4-Methylquinolizidine.—This compound, together with 1-(2′-piperidyl)-4-pentanol, was obtained by reduction of 1-(2-pyridyl)-pentanone-4 in the presence of Raney nickel catalyst at 150° and 250 lb. hydrogen pressure. Results were substantially the same as those recently reported by Boekelheide and Rothchild.[2b]

The hydrochloride of 4-methylquinolizidine melted above 360°.[14]

Anal. Calcd. for $C_{10}H_{19}N\cdot HCl$: C, 63.27; H, 10.62; Cl, 18.68. Found: C, 63.27; H, 10.57; Cl, 18.70.

3-Acetyl-1-(2′-pyridyl)-4-pentanone.[15]—A mixture of 50 g. of acetylacetone, 1.5 g. of sodium and 108 g. of 2-vinylpyridine was refluxed for seven hours. Distillation gave 57.1 g. of yellow oil boiling at 90–127° at 1.1 mm. and 50.7 g. of red glassy residue. Redistillation of the oil gave 14.1 g. of 1-(2′-pyridyl)-4-pentanone boiling at 84–118° at 1 mm. and 37.4 g. of 3-acetyl-1-(2′-pyridyl)-4-pentanone boiling at 118–119° at 1.0 mm.

The product gives a red color with alcoholic ferric chloride and reacts exothermically with phenylhydrazine.

Piperidines of Table III.—These were prepared by Raney nickel reduction of the ketonitriles in ethanol or by reductive methylation of the piperidine with formalin and a palladium–carbon catalyst in the manner previously described for compounds of Table II.

Acknowledgment.—The author is indebted to Miss Audrey Fiescher and Mrs. Allan Lapierre for technical assistance and to Mr. Morris E. Auerbach and his staff for analytical results. We are happy to have had the opportunity, on several occasions, of discussing this work with Dr. C. F. Koelsch, and we are especially indebted to Dr. C. M. Suter for his encouragement during this investigation.

Summary

δ-Ketonitriles have been prepared by Michael condensations involving (a) the reaction of acrylonitriles with β-ketoesters, or (b) the reaction of vinyl ketones with cyanoacetic esters.

Catalytic reduction of these ketonitriles has led to the formation of piperidines and bicyclo nitrogen compounds.

RENSSELAER, N. Y. RECEIVED NOVEMBER 18, 1949

(14) Lukes and Sorm, *Coll. Czech. Chem. Comm.*, **12**, 356 (1947).

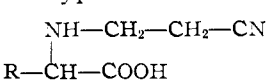
(15) Although the preparation of this compound in 16% yield was recently reported by Boekelheide and Rothchild,[2b] they stated that only a small amount of 1-(2′-pyridyl)-4-pentanone and none of the required product was obtained when an attempt was made to effect condensation according to the method used by Doering and Weil[8] to condense 2-vinylpyridine and acetoacetic ester. Since we independently found that this latter method, when applied to acetylacetone, gives 39% of 3-acetyl-1-(2′-pyridyl)-4-pentanone, the procedure for the preparation of this compound is included.

[CONTRIBUTION FROM THE NORTHERN REGIONAL RESEARCH LABORATORY,[1] PEORIA, ILLINOIS]

Cyanoethylation of Alpha Amino Acids. I. Monocyanoethyl Derivatives[2]

BY L. L. MCKINNEY, E. H. UHING, E. A. SETZKORN AND J. C. COWAN

The condensation of acrylonitrile with alpha amino acids offers a possibility for increasing their functionality by yielding monocyanoethyl derivatives of the type



Compounds of this type have not been described. However, the patent literature[3] indicates that acrylonitrile reacts with glycine in aqueous solution in the presence of acidic catalysts such as copper acetate or mineral acids. By employing the methods prescribed, no reaction was observed between glycine hydrochloride and acrylonitrile in aqueous solution. Upon refluxing glycine for five hours with excess acrylonitrile and 0.01 equivalent of copper acetate, we observed that 0.4 equivalent of acrylonitrile reacted. The reaction products proved difficult to isolate and this line of attack was dropped.

Preliminary experiments were then conducted to determine optimum conditions for obtaining the N^{α}-cyanoethyl derivatives of amino acids by condensing with acrylonitrile. In the preliminary work, the reactions were followed by observing the depression of the basicity of the amino group as indicated by comparing titration curves of the reaction mixtures with those for the amino acids. This procedure was chosen because the literature[4] indicates that some question exists as to the reliability of Kjeldahl determinations for nitrile nitrogen and because the similar solubility of alpha amino acids and their monocyanoethyl derivatives make separation difficult when both are present in the reaction mixture. These titrations indicated that no reaction occurred when glycine was refluxed with excess acrylonitrile in the presence of catalytic amounts of sodium methoxide, or when aqueous solutions were refluxed with or without hydrochloric acid. When sodium hydroxide was added to aqueous solutions of glycine containing one equivalent of acrylonitrile and the mixture was allowed to stand for twenty-four hours at room temperature, the depression of the basic portion of the titration curve was directly proportional to the amount of sodium hydroxide used, up to one equivalent.

(1) One of the laboratories of the Bureau of Agricultural and Industrial Chemistry, Agricultural Research Administration, U. S. Department of Agriculture. Article not copyrighted.

(2) Presented before the Division of Biological Chemistry at the 116th meeting of The American Chemical Society, Atlantic City, New Jersey, September 18–23, 1949.

(3) (a) U. Hoffmann and B. Jacobi, U. S. Patent 1,992,615, Feb. 2, 1935; (b) J. Y. Johnson, British Patent 404,744, July 27, 1933.

(4) (a) E. L. Rose and H. Ziliollo, *Ind. Eng. Chem., Anal. Ed.*, **17**, 211 (1945); (b) H. S. Davis and O. F. Wiedeman, *Ind. Eng. Chem.*, **37**, 482 (1945); (c) A. Friedrich, E. Kühass and R. Schurch, *Z. physik. Chem.*, **216**, 68 (1933); (d) P. Fleury and H. Levaltier, *Bull. soc. chim.*, **37**, 330 (1925).

TABLE I

N$^{\alpha}$-CYANOETHYL DERIVATIVES OF ALPHA AMINO ACIDS

Amino acid	M. p.,[a] °C.	Solubility, g./100 ml. solvent[d] Water t, °C.	Water Soly.	Water t, °C.	Water Soly.	Ethanol t, °C.	Ethanol %	Ethanol Soly.	Molecular formula	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Nitrogen Calcd.	Nitrogen Found
Glycine	190–191 (dec.)	R[b]	27	Hot	V. sol.	R	70	0.25	$C_5H_8O_2N_2$	46.9	46.8	6.29	6.10	21.9	21.9
DL-Alanine	249–250 (dec.)	R	14	Hot	V. sol.	R	50	2.5	$C_6H_{10}O_2N_2$	50.7	50.7	7.09	6.96	19.7	19.9
DL-Valine	252–253 (dec.)	R	1.28	73	6.25	R	50	0.12	$C_8H_{14}O_2N_2$	..	..	..	..	16.4	16.3
L-Leucine	249–250 (dec.)	5	0.44	70	0.98	70	99	0.15	$C_8H_{16}O_2N_2$	58.7	58.3	8.75	8.49	15.2	15.2
DL-Isoleucine	211–212 (dec.)	R	1.90	100	3.72	R	99	0.35	$C_8H_{16}O_2N_2$	..	..	..	..	15.2	15.1
DL-Phenylalanine	228–230 (dec.)	R	0.7	90	3.54	R	99	Insol.	$C_{12}H_{14}O_2N_2$	66.0	65.6	6.47	6.48	12.8	12.8
L-Tyrosine	238–239 (dec.)	5	0.07	100	0.21	75	95	0.018	$C_{12}H_{14}O_3N_2$	61.5	60.6	6.02	5.97	12.0	11.9
DL-Methionine	246–247 (dec.)	5	1.1	80	3.44	R	99	0.10	$C_8H_{14}O_2N_2S$	47.5	47.5	6.98	6.99	13.8	13.8
DL-Aspartic acid	187–188 (dec.)	5	6.7	85	32.6	R	95	Insol.	$C_7H_{10}O_4N_2$	45.2	45.1	5.41	5.48	15.0	15.0
L-Glutamic acid	119–120 (dec.)	5	8.74[c]	..	....	R	99	1.0	$C_8H_{12}O_4N_2$	48.0	47.8	6.04	6.10	14.0	13.9
L-Pyroglutamic acid	122.5–124	7	49.6	..	....	R	99	29.7	$C_8H_{10}O_3N_2$	52.7	53.0	5.53	5.54	15.4	15.4
L-Proline	137–140	R	Sol.	..	....	R	99	Sol.	$C_8H_{12}O_2N_2$	57.1	56.5	7.19	6.95	16.7	16.6

[a] Corrected. [b] R = room temp. (25–27°). [c] The anhydrous form was used and excess crystallized out as the monohydrate. [d] Acetone soly.: Proline derivative, Sol.; pyroglutamic derivative 45.4^{50}°. All others less than 0.2 g./100 ml. Ether soly.: Proline derivative, Sol.; pyroglutamic derivative 0.7^{25}°. All others less than 0.3 g./100 ml.

Therefore, it appeared that acrylonitrile reacted with the alkali metal salt of the amino acid and that catalytic amounts of base did not suffice. The same results were obtained with trimethylbenzylammonium hydroxide.

Experimental

Materials.—A practical grade of acrylonitrile was used without removing the inhibitor (b. p. 75–77°. *Anal.* Calcd.: C, 67.9; H, 5.66; N, 26.4. Found: C, 67.6; H, 5.62; N, 26.3). Commercial amino acids were used without purification, after nitrogen analysis indicated better than 98% purity.

Analyses.—Melting points, solubilities and analyses of the derivatives are recorded in Table I. Melting points were determined by the capillary method and were corrected. In agreement with the findings of Davis and Wiedeman,[4b] the standard Kjeldahl–Gunning–Arnold method[5] was found reliable for the nitrogen determinations. The reactions were followed by removing an aliquot from the reaction mixture, evaporating unreacted acrylonitrile, and determining Kjeldahl nitrogen. In all cases the Kjeldahl nitrogen value of the purified product was checked against nitrogen values determined by the Dumas method. In general, the Kjeldahl values were slightly lower than Dumas values.

Monocyanoethyl Derivatives of Neutral α-Amino Acids.—The alpha amino acid was suspended in water in an Erlenmeyer flask, and an aqueous solution of sodium or potassium hydroxide,[6] containing one equivalent of base was added, care being taken to keep the temperature below 30°. To the cold alkaline solution 1.0 to 1.1 equivalents[7] of acrylonitrile was added and the mixture shaken until homogeneous. A rise in temperature was usually observed when the acrylonitrile was added. Either portionwise addition or cooling was necessary to keep the temperature below 30°. Higher temperatures caused side reactions[8] which reduced the yields of the monocyanoethyl derivatives. After the solution had stood overnight at room temperature or at 5° (refrigerator) an aliquot was withdrawn, excess acrylonitrile evaporated, and Kjeldahl nitrogen analyses made to determine the extent of reaction. With leucine, isoleucine, methionine and tyrosine, it was necessary to warm the reaction mixture under reflux to 50–60° for two hours to complete the reaction. An equivalent amount of either glacial acetic or concentrated hydrochloric acid[9] was added while keeping the temperature below 30°. The products were isolated as follows:

N-(2-Cyanoethyl)-glycine.—The volume was reduced to 200 ml. per mole and 5 volumes of 95% ethanol added. After standing overnight in the refrigerator (5°), the crystals were filtered off and washed with 95% ethanol; yield 87%. Kjeldahl N: calcd. 21.88; found 21.36. Recrystallization was effected by dissolving in 100 ml. of hot water (for 1 mole) and adding 2 volumes of 95% ethanol. Fine needle-like crystals were obtained; over-all yield 84.5%.

N-(2-Cyanoethyl)-DL-alanine.—One mole (89.1 g.) of DL-alanine was used and the volume after acidification was 200 ml. Upon adding 270 ml. of 95% ethanol, immediate crystallization occurred. After standing for one hour at 5°, 114 g. of crystals was removed. A second crop of 10 g. was recovered by evaporating the filtrate to a sirup and adding 240 ml. of 95% ethanol to give a total yield of 87.4% of the crude product; calcd. N, 19.69. Found: N, 19.25. Recrystallization was effected by dissolving in 312 ml. of water at 80° and adding 300 ml. of 95% ethanol; over-all yield 117 g. (82.5%).

N-(2-Cyanoethyl)-DL-valine.—After acidification, 95% ethanol was added as for alanine. The crude derivative was recrystallized from hot water.

N-(2-Cyanoethyl)-L-leucine.—Voluminous precipitation occurred upon acidification. After standing in the refrigerator overnight, the mixture was filtered and the precipitate washed free of chloride ions with ice water; yield 75%; N, calcd. 15.20; found, 14.87; m. p. 242–243° dec. The washings and filtrate were combined and evaporated for a second and third crop to give a total yield of 91% of the crude product. Crystallization was effected by dissolving 9.8 g. in 1 l. of hot water to give 5 g. of crystals.

N-(2-Cyanoethyl)-DL-isoleucine.—The crude product was isolated as described for leucine for a yield of 86%; N, calcd. 15.20; found, 15.05. Recrystallization was effected by dissolving 18.5 g. in 500 ml. of boiling water; recovery was 69%.

N-(2-Cyanoethyl)-DL-phenylalanine.—The product was isolated in the same manner as the leucine derivative; total yield 92%.

N-(2-Cyanoethyl)-DL-methionine.—The product was isolated as described for the leucine derivative yield of crude product 98%. Crystallization was effected by dissolving 190 g. in 4 l. of boiling water; recovery 91%.

N-(2-Cyanoethyl)-L-tyrosine.—The product was isolated as described above. The precipitate was quite pure

(5) Method of Analysis, *A. O. A. C.*, 5th Ed., 1940.

(6) Where the barium salt is soluble, barium hydroxide may be used, for example, with glycine. After completion of the reaction, an equivalent amount of sulfuric acid is added and the barium sulfate removed by centrifuging, leaving a solution containing only the product.

(7) Best yields were obtained when exact equivalents were used with glycine, alanine and phenylalanine. With valine, leucine, isoleucine, methionine and tyrosine, a slight excess of acrylonitrile was preferred.

(8) Probably formation of dicyanoethyl derivatives leaving unreacted amino acid.

(9) Acetic acid was preferred for glycine, alanine and valine while hydrochloric acid gave best results with the insoluble derivatives.

(see Table I); yield 93%. No suitable solvent was found for crystallizing. However, fine needles were obtained by adding hydrochloric acid to an aqueous suspension, then adding pyridine or aniline to remove the acid.

Monocyanoethyl Derivatives of Acidic α-Amino Acids.—With these derivatives, it was necessary to avoid the use of excess heat to prevent the formation of uncrystallizable sirups.

N-(2-Cyanoethyl)-DL-aspartic Acid.—One mole (133.1 g.) of DL-aspartic acid was suspended in 100 ml. of water and 2 moles of sodium hydroxide, dissolved in 100 ml. of water, was added. An ice-bath was used to keep the temperature below 20°. Acrylonitrile (1.1 mole) was added and the reaction mixture shaken for thirty minutes at room temperature, then allowed to stand fifteen hours at room temperature. Nitrogen analysis indicated the reaction had gone to completion. Two moles of concentrated hydrochloric acid was added slowly with shaking while the temperature was kept below 20°. The product slowly crystallized at 5°. After two days it was filtered, to yield 159 g. (85%) containing 14.37% nitrogen (calcd. 15.04). After recrystallization from hot water, the nitrogen was 14.98% with a recovery of 77%.

Dipotassium N-(2-Cyanoethyl)-DL-aspartate.—This salt was obtained in quantitative yield by adding one equivalent of acrylonitrile to an aqueous solution of dipotassium DL-aspartate. After standing overnight the mixture was heated to 50° under reflux for two hours and then evaporated to dryness under reduced pressure to give a crystalline salt.

Anal. Calcd.: C, 32.01; H, 3.07; N, 10.7; K, 29.8. Found: C, 32.0; H, 3.2; N, 10.5; K, 29.0.

N-(2-Cyanoethyl)-L-glutamic Acid.—One mole (147.13 g.) of L-glutamic acid was suspended in 100 ml. of water and 2 moles of sodium hydroxide, dissolved in 200 ml. of water, was added slowly with the temperature kept below 20°. One mole (65.6 ml.) of acrylonitrile was added and the mixture shaken for a few minutes before placing it in the refrigerator (5°) overnight. A small layer of unreacted acrylonitrile was still present the next morning. The mixture was allowed to warm up to room temperature, then was shaken for six hours. After the volume had been made up to 500 ml., an analysis of an aliquot indicated that 0.98 mole of acrylonitrile had reacted. Two moles of concentrated hydrochloric acid was added slowly with the temperature kept below 10°.[10] A precipitate formed immediately. After standing overnight at 5°, the precipitate was filtered off and air-dried for twenty-four hours[11] (Found: N, 12.75; calcd. for the monohydrate, N, 12.83). The precipitate weighed 148.2 g. A second crop of 16 g. was obtained by adding acetone and cooling (total yield 76%). The filtrate yielded 17 g. of the pyrrolidone derivative accounting for 85% of the total nitrogen. Forty grams of the crude product dissolved in 250 ml. of water at 35° and cooled in an ice–salt-bath, yielded fine needles. After drying for twelve hours in vacuum at 5°, the needles weighed 30 g. (Found: N, 12.83; calcd. for monohydrate, N, 12.83). One molecule of water was removed from the needles on standing in a vacuum desiccator over phosphorus pentoxide for twenty-four hours, when air-dried for five days, or when suspended in ether overnight. X-Ray diffraction patterns showed a different crystalline structure for the air-dried sample while the ether-dried sample was amorphous. Attempts to determine the solubility of N-(2-cyanoethyl)-L-glutamic acid in water at room temperature were unsuccessful because the compound changed to N-(2-cyanoethyl)-L-pyroglutamic acid within a few hours.

N-(2-Cyanoethyl)-2-L-pyrrolidone-5-carboxylic Acid [N-(2-Cyanoethyl)-L-pyroglutamic Acid].—N-(2-Cyanoethyl)-L-glutamic acid (hydrate or anhydrous form) was quantitatively converted to the pyrrolidone by (1) treating with hot acetone (*ca.* 50°) or by (2) heating in a vacuum oven at 130° for two hours. The pyrrolidone derivative was best prepared by treating acrylonitrile with glutamic acid (1 mole) as described above. After acidification, the reaction mixture was evaporated to dryness under reduced pressure. Hot acetone (300–400 ml.) was added to the residue to obtain the pyrrolidone, which is soluble in acetone. The salt was then filtered off and ether was added to the acetone solution to incipient crystallization. After cooling on Dry Ice 145 g. of the product was obtained (*Anal.* Calcd.: N, 15.37; neut. equiv., 182.2. Found: N, 15.28; neut. equiv., 183). A second crop of 17 g. was obtained by evaporating the filtrate for a total yield of 90%.

Dipotassium N-(2-Cyanoethyl)-L-glutamate.—This compound was prepared in quantitative yield by adding one equivalent of acrylonitrile to an aqueous solution of dipotassium L-glutamate and allowing the reaction mixture to stand at room temperature for twenty-four hours. Upon evaporating the mixture to dryness under reduced pressure, a white crystalline salt was obtained.

Anal. Calcd.: C, 34.8; H, 3.65; N, 10.0; K, 28.3. Found: C, 34.8; H, 3.67; N, 10.0; K, 27.5.

N-(2-Cyanoethyl)-L-proline.—L-Proline (0.05 mole) was dissolved in 100 ml. of water containing one equivalent of potassium hydroxide. Acrylonitrile (0.076 mole) was added and the mixture allowed to stand at room temperature with occasional shaking for two days. One equivalent of hydrochloric acid was added and the solution evaporated to dryness under reduced pressure. The residue was taken up in absolute ethanol and the potassium chloride filtered off. The product failed to crystallize from ethanol. The solution was evaporated to a sirup under reduced pressure, taken up in benzene and allowed to evaporate at room temperature. A crop of crystals was obtained. The crude product recrystallized from hot acetone yielded 1.5 g. (17% yield) of N-(2-cyanoethyl)-L-proline.

Discussion

Because of the similarities in solubility (see Table I) of the monocyanoethyl derivatives and the free amino acids, separation is difficult. To obtain pure derivatives the reaction must go to completion. Titration curves from reaction mixtures were identical with those of the isolated product, indicating that the reaction was quantitative. Nitrogen analysis of reaction mixtures also indicated that one equivalent of acrylonitrile was readily taken up by the amino acids. Where the reaction was sluggish, a slight excess of acrylonitrile was used.

The role of alkali appears to be that of producing the uncharged amino group which is necessary for the condensation. With monocarboxylic amino acids, 0.5 equivalent of alkali did not give complete reaction when one equivalent of acrylonitrile was used and the isolated product was a mixture of the monocyanoethyl derivative and the free amino acid. Attempts to effect the reaction with monosodium (or potassium) salts of aspartic and glutamic acid resulted in an uptake of only 0.5 to 0.6 equivalent of acrylonitrile, even on refluxing. The reaction was quantitative with the dipotassium salt at room temperature. When 0.5 equivalent of sodium carbonate was added to an aqueous solution of glycine containing one equivalent of acrylonitrile and the mixture allowed to stand at room temperature four days, considerable carbon dioxide was liberated. Nitrogen analysis of an aliquot indicated that 0.91

(10) When the temperature was allowed to rise, uncrystallizable sirups were obtained.

(11) Previous attempts to prepare the compound indicated that it was unstable to heat.

equivalent of acrylonitrile had reacted. However, none of the monocyanoethyl derivative could be isolated in pure form. Several fractions, isolated in the solid state, appeared to be a mixture of free glycine and the expected derivative. The greater portion was an uncrystallizable sirup.

With valine, leucine, isoleucine, and tyrosine, an excess of acrylonitrile gave the monocyanoethyl derivative when the reaction was carried out at room temperature. With the other amino acids, there was a tendency for more than one equivalent of acrylonitrile to react, thereby reducing the yield of monocyanoethyl derivative. The monosodium salt of tyrosine is not very soluble in water; however, the heterogeneous mixture appeared to be as reactive toward acrylonitrile as when two equivalents of alkali was present.

Attempts to obtain the monocyanoethyl derivatives of arginine and histidine failed. The fractions obtained from the reaction mixture with arginine were low in nitrogen (20–22%) indicating a breakdown of the guanidino group. The acrylonitrile appeared to react with histidine to give more than one compound and none of the fractions gave constant melting points upon recrystallization.

Titration curves of representative monocyanoethyl derivatives are shown in Figs. 1, 2 and 3.

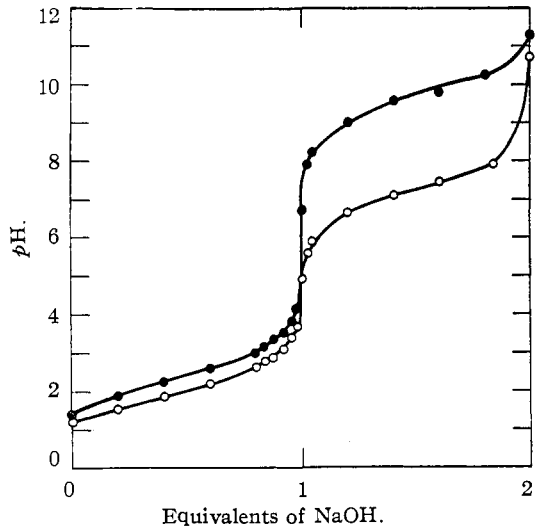


Fig. 1.—Titration curves: ●, DL-alanine; O, N-(2-cyanoethyl)-DL-alanine.

These curves were obtained with a glass electrode and are uncorrected. The depression of the basic character of the alpha amino group is evident.

In all cases the β-cyanoethyl derivatives melted lower than the parent amino acids. The differences in melting points ranged from 35° (methionine) to 90° (aspartic acid). With the exception of those from proline and pyroglutamic acid, all the derivatives exhibited Zwitterionic properties and melted with decomposition.

The derivatives appeared to be stable to both

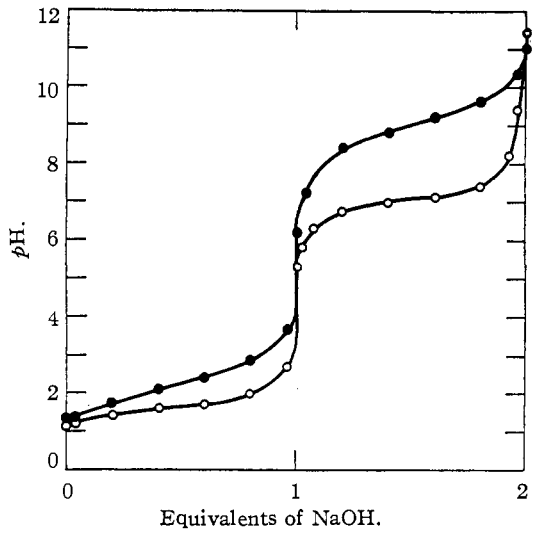


Fig. 2.—Titration curves: ●, DL-methionine; O, N-(2-cyanoethyl)-DL-methionine.

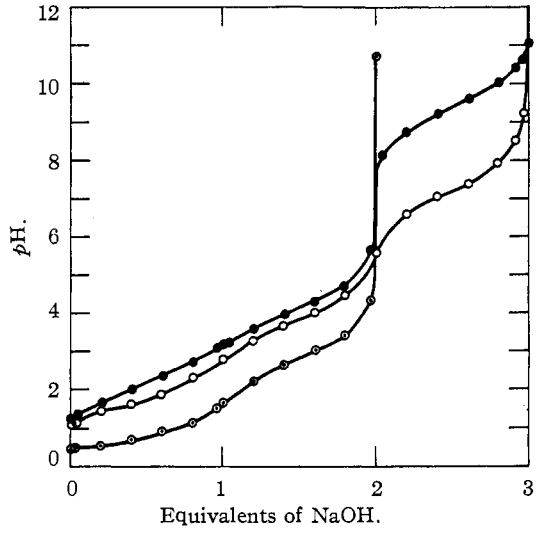


Fig. 3.—Titration curves: ●, L-glutamic acid; O, N-(2-cyanoethyl)-L-pyroglutamic acid; ⊙, N-(2-cyanoethyl)-L-glutiminic acid.

acid and alkali. Boiling with 20% hydrochloric acid and 40% sulfuric acid resulted in no great change other than hydrolysis of the nitrile group. Boiling with strong alkali and measuring the ammonia liberated was used as a method for determining nitrile nitrogen. There was no indication of decomposition or dissociation of the cyanoethyl group.

Racemization apparently did not occur during the reaction as the derivatives were optically active. Data on the optical rotation of the L-amino acids and their derivatives are recorded in Table II. With the exception of the L-glutamic acid derivative the optical rotation of these solutions remained constant on standing for two weeks at room temperature.

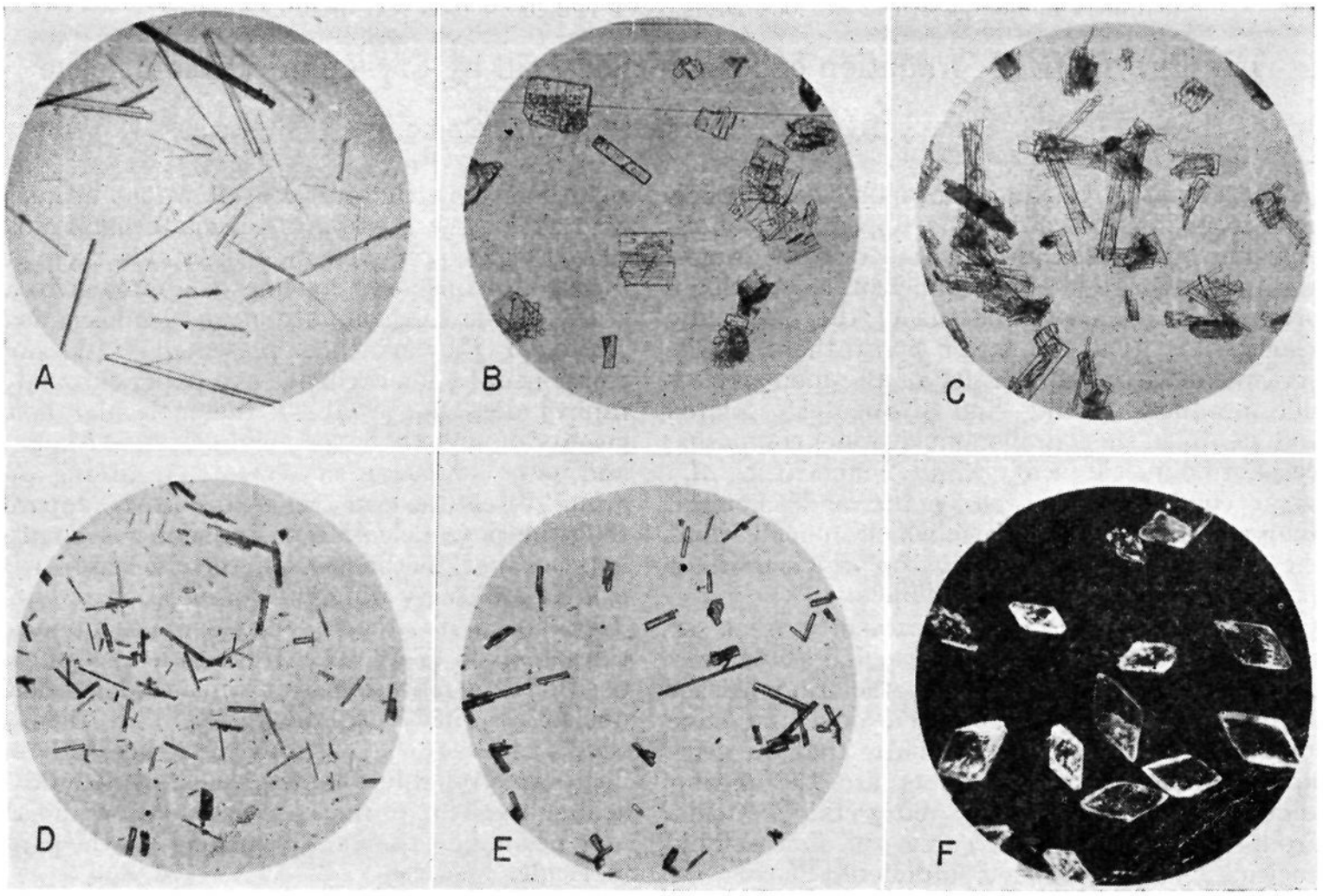


Fig. 4.—A, N-(2-Cyanoethyl)-DL-alanine ×50; B, N-(2-cyanoethyl)-DL-methionine ×100; C, N-(2-cyanoethyl)-DL-phenylalanine ×100; D, N-(2-cyanoethyl)-DL-aspartic acid ×120; E, N-(2-cyanoethyl)-L-glutamic acid H_2O ×120; F, N-(2-cyanoethyl)-L-pyroglutamic acid ×5.

TABLE II

OPTICAL ROTATIONS OF L-AMINO ACIDS AND THEIR N-MONOCYANOETHYL DERIVATIVES

Compound	$[\alpha]^{23}D$	Concn., *M*	Solvent, *N*
L-Leucine	+16.1	0.1	0.4 HCl
N-(2-Cyanoethyl)-L-leucine	+25.9	.1	.4 HCl
L-Glutamic acid	+31.8	.1	.4 HCl
N-(2-Cyanoethyl)-L-glutamic acid	+25.1	.1	.4 HCl
N-(2-Cyanoethyl)-L-pyroglutamic acid	− 7.3	.1	.4 HCl
L-Tyrosine	−14.35	.1	.205 NaOH
N-(2-Cyanoethyl)-L-tyrosine	+12.37	.1	.205 NaOH

Acknowledgment.—The authors are indebted to C. H. VanEtten and Mary B. Wiele of the Microanalytical Section for carbon and hydrogen analyses and Dumas nitrogen determinations.

Summary

1. A series of N-monocyanoethyl derivatives of α-amino acids has been prepared by treatment of aqueous solutions of the alkali (or alkaline earth) metal salts with acrylonitrile. N-Monocyanoethyl derivatives of the following amino acids are reported: glycine, DL-alanine, DL-valine, L-leucine, DL-isoleucine, DL-phenylalanine, L-tyrosine, DL-methionine, DL-aspartic acid, L-glutamic acid, L-pyroglutamic acid, and L-proline.

2. With the exception of proline, one equivalent of acrylonitrile was readily taken up and the reaction appeared to be nearly quantitative.

3. With the exception of proline and pyroglutamic acid, the solubilities of the monocyanoethyl derivatives were similar to those of the parent amino acid. They exhibited Zwitterionic properties, melted with decomposition from 30 to 90° lower than the parent amino acids and were insoluble in organic solvents.

4. Titration curves of the derivatives exhibited the expected depression of basicity of the α-amino group.

5. Arginine and histidine failed to yield monocyanoethyl derivatives under the conditions used for neutral and acidic amino acids.

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