in 65 ml. of dry benzene was allowed to react at room temperature in the absorption train. The reaction rate was very slow, and in 188 hours only 0.247 g. (7.8%) of carbon dioxide was evolved.

Under similar conditions, a solution of 9.71 g. (0.0698 mole) of bromoacetic acid and 7.8 g. (0.0722 mole) of DMP in 62 ml. of freshly distilled nitrobenzene reacted much more rapidly, with 0.783 g. (25.5%) of carbon dioxide evolved in 146.5 hours.

With either solvent, 1,2,5-trimethylpyrazinium bromide was obtained in only slightly less than equivalent (based on carbon dioxide) yield.

Quaternization and Decarboxylation in Glacial Acetic Acid.—Solutions of bromoacetic acid and DMP in water or alcohols reddened when standing even when cold. Glacial acetic solutions reddened only slowly even when heated.

A solution of 10.1 g. (0.0726 mole) of bromoacetic acid and 9.7 g. (0.0898 mole) of DMP in 25 ml. of glacial acetic acid was heated on a steam-bath for 2.5 hours. The clear red solution was cooled and 75 ml. of ether added; yield of pale pink precipitate of impure 1,2,5-trimethylpyrazinium bromide, ether washed and air dried, 12.8 g. (87%), m.p. 212° dec.

Reaction of DMP with α-Bromopropionic Acid.—A solution of 9.3 g. (0.0608 mole) of α-bromopropionic acid in 30 g. (0.278 mole) of DMP was allowed to react at room temperature in the absorption train. The rate of reaction was very slow, with 0.020 g. of carbon dioxide corresponding to 0.75% reaction in 25.2 hours. Only a few small crystalline conglomerates formed on the walls of the flask.

The temperature of the reaction was then raised to 95–100°. Tan crystals formed steadily and carbon dioxide was evolved.

After 24 hours, 0.581 g. (21.7%) of carbon dioxide had been collected; yield 2.1 g. (15.9% as 1-ethyl-2,5-dimethylpyrazinium bromide). On recrystallizing from methanol-ether, 1.8 g. (13.6%) of fine tan needles, m.p. 182° dec., was obtained. This gave no depression in a mixed melting point with the quaternary salt from ethyl bromide and DMP.

Anal. Calcd. for $C_8H_{13}N_2Br$: N, 12.90. Found: N, 13.13.

Reaction of DMP with Chloroacetic Acid.—Chloroacetic acid gave no visible reaction or decarboxylation at room temperature. At 95–100°, about 5% of the theoretical of carbon dioxide was collected in 3 hours and a tarry black precipitate was formed.

Reaction of DMP with Halobutyric Acids.—Neither bromobutyric nor iodobutyric acids dissolved in DMP gave precipitates or evolved carbon dioxide at room temperature. A small amount of carbon dioxide, about 1% after 4 hours, was obtained with iodobutyric acid in DMP at 95–100°. This was accompanied by a small amount of tarry black precipitate.

Reaction of Pyrazine with Bromoacetic Acid.—A solution of 6.25 g. (0.0450 mole) of bromoacetic acid and 3.732 g. (0.0466 mole) of pyrazine in 45 ml. of freshly distilled nitrobenzene was allowed to react at room temperature in the reaction train. A fine dark brown sludge formed steadily. In 45.0 hours, 0.216 g. (10.9%) of carbon dioxide was evolved. The precipitate was filtered with suction and washed with acetone. It was virtually insoluble in alcohols (even in methanol). It was not decolorized by boiling in aqueous solution with charcoal. On adding excess acetone to the brown aqueous solution the dark brown precipitate was recovered. It turned tarry while air-drying on the filter paper; estimated yield 1 g.

Reaction of Quinoxaline with Bromoacetic Acid.—Mixtures of quinoxaline and bromoacetic acid in the melt bubbled above 60° and gave a tarry product. Solutions of quinoxaline and bromoacetic acid in minimum amounts of acetone or ethanol slowly evolved carbon dioxide and formed black tars from which no crystalline components could be separated.

WESTFIELD, N. J.

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[4] H. L. Fisher, "Laboratory Manual of Organic Chemistry," 4th Ed., John Wiley and Sons, Inc., New York, N. Y., 1938, p. 307.

[5] C. Stoehr, *J. prakt. Chem.*, [2], **47**, 462 (1893).

[6] All analyses were performed by R. E. Schachat in the Brooklyn Polytechnic Microanalytical Laboratory.