senting some sort of competitive effect in a system one of the components of which was perhaps a serine-containing peptide. The serine which showed the effect was racemic (DL) and it was recently suggested to us by Dr. E. Brand that the action might be different with the D and L forms of the amino acid. Through the courtesy of Drs. Brand, Folch-Pi, and du Vigneaud two specimens of pure L-serine and one of D-serine were made available to us and it was readily possible to demonstrate that this was indeed the case. The following protocol presents the titers of toxin obtained in terms of flocculating units per ml.

		Units
1	Regular medium[3]	110
2	Regular medium + DL serine 1 mg.	90
3	Regular medium + DL serine 2 mg.	70
4	Regular medium + DL serine 4 mg.	40
5	Regular medium + L serine (sample 1) 1 mg.	110
6	Regular medium + L serine (sample 1) 2 mg.	110
7	Regular medium + L serine (sample 1) 4 mg.	110
8	Regular medium + L serine (sample 2) 1 mg.	110
9	Regular medium + L serine (sample 2) 2 mg.	110
10	Regular medium + L serine (sample 2) 4 mg.	110
11	Regular medium + D serine 0.5 mg.	100
12	Regular medium + D serine 1.0 mg.	65
13	Regular medium + D serine 2.0 mg.	38

The identity and purity of the compounds used were attested by analytical and rotational data provided with the specimens, and were further grossly checked by means of paper chromatograms of all specimens, which showed identical behavior.

At present, there is no evidence to explain the mechanism of this phenomenon. So far as it has been possible to demonstrate, the unnatural forms of the other amino acids do not produce a similar effect. In view of the specific nephrotoxic effect of D-serine[4] and of recent observations[5] on specific growth inhibition of *E. coli* by the same substance, it seems worth while to place on record this further instance of interference in a biological system by this amino acid without in any way suggesting that the three may be related.

The writers hope to be able to report later on further details of this mechanism as it relates to tetanus toxin formation.

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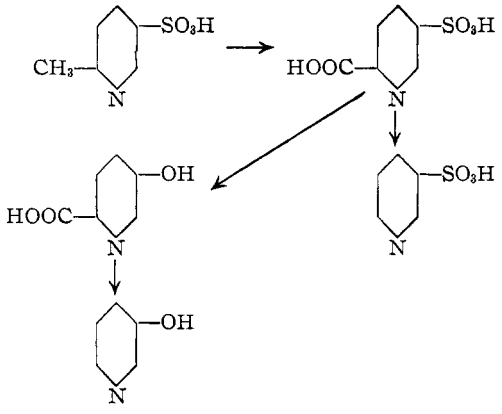
Carboxylic Acids of 3-Pyridinesulfonic Acid and Their Salts

BY BERNARD F. DUESEL AND JOHN V. SCUDI

The current shortage of refined pyridine led us to investigate the use of the picolines as a source of raw material for pyridine intermediates. The picolines are more readily available, and they can be easily sulfonated[1,2,3,4] in the presence of a suitable catalyst to give mainly 3-pyridinesulfonic acid derivatives. We have oxidized these derivatives and have obtained the corresponding carboxypyridinesulfonic acids. Certain of these are of commercial importance; for example, 6-carboxy-3-pyridinesulfonic acid, made from α-picoline, can be decarboxylated in nearly quantitative yield to give 3-pyridinesulfonic acid, an intermediate in the preparation of niacin and niacinamide.

The picolinesulfonic acids were prepared according to known methods[1,2,3,4] with or without modification and the products were oxidized. Lower yields were obtained following the acid manganese dioxide method of Biswell and Wirth[5] than were obtained using a simple alkaline permanganate oxidation. Other methods investigated included the selenium oxidation procedure of Woodward, *et al.*,[6] and the hydrogen peroxide method of Stiks and Bulgach.[7] Neither of these proved as convenient as the permanganate method for laboratory preparations.

Since pyridine is known to sulfonate predominantly in the beta position, the structures of the mono-sulfonic acids obtained from the β- and γ-picolines follow directly. With α-picoline, however, two β-positions are available for sulfonation. That the main product was 6-methyl-3-pyridinesulfonic acid may be inferred from the work reported by Graf.[8] Its structure was demonstrated by means of the reactions



Oxidation of the picoline sulfonic acid gave a sulfopicolinic acid (m. p. 287°) which is not readily differentiated from the known[9] 3-sulfopicolinic

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acid (m. p. 282°). Caustic fusion of the sulfopicolinic acid gave a hydroxypicolinic acid (m. p. 269–270°), which is not identical with the 3-hydroxypicolinic acid reported by Kirpal,[10] but which corresponds to the 5-hydroxypicolinic acid reported by Bellman[11] and Urbanski.[12] The 5-hydroxypicolinic acid in turn establishes the structure of the picolinesulfonic acid as 6-methyl-3-pyridinesulfonic acid.

Experimental

6-Carboxy-3-pyridinesulfonic Acid.—Commercial grade 2-picoline, obtained from the Barrett Company, was sulfonated in 69% yield by means of the method of McElvain and Goese with the heating time reduced from twenty-four to five hours. The yield of 69% with a loss of 6% α-picoline may be compared with a 45% yield with a 12% loss upon twenty-four hours of heating.

87.5 g. of sodium 6-methylpyridine-3-sulfonate was dissolved in 3 liters of distilled water; 175 g. of potassium permanganate was added in portions over a one and one-half hour period while the mixture was stirred and heated at 70°. The reaction was over in three hours. The manganese dioxide was filtered off, and the filtrate was evaporated to a volume of one liter. Dilute hydrochloric acid was added to *p*H 6.0. A solution of 20% barium chloride was added to maximum precipitation of the barium salt of the carboxypyridinesulfonic acid. The barium salt, filtered and washed with warm water, was suspended in 500 cc. of boiling water and dilute sulfuric acid added to remove the barium. Evaporation of the filtrate gave crystals of 6-carboxy-3-pyridinesulfonic acid m. p. 287° dec. The yield was 64 g. or 70% of the theoretical.

Anal. Calcd. for $C_6H_5NO_5S$: N, 6.89; titration equivalent, 101.5. Found: N, 6.85; titr. equiv., 102; pKa_1, 1.65; pKa_2, 3.46; pKb, 12.68.

5-Hydroxypicolinic Acid.—Five grams of 6-carboxy-3-pyridinesulfonic acid was mixed in a nickel crucible with 20 g. of sodium hydroxide pellets and 4 cc. of water. The mixture was stirred and heated at 220° for one hour. The reaction mass was diluted to 250 cc. with hot water. Addition of dilute hydrochloric acid to *p*H 5 gave 3 g. of fine white needles. Recrystallization from 250 cc. of hot water gave 2.6 g. of a crystalline monohydrate. When dried at 130° overnight, the product changed to a white powder which melted at 269–270° dec. It gave a characteristic red color with ferric chloride solution.

Anal. Calcd. for $C_6H_5NO_3$: N, 10.1. Found: N, 10.1.

On heating *in vacuo* at 280–300°, carbon dioxide was evolved and 3-hydroxypyridine, m. p. 128–129°, was obtained on distillation.

Decarboxylation of 6-Carboxy-3-pyridinesulfonic Acid.—Ten grams of potassium 6-carboxypyridine-3-sulfonate was suspended in 50 cc. of mineral oil. The temperature was adjusted to 240°, and the suspension was stirred for two and one-half hours until the evolution of carbon dioxide ceased. The solid was filtered and washed free of oil with ligroin. The product was dissolved in 50 cc. of water and treated with Norit A. After removing the Norit, the filtrate was concentrated to the point of crystallization when an equal volume of alcohol was added. Potassium 3-pyridinesulfonate was obtained in nearly quantitative yield. Conversion of the salt to the free acid gave 3-pyridinesulfonic acid, m. p. 354° dec.

Anal. Calcd. for $C_5H_5NO_3S$: S, 20.1; titration equivalent, 159.2. Found: S, 20.1; titr. equiv., 159.5.

Potassium 4-carboxypyridine-3-sulfonate can be decarboxylated in the same way.

5-Carboxy-3-pyridinesulfonic Acid.—3-Methyl-5-pyridinesulfonic acid was prepared according to McElvain and Goese,[3] using 3-picoline obtained from Reilly Tar and Chemical Corporation; 13.5 g. of the product was dissolved in 300 cc. of water, and 22 g. of potassium permanganate was added portionwise over a two-hour period with stirring at 100°. On heating another hour, the permanganate color disappeared. The manganese dioxide was removed, and the filtrate was adjusted to *p*H 6.5 with hydrochloric acid. An excess of 20% barium chloride solution was added. The solution was concentrated and filtered. The precipitate weighed 7 g. and proved to be barium oxalate. Concentration of the filtrate to 20 cc. gave a precipitate of the barium salt of 5-carboxy-3-pyridinesulfonic acid. Following treatment with dilute sulfuric acid and recrystallization from an alcohol–water mixture, the acid, melting at 335° dec., was obtained.

Anal. Calcd. for $C_6H_5NO_5S$: N, 6.89; titration equivalent, 101.5. Found: N, 6.86; titr. equiv., 102.

4-Carboxy-3-pyridinesulfonic Acid.—4-Picoline, b. p. 143–145°, obtained from Eastman Kodak Co., was sulfonated according to Webb and Corwin[4]; 39 g. of the sodium-4-methylpyridine-sulfonate was dissolved in 1040 cc. of water, and 78 g. of potassium permanganate was added over a period of six hours at 60°. The excess of permanganate was discharged by addition of alcohol. The manganese dioxide was removed, and the clear filtrate was passed through a column of Amberlite resin IR-100 to remove sodium and potassium ions. The filtrate, which was strongly acid, was evaporated to a volume of 100 cc. and cooled; 7.2 g., or 17.8% of 4-carboxy-3-pyridinesulfonic acid was obtained as white crystals. On recrystallization from alcohol–water, the melting point was 315–316° dec. Sucharda and Troszkiewicz,[9] who prepared this product through an oxidation of 4-carboxy-3-pyridylmercaptan, reported a melting point of 318°.

Anal. Calcd. for $C_6H_5NO_5S$: N, 6.89; titration equivalent, 101.5. Found: N, 6.78; titr. equiv., 102.

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Note on Friedel–Crafts Copolymerization

BY R. E. FLORIN

Results similar to those reported by Alfrey and Wechsler[1] have been obtained upon the system styrene (M_1)/2,5-dichlorostyrene (M_2), copolymerized at 0° in ethyl chloride solution, with aluminum chloride as catalyst. Under these conditions, $r_1 = 14.8 \pm 2$ and $r_2 = 0.34 \pm 0.2$. The reactivity ratios were evaluated by the procedure of Mayo and Lewis[2] from basic data shown in Table I.

Under the same general conditions, styrene/vinylidene chloride in all ratios yields only polystyrene, vinyl *n*-butyl ether/vinylidene chloride yields only the polyether, and styrene/vinyl *n*-butyl ether yields liquid products at low styrene ratios and semi-solid products at high styrene ratios, whose refractive indices are always close to that of the polyether.

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