TABLE I

ACETYLATED ALDONIC ACIDS

Acid	Salt	Yield, %	Product M.P.	Product $[\alpha]_D^{20-25}$ in chloroform	Reported Constants M.P.	Reported Constants $[\alpha]_D$ in chloroform	Reference
Arabinonic	K^+	78					
	Ca^{++}	76	135–136°	+32.0°	135–136°	+32.5°	(5)
	Zn^{++}	78					
Gluconic	K^+	78					
	NH_4^+	65	110–112	+11.8	110–111	+11.5	(8)
	Ca^{++}	77					
Galactonic	K^+	76	129–130	+12.1	131.2	+12.0	(6)
	$Ca^{++}\cdot 5H_2O$	82					
Mannonic	NH_4^+	71	74–76[7]	+25.1	75–76[7]	+24.8	(5)

N-(β-Picolyl)glycine, *N*-(β-Picolyl)-β-aminopropionic Acid, and Their Methyl Derivatives

HARVEY N. WINGFIELD, JR.

Received February 15, 1960

The compounds *N*-(β-picolyl)glycine, *N*-(β-picolyl)-β-aminopropionic acid, and corresponding methyl derivatives were synthesized for comparison with the metabolic products of nicotine found in the urine of dogs after administration of nicotine. Since no reference to these compounds could be found in the literature, their synthesis is reported here.

EXPERIMENTAL

N-(β-Picolyl)glycine. Glycine ethyl ester hydrochloride (14 g., 0.1 mole) was dissolved in the minimum quantity of water and treated with 8.4 g. (0.1 mole) of sodium bicarbonate. Alcohol was added and the precipitated sodium chloride was removed by filtration, collecting the filtrate in a hydrogenation bottle. Pyridine-β-carboxaldehyde (10 g., 0.1 mole) was added and the mixture was hydrogenated, employing 100 mg. of palladium catalyst.[1] After the hydrogenation was completed the catalyst was filtered, and most of the solvent was evaporated under vacuum. The residual ester was washed with water, dissolved in acetone, and the insoluble material was removed by filtration. The acetone was evaporated under vacuum and the residue was dissolved in chloroform. After filtering and again removing the solvent, *N*-(β-picolyl)glycine ethyl ester remained as a viscous yellow oil. The yield of crude product was 50–60%. Attempts to distill the ester resulted in decomposition.

Several batches of the ester were combined in a flask, acidified with 15% sulfuric acid, and refluxed for 48 hr. The hydrolyzate was decolorized by boiling with activated charcoal and filtering. Sulfuric acid was removed by making the solution alkaline with barium hydroxide and filtering, and the excess barium hydroxide was removed by treating the solution with carbon dioxide, boiling, and filtering. Residual traces of barium were removed by treating the solution with a very small amount of cadmium sulfate, and precipitating the excess cadmium with hydrogen sulfide. The filtrate was evaporated under vacuum, the acid residue was dissolved in a minimum amount of water, and the *N*-(β-picolyl)lgycine was precipitated with alcohol-acetone. After several recrystallizations in this manner, the acid, m.p. 209–210° dec., was dried overnight for analysis.

Anal. Calcd. for $C_8H_{10}N_2O_2$: C, 57.83; H, 6.02. Found: C, 57.71; H, 6.13.

The thiohydantoin, m.p. 176–177° dec., was prepared from azobenzene isothiocyanate by the method of Ramachandran and McConnell.[2]

Anal. Calcd. for $C_{21}H_{17}N_5OS$: C, 65.11; H, 4.39. Found: C, 64.94; H, 5.07.

N-Methyl-N-(β-picolyl)-glycine. A mixture of 0.2 mole of *N*-(β-picolyl)glycine ester and 100 ml. of formaldehyde was placed in a pressure bottle wth 70–75 g. Raney nickel catalyst and reduced with hydrogen at a gage pressure of 45 p.s.i. Absorption of hydrogen ceased after 3 hr. The catalyst was removed by filtration, and the solution evaporated to near dryness under vacuum. The residue was hydrolyzed by refluxing for several days with 15% sulfuric acid. After decolorization with activated carbon, the *N*-methyl-*N*-(β-picolyl)glycine was recovered by the same procedure employed with *N*-(β-picolyl)glycine. The yield of crude material was nearly quantitative. The methylated compound, m.p. 175–176°, was more soluble in alcohol than the unmethylated.

Anal. Calcd. for $C_9H_{12}N_2O_2$: C, 60.00; H, 6.66. Found: C, 59.90; H, 7.03.

The chloroplatinate, m.p. 217° dec., was recrystallized from alcohol-water.

Anal. Calcd. for $C_9H_{14}N_2O_2Cl_6Pt$: C, 18.31; H, 2.37; Pt, 33.05. Found: C, 18.43; H, 2.98; Pt, 32.81.

N-(β-Picolyl)-β-aminopropionic acid (chloroplatinate and thioureide). β-Picolylamine (54 g., 0.5 mole) was chilled in an Erlenmeyer flask and 25 g. (0.47 mole) of acrylonitrile was added dropwise over a period of 2 hr. The mixture was allowed to come to room temperature and left standing for several days with occasional shaking. Fractional distillation of the mixture under 5 mm. pressure gave three fractions: (1) 95–96° (unchanged amine), (2) 165–170°, (3) above 170°. Fraction 2, which represented a yield of about 30%, was refluxed about 20 hr. with 15% sulfuric acid. The sulfuric acid was removed by treating with excess barium hydroxide and filtering. The filtrate was evaporated to a small volume and extracted three times with chloroform, thus removing a small amount of picolylamine. The aqueous solution was treated with carbon dioxide, boiled, and filtered to remove barium. The filtrate was evaporated to a small volume. After standing several weeks in a vacuum desiccator, the liquid solidified to a waxy mass. The material was dissolved in absolute alcohol and precipitated with acetone. The yield of a product, which still contained a

(1) Later, it was found that Raney nickel catalyst gave better results.

(2) L. K. Ramachandran and W. B. McConnell, *J. Am Chem. Soc.*, **78**, 1255 (1956).

trace of barium, was 10–12%. A satisfactory analysis could not be obtained even after repeated recrystallizations. The acid decomposed in the neighborhood of 270°. The chloroplatinate, decomposing above 250°, was prepared and recrystallized from alcohol-water.

Anal. Calcd. for $C_9H_{14}N_2O_2Cl_6Pt$: C, 18.31; H, 2.37; Pt, 33.05. Found: C, 18.71; H, 2.57; Pt, 33.19.

The thioureide, m.p. 174–176° dec., was prepared from azobenzene isothiocyanate.[2]

Anal. Calcd. for $C_{22}H_{21}N_5O_2S$: C, 63.01; H, 5.01. Found: C, 63.13; H, 5.29.

N-(β-Picolyl)-β-methylaminopropionitrile. β-Picolylmethylamine (25 g., 0.2 mole) was dissolved in 150 ml. of benzene contained in a three-necked flask fitted with stirrer, dropping funnel, and reflux condenser. Four or five pellets of potassium hydroxide were added and then a solution of 21.2 g. (0.4 mole) of acrylonitrile was added slowly while stirring. After 2 days at room temperature, the mixture was refluxed on the steam bath for several days. The insoluble material was removed by filtration, and the benzene was evaporated. On distillation of the thick residue in vacuum, the nitrile distilled as a slightly turbid liquid at 121–125° (1 mm.). The chloroplatinate, m.p. 228° dec., was recrystallized from alcohol-water.

Anal. Calcd. for $C_{10}H_{15}N_3Cl_6Pt$: C, 20.61; H, 2.58; Pt, 33.50. Found: C, 20.45; H, 2.57; Pt, 33.32.

N-(β-Picolyl)-β-methylaminopropionic acid. The nitrile, prepared above, was hydrolyzed by refluxing with 50% sulfuric acid. The hydrolyzate was treated with barium hydroxide, filtered, and the filtrate treated with carbon dioxide and again filtered to remove the barium. The filtrate was evaporated, and the residue dissolved in chloroform and filtered. Evaporation of the chloroform left the crude product that did not crystallize. Even after standing 6 months in a vacuum desiccator, it remained a viscous liquid. The dihydrochloride was prepared by the method of Liwschitz, Zilkha and Shahak.[3] This compound is a white crystalline solid, melting at 205–206° with slight decomposition.

Anal. Calcd. for $C_{10}H_{16}N_2O_2Cl_2$: C, 45.11; H, 6.01. Found: C, 44.97; H, 5.98.

The chloroplatinate, decomposing without melting, was recrystallized from alcohol-water.

Anal. Calcd. for $C_{10}H_{18}N_2O_2Cl_6Pt$: C, 19.96; H, 2.66; Pt, 32.45. Found: C, 19.61; H, 2.71; Pt, 32.44.

Acknowledgment. The author wishes to thank Mrs. Joyce Booth for the microanalyses.

DEPARTMENT OF RESEARCH AND DEVELOPMENT
THE AMERICAN TOBACCO CO.
RICHMOND, VA.

(3) Y. Liwschitz, A. Zilkha, and I. Shahak, *J. Org. Chem.*, **21**, 1530 (1956).

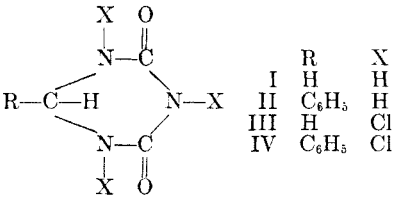
Chlorination of 2,4-Dioxohexahydro-1,3,5-triazines

FRANK B. SLEZAK, ALFRED HIRSCH, LEWIS I. KRIMEN,[1] AND HENRY A. MCELRAVY, JR.

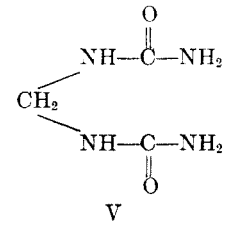
Received February 19, 1960

During the course of studying various *N*-halogen compounds, suitable methods of preparing *N*-chlorohexahydro-*s*-triazines became of interest to us.

(1) Present address: Nalco Chemical Co., Chicago, Ill.



	R	X
I	H	H
II	C_6H_5	H
III	H	Cl
IV	C_6H_5	Cl



V

Our attempts to prepare 2,4-dioxohexahydro-1,3,5-triazine (I) by previously described methods[2,3] were unsatisfactory because of low yield and purity of product. A far more convenient method was devised whereby crude, dry methylenediurea (V) was cyclized in a stirred, refluxing diluent such as nitrobenzene, *n*-hexyl ether, or the dibutyl ether of diethylene glycol (dibutyl Carbitol). Nitrobenzene seemed most convenient to use. The methylenediurea was prepared by a simplification of the method described by Kadowaki.[4] The method of Krassig and Egar[5] was used to prepare 6-phenyl-2,4-dioxohexahydro-1,3,5-triazine (II).

It was found that the efficiency of the halogenation in an aqueous medium was dependent on the *p*H and on the temperature at which the halogenation was carried out. Chlorination of I and II, to the novel III and IV respectively, gave the best results when the reactions were carried out in the range *p*H 1–3 and at ice temperatures. Chlorination at higher *p*H ranges and/or at higher temperatures resulted in diminished yields of product.

1,3,5-Trichloro-2,4-dioxohexahydro-1,3,5-triazine (III), in concentrations as low as 1 p.p.m., completely inhibited the growth of the test organisms *Erwinia amylovora*, *Xanthomonas phaseoli*, *Micrococcus pyrogenes* var. *aureus*, and *Escherichia coli*.[6]

EXPERIMENTAL[7]

Methylenediurea (V). Water (1500 ml.), urea (1200 g., 20 moles), 40% aqueous formaldehyde (250 ml., 3.32 moles),

(2) O. Diels and R. Lichte, *Ber.*, **59B**, 2778 (1926).

(3) H. Fahrenhorst and H. Scheuermann, German Patent **694,823** (1940).

(4) H. Kadowaki, *Bull. Chem. Soc. Japan*, **11**, 248 (1936); *Chem. Abstr.*, **30**, 5944.[6]

(5) H. Krassig and G. Egar, *Makromol. Chem.*, **18/19**, 195 (1956).

(6) Biological data provided by Dr. Paul H. Schuldt of the Boyce Thompson Institute for Plant Research, Inc., Yonkers, N. Y.

(7) All melting points are uncorrected. Elemental analyses by Diamond Alkali Company Research Analytical Laboratory. Available halogen determinations by sodium thiosulfate titration. The theoretical percent available halogen is taken as twice the weight percent of halogen attached to nitrogen.