NOTES

N-Derivatives of *p*-Arsanilic Acid

BY C. K. BANKS, JOHN CONTROULIS AND W. F. HOLCOMB

In a previous study[1] attempts were made to synthesize N-triazinylaminobenzenearsonic acids by reaction of *p*-arsanilic acid with various compounds known to produce melamine. None of the reaction products proved to be the desired compound but several new and interesting arsenicals were isolated and identified.

When cyanogen bromide was treated with *p*-arsanilic acid under neutral conditions, hydrobromic acid was produced and a reaction product of the composition $NCNHC_6H_4AsO_3H_2$ was isolated. On hydrolysis in dilute alkali, it gave *p*-carbamidobenzenearsonic acid, identical with the reaction product obtained from potassium cyanate and *p*-arsanilic acid.[2] Sticklings has reported[3] the isolation of *p*-carbamidobenzenearsonic acid from the interaction of cyanogen bromide and *p*-arsanilic acid but apparently did not isolate the intermediate cyanamido compound. *p*-Cyanamidobenzenearsonic acid also reacted with alcoholic hydrogen chloride to give a substance with the properties of an imino ether. Ammonolysis with alcoholic ammonia converted the imino ether to a substance having the properties of a guanidine but which failed to crystallize. A solution of this gummy product could also be hydrolyzed to the carbamido derivative.

Dicyandiamide also condensed with *p*-arsanilic acid in neutral solution to give 4-biguanidobenzenearsonic acid. After the biguanido compound had been heated with 4 *N* hydrochloric acid, 4-guanylcarbanido- or 4-carbamylguanidobenzenearsonic acid hydrochloride crystallized upon cooling the solution. Further hydrolysis resulted in complete decomposition to arsanilic acid.

4-Cyanamidobenzenearsonic Acid.—*p*-Arsanilic acid (108 g.) and sodium hydroxide (20 g.) were dissolved in water (500 ml.). A solution of potassium cyanide (65 g.) in water (500 ml.) was treated with bromine (*ca.* 160 g.) until a faint bromine color was evident. The solution of cyanogen bromide was added to the solution of arsanilic acid with cooling and the resulting mixture allowed to stand forty-eight hours at room temperature. The product crystallized as a yellow granular mass and was dissolved in hot water, charcoaled, filtered and the filtrate cooled to yield 85 g. (70%) of the colorless, crystalline material. The compound was insoluble in cold water but soluble in hot water and in acids and alkalies with decomposition.

Anal. Calcd. for $C_7H_7AsN_2O_3$: As, 30.95; N, 11.58. Found: As, 30.98; N, 11.62.

Five grams of 4-cyanamidobenzenearsonic acid was dissolved in sodium hydroxide, filtered and the resulting solution made acid to congo red paper. The resulting crystalline solid was identical in properties and analysis with 4-carbamidobenzenearsonic acid.

Anal. Calcd. for $C_7H_9AsN_2O_4$: As, 28.70. Found: As, 28.82.

4-Biguanidobenzenearsonic Acid.—*p*-Arsanilic acid (217 g.) was dissolved in hot water (1000 ml.) with sufficient sodium hydroxide to give a solution of *p*H 4.8. Dicyandiamide (200 g.) was added and the solution refluxed for two hours and then cooled. The product crystallized in small granules (150 g.) which were recrystallized from hot water. The compound was soluble in dilute acids and alkalies and could be recovered unchanged from such solutions.

Anal. Calcd. for $C_8H_{12}As_2O_3$: As, 24.87; N, 23.26. Found: As, 24.79; N, 23.02.

4-Guanylcarbamido Acid or Carbamylguanidobenzenearsonic Acid Hydrochloride.—4-Biguanidobenzenearsonic acid (50 g.) was refluxed for thirty minutes in 4 *N* hydrochloric acid (375 ml.). The hydrochloride, which crystallized from the cold solution, was recrystallized from dilute hydrochloric acid, yield 25 g.

Anal. Calcd. for $C_8H_{12}AsClN_4O_4$: As, 22.20; N, 16.58. Found: As, 22.22; N, 16.30.

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(1) Banks, Grulzit, Tillitson and Controulis, THIS JOURNAL, **66**, 1771 (1944).

(2) German Patent 213,155.

(3) Sticklings, *J. Chem. Soc.*, 3131 (1928).

The Preparation of α-Phenyl-β-benzoylpropionic and α,γ-Diphenylbutyric Acids

BY ROBERT H. BAKER AND WILLIAM W. JENKINS

In connection with another problem it was desirable to synthesize a large quantity of α,γ-diphenylbutyric acid. Alkaline hydrolysis of the easily available α-phenyl-β-benzoylpropionitrile[1] was found to be more reliable than acid hydrolysis[2] and the catalytic reduction of the resulting α-phenyl-β-benzoylpropionic acid was superior to the Clemmensen method of producing the α,γ-diphenylbutyric acid.[3]

α-Phenyl-β-benzoylpropionic Acid.—To a paste of 70 g. (0.3 mole) of α-phenyl-β-benzoylpropionitrile and 15 ml. of ethanol was added 350 ml. of 10% aqueous sodium hydroxide solution. The mixture was refluxed for six hours, then the almost clear solution was diluted with 2.5 liters of water and clarified by filtration with Norit. Acidification of the filtrate with glacial acetic acid to incipient crystallization followed by complete precipitation with hydrochloric acid gave 58 g. (76.7%) of crude acid, m. p. 148–149°.

The crude acid, 66 g. from this and another run, was crystallized from 400 ml. of hot chloroform by adding 500 ml. of petroleum ether (b. p. 60–70°) and allowing the solution to stand at 40° overnight. The yield of white crystals was 65 g., m. p. 150–151° (reported[2] 152–153°).

A similar run with 65 g. of the nitrile gave 64 g. (90%) of the crystallized acid, m. p. 150–151°.

α,γ-Diphenylbutyric Acid.—To a warm solution of 25.4 g. (0.10 mole) of α-phenyl-β-benzoylpropionic acid in 100 ml. of glacial acetic acid was added 2 ml. of 60%

(1) "Organic Syntheses," Coll. Vol. II, John Wiley & Sons, Inc., New York, N. Y., 1943, p. 498.

(2) Lapworth and Wechsler, *J. Chem. Soc.*, **97**, 38 (1910); Hahn and Lapworth, *ibid.*, **85**, 1355 (1904).

(3) Kohler and Kimball, THIS JOURNAL, **55**, 4632 (1933).

perchloric acid[4] and 0.5 g. of 5% palladium-on-charcoal (Wilkens-Anderson Co.). The still warm solution was shaken with hydrogen at 30–35 lb. pressure until 0.2 mole had been absorbed, about one hour. After removal of the catalyst the solution was heated to 75° and diluted with water until cloudy. Upon seeding and cooling, finally to 15°, the acid generally precipitated as an oil which later solidified. After drying *in vacuo* over solid sodium hydroxide the granular product weighed 20 g. It was dissolved in 130 ml. of petroleum ether (b. p. 60–70°) and treated with Norit to yield 19.8 g. (82.5%) of white needles, m. p. 74.5–75° (reported[3], 75°).

Four additional reductions were run as above and the reaction mixtures were combined and worked up to give the acid in 89% yield.

(4) The efficacy of perchloric acid in promoting hydrogenolysis was first recognized by Karg and Marcus, *Ber.*, **75**, 1850 (1942).

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2,5-Diamino-1,4-benzoquinones[1]

BY JOHN H. BILLMAN, DONALD G. THOMAS AND DAVID K. BARNES

The reaction of aromatic and aliphatic amines with 1,4-benzoquinone has long been known. Perhaps the most important incentive for the extensive study which has been made on this type of reaction is due to the close relationship between aromatic aminoquinones and dyes of commercial importance.[2] Since compounds of this type had not been examined for antimalarial activity, several of them have now been prepared by the following typical procedure.

2,5-Disulfapyridino-1,4-benzoquinone.—To a solution of 5 g. (0.04 mole) of 1,4-benzoquinone in 100 ml. of hot 95% ethanol was added 10.0 g. (0.04 mole) of sulfapyridine and one ml. of concentrated hydrochloric acid. The reaction proceeded smoothly and crystals precipitated when the solution was cooled. The product was filtered by suction and washed thoroughly with hot alcohol until the filtrate was almost colorless. The yield was 8 g. or 66%.

The following compounds were prepared and their antimalarial activity tested.

TABLE I

2,5-DIAMINO-1,4-BENZOQUINONES

Amine used	M. p., [a] °C.	Mol. ratio quinone/amine	% Nitrogen Calcd.	% Nitrogen Found
Aniline	345	2/1		[b]
Ethanolamine	262	3/2		[c]
β-Phenylethylamine	208	3/1	8.09	8.02
p-Anisidine	300	1/1	8.00	8.09
Sulfapyridine	218–220	1/1	13.82	14.09

[a] Determined on a Maquenne block, uncorrected decomposition points. [b] Previously prepared by Willstätter and Majima, *Ber.*, **43**, II, 2591 (1910). [c] Previously prepared by Kansas and Inagawa, *J. Pharm. Soc. Japan*, **58**, 347–352 (1938).

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(1) This work was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and Indiana University at Bloomington, Indiana.

(2) Suida and Suida, *Ann.*, **416**, 113 (1918).

(*p*-Halogenophenyl)-trimethylsilanes

BY CHARLES A. BURKHARD

(*p*-Chlorophenyl)-trimethylsilane and (*p*-bromophenyl)-trimethylsilane have been prepared by the following reaction.

$$(CH_3)_3SiCl + p\text{-}XC_6H_4MgBr \longrightarrow p\text{-}(CH_3)_3SiC_6H_4X + MgBrCl$$

Grüttner and Krause[1] have prepared the corresponding triethyl compounds and (*p*-chlorophenyl)-tri-*n*-propylsilane by reaction of the alkyl Grignard reagent with the corresponding *p*-halogenophenyltrichlorosilane.

(*p*-Chlorophenyl)-trimethylsilane.—*p*-Chlorophenylmagnesium bromide was prepared by the reaction of 382 g. of *p*-chlorobromobenzene with 50 g. of magnesium turnings in 700 ml. of anhydrous ether. To this was added dropwise with stirring 220 g. of chlorotrimethylsilane. The solution was kept at reflux to ensure complete reaction. The compound was recovered by rectification; yield 305 g., 83%, b. p. 119–120° (50 mm.), d^{20}_4 1.0282, $n^{20}D$ 1.5128.

Anal.[2] Calcd. for $C_9H_{13}SiCl$: Cl, 19.20. Found: Cl, 19.3.

(*p*-Bromophenyl)-trimethylsilane.—*p*-Bromophenylmagnesium bromide was prepared by the reaction of 177 g. of *p*-dibromobenzene with 18.8 g. of magnesium turnings in 300 ml. of anhydrous ether. To this was added 81 g. of chlorotrimethylsilane with stirring. The solution was kept under reflux to ensure complete reaction. The compound was recovered by rectification; yield 90.5 g., 53%; b. p. 146–148° (50 mm.), d^{20}_4 1.2197, $n^{20}D$ 1.5302.

Anal. Calcd. for $C_9H_{13}SiBr$: Br, 34.87. Found: Br, 34.2.

(1) Grüttner and Krause, *Ber.*, **50**, 1559 (1917).

(2) The author is indebted to Dr. E. W. Balis and Mr. L. B. Bronk for analyses.

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The Preparation of Mercaptans from Alcohols[1]

BY ROBERT L. FRANK AND PAUL V. SMITH

The preparation of isothiouronium salts by the direct action of thiourea and halogen acids on alcohols, first recorded by Stevens[2] and developed by Johnson and Sprague,[3,4] is herein further described as a step in the synthesis of mercaptans (I–III).

$$ROH + H_2NCSNH_2 + HX \longrightarrow$$

I

$$RSC(=NH)NH_2 \cdot HX \xrightarrow{NaOH} RSH$$

II III

Our experiments comparing hydrochloric and hydrobromic acids in this reaction have shown a great advantage in the use of the latter for making primary mercaptans. *n*-Dodecyl mercaptan, for

(1) This investigation was carried out under the sponsorship of the Office of Rubber Reserve, Reconstruction Finance Corporation, in connection with the Government Synthetic Rubber Program.

(2) Stevens, *J. Chem. Soc.*, **81**, 79 (1902).

(3) Johnson and Sprague, THIS JOURNAL, **58**, 1348 (1936).

(4) Sprague and Johnson, *ibid.*, **59**, 1837 (1937).