ally; periods of a day or night at 110, 320 and 540° were adequate when followed by ten-minute heatings to constant weight at about 800°. These analyses showed that the ratio of sodium to acid hydrogen was 0.500 ± 0.001 for the monosodium salt, and 2.002 ± 0.001 for the disodium salt. The analyses also indicated a formula weight of 215.4 for the monosodium salt and 263.5 for the disodium salt. The former figure is somewhat more than 214.1, the formula weight of anhydrous monosodium citrate, while the latter figure indicates that the disodium salt contained 1.5 moles of water, which would make the calculated value 263.1. The air-dried preparations of both salts lost less than 0.5% in weight at 70 or 110°, and also remained constant in weight when kept over a saturated sodium chloride solution at room temperature. The monosodium salt became caked on standing in a stoppered bottle, but titration of the caked material did not reveal any absorption of moisture. The disodium salt could be dried more rapidly after washing with 95% alcohol, which did not remove the 1.5 moles of water. Alcohol withdrew a little acid from the monosodium salt. None of the preparations of either salt had the composition of the monohydrates reported by Heldt[1] and Salzer.[2]

These acid citrates differ from many other acid salts, such as the phosphates, in one important respect. Either of the acid citrates by itself forms a well buffered solution in water. The following *p*H values were obtained for 0.1 and 0.01 *M* solutions at 25°: monosodium citrate, 3.70 and 3.88; disodium citrate, 4.96 and 5.30, respectively. These values, which were checked within 0.003 *p*H with solutions made from three different preparations of each salt, were obtained by means of a carefully tested glass electrode in a water-jacketed cell with liquid junction, similar to that described in a previous paper.[4] They are based on a *p*H value of 4.008 for 0.05 *M* potassium acid phthalate.

Reliable solutions may also be obtained, without isolating the acid salts, from carefully standardized solutions of citric acid and sodium hydroxide, according to Sörensen.[5]

---

(4) D. I. Hitchcock and A. C. Taylor, This Journal, **59**, 1812 (1937).

(5) S. P. L. Sörensen, *Biochem. Z.*, **21**, 131 (1909).

Laboratory of Physiology
Yale University School of Medicine
New Haven, Connecticut
Received December 5, 1945

Studies on the Willgerodt Reaction. I. Some Extensions of the Reaction

By John A. King and Freeman H. McMillan

Nearly sixty years ago Willgerodt[1,2] discovered the reaction which has come to bear his name: treatment of an aliphatic aromatic ketone with yellow ammonium sulfide at a moderately high temperature in a sealed tube to effect the transformation of the ketone to an aralkyl amide. Until Cavalieri, Pattison and Carmack[3] announced, last October, their application of the reaction to purely aliphatic and to alicyclic–aliphatic ketones, the assumption had always been implied that the reaction was confined to aromatic–aliphatic ketones. We have likewise found that this assumed restriction does not exist.

$$\mathrm{C_6H_5COCH_3} \xrightarrow{\mathrm{(NH_4)_2S_x}} \mathrm{C_6H_5CH_2CONH_2}$$

When phenylacetone was treated with yellow ammonium sulfide under the same conditions as used by Willgerodt and Merk[4] for propiophenone the product was β-phenylpropionamide.

$$\begin{tikzcd} \mathrm{C_6H_5CH_2COCH_3} \arrow[r, "\mathrm{(NH_4)_2S_x}"] & \mathrm{C_6H_5CH_2CH_2CONH_2} & \mathrm{C_6H_5COCH_2CH_3} \arrow[l, "\mathrm{(NH_4)_2S_x}"'] \end{tikzcd}$$

After it was thus shown that the carbonyl group of the ketone did not need to be adjacent to the aromatic ring for the reaction to occur, it seemed of interest to determine if compounds of the next lower state of oxidation would undergo the reaction. It was found that both phenylmethylcarbinol and its dehydration product, styrene, gave phenylacetamide in approximately the same yield as did acetophenone, under the conditions of Willgerodt and Merk.[4]

$$\begin{tikzcd} \mathrm{C_6H_5COCH_3} \arrow[dr] & \mathrm{C_6H_5CHOHCH_3} \arrow[d] & \mathrm{C_6H_5CH{=}CH_2} \arrow[dl] \\ & \mathrm{C_6H_5CH_2CONH_2} & \end{tikzcd}$$

Work on this reaction is being continued.

Experimental[5]

Yellow ammonium sulfide was prepared according to the directions of Willgerodt and Merk. Concentrated ammonium hydroxide (200 cc.) was saturated at room temperature with hydrogen sulfide. To the solution, which weighed 244 g., there was added 24.4 g. of sulfur, which was stirred into solution.

Phenylacetone was prepared by the method used by Baker[6] for 1-anisyl-2-butanone. The same material was also prepared much more easily by the method of Magidson and Garkusha.[7] When the preparation was carried out on a scale four times as large as reported by Magidson and Garkusha there was obtained, in addition to phenylacetone, b. p. 88–92° (6 mm.), 37 g. of a fraction, b. p. 171–179° (6 mm.), which gave an oxime, m. p. 119–122°. The oxime of *s*-diphenylacetone is variously reported[8] to melt from 118 to 125°.

Phenylmethylcarbinol was prepared by aluminum isopropoxide reduction of acetophenone, by the procedure of Lund[9]; the product boiled at 77–81° (5 mm.).

The styrene used was Eastman Kodak Co. White Label material.

Phenylacetone and Ammonium Polysulfide.—Phenylacetone (3.0 g.) and ammonium polysulfide (15 g.) were heated for five hours at 210 ± 5° in a pressure tube.[10] The solid material removed from the tube weighed 2.0 g. (60% crude) and melted at 86–89°; two recrystallizations of the material from water raised its melting point to 101.5°. When it was mixed with an authentic sample of

---

(1) Willgerodt, *Ber.*, **20**, 2467 (1887).

(2) Willgerodt, *ibid.*, **21**, 534 (1888).

(3) Cavalieri, Pattison and Carmack, This Journal, **67**, 1783 (1945).

(4) Willgerodt and Merk, *J. prakt. Chem.*, [2] **80**, 192 (1909).

(5) Melting points and boiling points are uncorrected.

(6) Baker, This Journal, **65**, 1576 (1943).

(7) Magidson and Garkusha, *J. Gen. Chem., U. S. S. R.*, **11**, 339 (1941); *C. A.*, **35**, 5868 (1941).

(8) Beilstein, "Handbuch der organischen Chemie," 4th ed., **7**, 446 (1925); First Supplement, **7–8**, 238 (1931).

(9) Lund, *Ber.*, **70B**, 1520 (1937).

(10) The tube used was of a design suggested by Dr. J. S. Buck, Associate Director of Chemical Research of these Laboratories. An ordinary 13-inch Pyrex Carius tube was drawn down on the open end and had sealed to it an 8-inch length of 10-mm. OD-5 mm. ID Pyrex tubing. After the tube was filled the smaller tube was sealed on the end. A pressure tube of this type can be used six or eight times before another length of the smaller tubing needs to be sealed on and can be used a great many times, as contrasted with the ordinary Carius tube which has a relatively short life.

β-phenylpropionamide,[11] m. p. 100–100.5°, the mixture melted at 100.5–101°.

Phenylmethylcarbinol and Ammonium Polysulfide.—Phenylmethylcarbinol (3.0 g.) and ammonium polysulfide (15 g.) were heated four hours at 210 ± 5° in a pressure tube. The solid material was removed by filtration and the mother liquor was extracted with ether from which there was obtained more of the product. The crude product (wt. 1.6 g., 48% yield, crude) was recrystallized once from water to give white plates, m. p. 156.5–157°, undepressed when mixed with an authentic sample of phenylacetamide.

Styrene and Ammonium Polysulfide.—Styrene (3.0 g.) and ammonium polysulfide (15 g.) were heated four hours at 210 ± 5° in a pressure tube. The crude product, isolated as above, weighed 1.64 g. (49% yield, crude); after recrystallization from water it melted at 156–157°, undepressed when mixed with an authentic sample of phenylacetamide.

---

[11] Conrad, *Ann.*, **204**, 174 (1880); Hofmann, *Ber.*, **18**, 2740 (1885).

RESEARCH LABORATORIES
WINTHROP CHEMICAL COMPANY, INC.
RENSSELAER, NEW YORK
RECEIVED AUGUST 23, 1945

Preparation of 6-Methylpyrazine-2-carboxylic Acid

BY FREDERICK LEONARD AND PAUL E. SPOERRI

In the course of our studies on pyrazine carboxylic acids it was of interest to prepare the 6-methylpyrazine-2-carboxylic acid. The related acid, 5-methylpyrazine-2,3-dicarboxylic acid, obtained by the oxidation of 2-methylquinoxaline had been described by Böttcher in 1913.[1] By considerable modification of Böttcher's oxidation procedure, followed by decarboxylation, we have been able to prepare the desired 6-methylpyrazine-2-carboxylic acid in satisfactory yields.

The mono carboxylic acid melted sharply at 138° with decomposition. Since Stoehr[2] found that 5-methylpyrazine-2-carboxylic acid melts at 200°, the substance we obtained can only be the isomeric 6-methylpyrazine-2-carboxylic acid.

Experimental

5-Methylpyrazine-2,3-dicarboxylic Acid.—Twenty-eight and eight-tenths grams of 2-methylquinoxaline was dissolved in 2400 cc. of water containing 8 g. of potassium hydroxide. To this solution at 50°, a solution of 176 g. of potassium permanganate in 1600 cc. of water, preheated to 50°, was added dropwise with good stirring. The addition took about two and one-half hours. The mixture was heated for an additional hour, 50 cc. of alcohol was added and heating continued for a half hour more. The filtrate from the manganese dioxide was concentrated to about 1 liter, made alkaline with concentrated ammonia, and a solution of 142 g. of calcium nitrate tetrahydrate in 200 cc. of water added. After the mixture had been digested on a steam-bath for one hour, the calcium oxalate was filtered off and washed with water. The combined filtrate and washings were made acid to congo red with 1:1 nitric acid and precipitated with a solution of 68 g. of silver nitrate in 200 cc. of water. The precipitated silver salt was filtered by suction and washed with water. It was suspended in water, acidified with acetic acid and treated with hydrogen sulfide at 60° with constant stirring for one and one-half hours. The silver sulfide was filtered off and washed. The combined filtrate and washings were partially decolorized with Norit A and evaporated to dryness *in vacuo* to yield 11 g. (39% yield) of 5-methylpyrazine-2,3-dicarboxylic acid, m. p. 163–164°. Recrystallized from an alcohol-ether mixture, the compound melted at 174–175°. It titrated as a strong acid and had a neutral equivalent of 93.0 (determined by potentiometric titration); calcd. 91.1. Aqueous solutions of this acid gave deep wine red colorations with ferrous sulfate.

Anal. Calcd. for $C_7H_6O_4N_2$: C, 46.15; H, 3.32; N, 15.36. Found: C, 46.40; H, 3.69; N, 14.33.

S-Benzylthiuronium salt prepared according to Donleavy[3]; m. p. 203–204°, after recrystallization from aqueous alcohol.

Anal. Calcd. for $C_{23}H_{26}O_4N_6S_2$: C, 53.65; H, 5.09; N, 16.34; S, 12.45. Found: C, 53.40; H, 5.09; N, 16.65; S, 12.10.

6-Methylpyrazine-2-carboxylic Acid.—One gram of 5-methylpyrazine-2,3-dicarboxylic acid was placed in a vacuum sublimation apparatus and was decarboxylated by heating to 175–185° at 1 mm. with simultaneous sublimation to yield 0.6 g. (82%) of 6-methylpyrazine-2-carboxylic acid, m. p. 135–140°. After two resublimations at 100–110° (1 mm.) the compound melted sharply at 138–140° (turbid melt which became clear at 144 with the evolution of a gas). Neutral equivalent by potentiometric titration was 136; calcd. 138. The ferrous sulfate color test gave orange coloration.

Anal. Calcd. for $C_6H_6O_2N_2$: C, 52.19; H, 4.38; N, 20.29. Found: C, 52.31; H, 4.21; N, 20.21.

---

[1] Böttcher, *Ber.*, **46**, 3084 (1913).

[2] Stoehr, *J. prakt. Chem.*, [2] **47**, 480 (1893).

[3] Donleavy, THIS JOURNAL, **58**, 1004 (1936).

CHEMISTRY DEPARTMENT
POLYTECHNIC INSTITUTE OF BROOKLYN
BROOKLYN 2, NEW YORK
RECEIVED OCTOBER 5, 1945

Interaction Energies and Thermochemical Data

BY JOHN R. LACHER[1]

Recently Aston, *et al.*,[2] have been able to calculate empirically the height of potential barriers hindering internal rotation. They assumed that the barrier was due to a repulsion between hydrogen atoms. Urey and Bradley,[3] in discussing the normal vibrations of carbon tetrachloride and similar compounds, found it necessary to assume the existence of repulsive forces between the atoms situated at the corners of a tetrahedron. These latter forces were in addition to those directed along and perpendicular to the chemical bonds. H. A. Stuart,[4] V. Deitz,[5] R. Serber,[6] and E. Mack[7] have already indicated that interaction energy due to the repulsion (and in some situations certainly due to the attraction) of certain groups should be taken into account in the interpretation of thermochemical data. It is desired here to illustrate and develop this idea further in connection with groups arranged tetrahedrally

---

[1] Present address: Department of Chemistry, University of Colorado, Boulder, Colorado.

[2] J. G. Aston, S. Isserow, G. J. Szasz and R. M. Kennedy, *J. Chem. Phys.*, **12**, 336 (1944).

[3] H. C. Urey and C. A. Bradley, Jr., *Phys. Rev.*, **38**, 1969 (1931).

[4] H. A. Stuart, *ibid.*, **38**, 1372 (1938).

[5] V. Deitz, *J. Chem. Phys.*, **3**, 58, 436 (1935).

[6] R. Serber, *ibid.*, **3**, 81 (1935).

[7] E. Mack, Jr., *J. Phys. Chem.*, **41**, 221 (1937).