The Preparation of Glycocyamidines from Substituted Cyanamides

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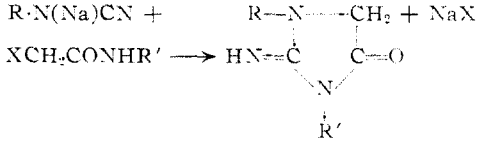
The chemical synthesis of substituted glycocyamidines by various modifications utilizing glycine derivatives as starting materials has been reported by several investigators.[1-5] A new route to these compounds was discovered during a study of the reactions of sodium arylcyanamides, when it was found that the latter reacted with haloacetamides to yield glycocyamidines in good yields



Several glycocyamidines carrying phenyl or *p*-chlorophenyl substituents in the 1-position were synthesized by means of this reaction, and in addition the *n*-octyl homolog of creatinine was prepared by allowing sodium *n*-octylcyanamide to react with chloroacetamide. When N-substituted α-haloacetamides were used, glycocyamidines substituted in the 3-position were produced.

Experimental

Cyanamides.—Phenylcyanamide,[6] 4-chlorophenylcyanamide,[7] and *n*-octylcyanamide[8] were prepared by methods appearing in the literature. They were converted to their sodium salts by dissolving in one equivalent of aqueous sodium hydroxide or by reaction with one equivalent of methanolic sodium methoxide in an inert organic solvent such as benzene, followed by removal of the organic solvent.

Glycocyamidines.—A solution of equimolecular proportions of an α-haloacetamide and the sodium salt of a monosubstituted cyanamide in a suitable solvent was prepared. The mixture was then either heated to reflux for several hours or allowed to stand at room temperature for several days. When the solvent was water, reaction at room temperature was preferred in order to avoid hydrolysis. If the product precipitated from the reaction mixture, it was isolated by filtration and washed free of sodium halide with water; if the product remained in solution, the solution was evaporated to dryness and the residue washed with water. The glycocyamidines produced were further purified by recrystallization.

The α-haloacetamides used were chloroacetamide, α-chloroacetanilide,[9] α-bromo-N-*n*-octylacetamide,[10] and α-chloro-4-nitroacetanilide.[11] The products prepared and the experimental details are listed in Table I.

The preparation of 1-phenylglycocyamidine was typical of the series: chloroacetamide (9.4 g., 0.1 mole) was dissolved in a solution of sodium phenylcyanamide (14 g., 0.1 mole) in water (100 ml.) and the clear solution was allowed to stand at room temperature. After 48 hours a nearly colorless, crystalline solid had separated from the reaction mixture. This was filtered and dried in a 65° oven, yield 9 g. (51%), m.p. 235–240° (dec.). Recrystallization from 2B ethanol (400 ml.) gave 5 g. of colorless plates, m.p. 239–243° (dec.). Comparable or better yields of 1-phenylglycocyamidine were obtained by refluxing for several hours in an organic solvent as the reaction medium in place of water:acetone (52% yield), ethyl acetate (71%), and acetonitrile (61%).

TABLE I

GLYCOCYAMIDINES PREPARED

Glycocyamidine	Reaction solvent	Time, hours	Temp., °C.	Yield, %	M.p.,[a] °C.	Analyses, % Calcd.	Found
1-Phenyl	Water[b]	48	25	51	239–243 (dec.)[c,d]	N 24.0	23.8
1,3-Diphenyl	Acetone	48	25	87	164–165[e]	N 16.7	16.8
1-Phenyl-3-*n*-octyl	Ethanol	2	Reflux	28	86–88[f]	N 14.6	14.8
1-Phenyl-3-*p*-nitrophenyl	Ethanol	3	Reflux	78	271–273[g]	N 18.9	18.9
1-*p*-Chlorophenyl	Water	48	25	67	275–278 (dec.)[h]	N 20.0	20.2
1-*n*-Octyl	Acetone	2	Reflux	64	239–244 (dec.)[i]	N 19.9	20.4

[a] Uncorrected. [b] Also prepared using acetone, ethyl acetate, and acetonitrile, respectively, as reaction media. [c] Ellinger and Matsuoka[1] report 235–236° (dec.). [d] Colorless plates from ethanol. [e] Colorless needles from acetone. [f] Colorless crystals, twice recrystallized from methanol. *Anal.* Calcd.: C, 71.1; H, 8.71. Found: C, 71.1; H, 8.87. [g] Yellow crystals from acetone. *Anal.* Calcd.: C, 60.8; H, 4.05. Found: C, 60.8; H, 4.25. [h] Tan crystals from acetone. *Anal.* Calcd.: Cl, 17.6. Found: Cl, 17.6. [i] Colorless crystals from ethanol.

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Preparation of Propane-1-C^{13}. Electroreduction of Acetone to Propane[1]

BY ALVIN S. GORDON AND SHELDON HEIMEL

Propane-1-C^{13} has been synthesized using $BaC^{13}O_3$ as the source of C^{13}. Starting with about 45 millimoles of $BaC^{13}O_3$ a 67.5% yield of propane-1-C^{13} based on $C^{13}O_2$ was obtained. The propane is 98–99.3% pure. The following steps were employed[2]

(1) This research is part of the work being done at the Bureau of Mines on Contract NA onr 25-47, supported by the Office of Naval Research and the Air Materiel Command.
(2) For complete experimental details order Document 3210 from American Documentation Institute, 1719 N St., N.W., Washington 6, D. C., remitting $1.00 for microfilm (images 1 inch high on standard 35 mm. motion picture film) or $1.00 for photocopies (6 × 8 inches) readable without optical aid.