

plus sodamide) or of $C_6H_5-CHLi-COONa^4$ to Schiff bases. (b) Addition of ethyl phenylacetate to Schiff bases in the presence of aluminum chloride, followed by alkaline hydrolysis.⁵⁻⁷

We wish to report that a simple mixture of phenylacetic acid and *N*-benzylidenemethylamine, after being heated at about 100°, affords I, Ar = C_6H_5 , R = CH_3 . No catalyst is necessary. A discussion of possible reaction mechanisms is postponed until we have determined the stereochemical nature (DL-erythro, DL-threo, or some mixture of these) of products formed by the various methods. Only malonic acid has previously been reported capable of adding without catalyst to a carbon-nitrogen double bond to give a beta amino acid.⁸

EXPERIMENTAL

2,3-Diphenyl-3-methylaminopropanoic acid. Equimolecular quantities of phenylacetic acid and *N*-benzylidenemethylamine^{9,10} are heated at 100° for 2 hr. in a flask equipped with a calcium chloride drying tube. The reaction mixture, which is almost completely solid at the end of the heating period, is cooled and treated with a 0.1M NaOH solution. Any alkali-insoluble material is removed by filtration. A stream of carbon dioxide gas is then passed through the alkali solution until the β -aminoacid precipitates. After being filtered, washed with water, and dried it melts at 200°.

Anal. Calcd. for $C_{16}H_{17}NO_2$: C, 75.27; H, 6.71; N, 5.49. Found: C, 74.81; H, 6.85; N, 5.30.

Yields are variable but may reach approximately 75%. Polymerization reactions of the imine, which appear to reduce the yield, may possibly be minimized by the use of an inert diluent.

The β -aminoacid dissolves in very dilute hydrochloric acid. When concentrated hydrochloric acid is added to such a solution, then the hydrochloride of the β -aminoacid precipitates. This substance is easily water soluble but only slightly soluble in fairly concentrated (3M or higher) hydrochloric acid. It melts sharply, but with decomposition, anywhere between 194.5° and 198°, depending on the rate of heating.

Anal. Calcd. for $C_{16}H_{18}ClNO_2$: C, 65.86; H, 6.22; Cl, 12.15; N, 4.80. Found: C, 65.89; H, 6.34; Cl, 11.99; N, 4.69.

A sample of β -aminoacid hydrochloride prepared by Mollov according to method (b) was reported to melt with decomposition at 190–191°. The free β -aminoacid was not described by Mollov.

CHEMISTRY DEPARTMENT
ADELPHI COLLEGE
GARDEN CITY, N. Y.

(4) N. Marécoff, G. Vassileff, and D. Ivanoff, *XVIIth International Congress of Pure and Applied Chemistry*, Paris, July 1957, Congress Handbook Vol. II, Division of Organic Chemistry, pp. 119–120.

(5) B. I. Kurtev and N. M. Mollov, *Doklady Akad. Nauk S.S.S.R.*, **101**, 1069 (1955).

(6) N. M. Mollov and B. I. Kurtev, *Doklady Akad. Nauk S.S.S.R.*, **102**, 287 (1955).

(7) N. M. Mollov, *Doklady Akad. Nauk S.S.S.R.*, **106**, 482 (1956).

(8) T. B. Johnson and J. E. Livak, *J. Am. Chem. Soc.*, **58**, 299 (1936).

(9) H. Zaunschirm, *Ann.*, **245**, 279 (1888).

(10) C. K. Ingold and C. W. Shoppee, *J. Chem. Soc.*, 1204 (1929).

Levulinic Acid. II.¹ Some Derivatives of 2-Aminoethyl Levulinate

ROGER STEVENS

Received July 10, 1957

In connection with other studies a series of esters of levulinic acid were required; most of these have been described previously. Attempts to prepare 2-aminoethyl levulinate by azeotropic esterification of a mixture of levulinic acid and ethanolamine only yielded a viscous gum which could not be distilled; hydrogenation of the same mixture gives 1-(ethan-2-ol)-5-methyl-2-pyrrolid-one.^{2,3} Using the azeotropic method, levulinic acid was successfully esterified with 2-dimethylaminoethanol, 2-diethylaminoethanol, and *N*-2-hydroxyethylphthalimide.

EXPERIMENTAL⁴

2-Dimethylaminoethyl levulinate. Levulinic acid (116 g., 1.0 mole), 2-dimethylaminoethanol (89 g., 1.0 mole), and benzene (100 ml.) were refluxed in a flask fitted with a Dean and Stark adaptor; water (18 ml.) separated in 24 hrs. The reaction product was washed with water, sodium bicarbonate, and dried. After removal of the solvent the ester had b.p. 156–158°/30 mm.; n_D^{23} 1.4395; yield 61 g. (33%).

Anal. Calcd. for $C_9H_{17}O_3N$: C, 57.73; H, 9.15; N, 7.49. Found: C, 57.32; H, 9.08; N, 6.90%.

2-Diethylaminoethyl levulinate. This ester was prepared in a similar manner and had b.p. 172–176°/30 mm., n_D^{27} 1.4435; yield 46%.

Anal. Calcd. for $C_{11}H_{21}O_3N$: C, 61.37; H, 9.83; N, 6.51. Found: C, 61.54; H, 9.45; N, 6.32%.

2-Phthalimidoethyl levulinate. *N*-2-hydroxyethyl phthalimide⁶ (95.5 g., 0.5 mole.) and levulinic acid (58 g., 0.5 mole.) in benzene (100 ml.) were refluxed for 48 hrs. in a flask fitted with a Dean and Stark adaptor; water (9.5 ml.) separated. After cooling the reaction mixture was washed twice with 2N sodium carbonate; at this stage the product crystallized and was collected by filtration. The dried product was recrystallized from ethanol m.p. 90–93°; yield 89 g. (62%).

Anal. Calcd. for $C_{15}H_{15}O_5N$: C, 62.28; H, 5.23; N, 4.84. Found: C, 62.58; H, 5.35; N, 4.91%.

BRITISH WEST INDIES SUGAR RESEARCH SCHEME
THE IMPERIAL COLLEGE OF TROPICAL AGRICULTURE
TRINIDAD, B. W. I.

(1) Part I. *J. Chem. Soc.*, in press.

(2) R. B. Moffett, *J. Org. Chem.*, **14**, 862 (1949).

(3) Y. Hachihama and I. Hayashi, *Technol. Rep. Osaka Univ.*, **4**, No. 108, p. 177 (1954).

(4) Analyses by Drs. Weiler and Strauss, Oxford.

(5) H. Wenker, *J. Am. Chem. Soc.*, **59**, 422 (1937).

Monomeric and Polymeric Compositions from Carbethoxymethyl Isocyanate¹

DONALD A. SMITH AND CORNELIUS C. UNRUH

Received July 15, 1957

Recent work in the field of synthetic polypeptides has provided improved techniques for the

(1) Communication No. 1915 from the Kodak Research Laboratories.

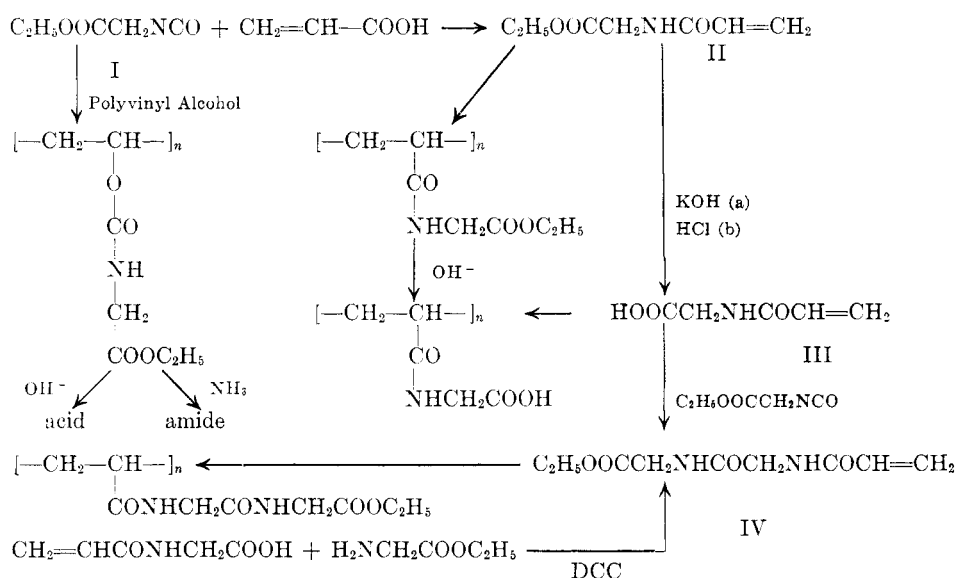
preparation of these materials. We have been concerned in the present work with the synthesis of polymers which have peptide side chains attached to a carbon-carbon backbone. To this end we have prepared ethyl acrylamidoacetate (II) by the reaction of carbethoxymethyl isocyanate with acrylic acid. This compound can be polymerized by free radical initiation and the resultant product saponified to the acid. The conversion of II to acrylamidoacetic acid (III) is accomplished by saponification in alcoholic potassium hydroxide and acidification of the isolated potassium salt in alcohol suspension. The acid (III) undergoes polymerization unless handled at low temperatures; however, the monomeric material can be separated from the polymer by cold recrystallization from acetonitrile.

EXPERIMENTAL

Ethyl acrylamidoacetate. To 100 g. (1.38 moles) of acrylic acid (stabilized with methylene blue) was added dropwise, with stirring, 140 g. (1.16 moles) of carbethoxymethyl isocyanate. During the addition, the temperature was kept at 38–42° by external cooling. When the addition was complete, the mixture was heated slowly to 60° and a few crystals of cupric acetate were added. This resulted in a brisk evolution of carbon dioxide and a rapid increase in temperature to 67°. The solution was allowed to stand 3 days, then heated briefly to 80°, and distilled under reduced pressure. The fraction boiling at 120–140° and 2–3.5 mm. was collected and redistilled from a few grams of Aranox No. 2. The yield of ethyl acrylamidoacetate, a colorless oil which crystallized on cooling, was 65 g. (36%), b.p. 111–114°/1 mm.

Anal. Calcd. for $C_7H_{11}NO_3$: C, 53.5; H, 7.01; N, 8.92. Found: C, 52.9; H, 7.1; N, 8.7.

Acrylamidoacetic acid. To a solution of 5.6 g. (0.1 mole) of



The appendage of a second glycine unit to the acid (III) is satisfactorily accomplished by reaction with a second equivalent of carbethoxymethyl isocyanate to give ethyl acrylamidoacetamidoacetate (IV). The identity of this compound was verified by preparing it from III and ethyl aminoacetate using dicyclohexylcarbodiimide, according to the method of Sheehan.² Attempts to saponify IV and continue the stepwise operation were unsuccessful, probably because of cyclization and/or polymerization.

As an alternative method, we attempted to build peptide side chains directly on a polymer chain. Carbethoxymethyl isocyanate (I) reacted smoothly with polyvinyl alcohol and other hydroxyl-containing polymers to give carbethoxymethyl urethans. These could be saponified readily, but the resulting polymeric acid on treatment with a second mole of the isocyanate (I) formed a cross-linked gel.

potassium hydroxide in 75 ml. of ethanol was added 15.7 g. (0.1 mole) of ethyl acrylamidoacetate. The crystalline potassium salt began to separate almost immediately. After vigorous stirring for 30 min., the mixture was filtered and the product washed with ethanol and dried *in vacuo*. Yield, 9.5 g. (57%).

Anal. Calcd. for $C_8H_9NO_3K$: C, 35.9; H, 3.6; N, 8.4. Found: C, 35.5; H, 4.1; N, 8.0.

A suspension of 35.0 g. (0.21 mole) of potassium acrylamidoacetate in 200 ml. of ethanol was chilled in a freezing mixture and treated with 22.5 ml. of 2.9*N* hydrochloric acid in ethanol so that the temperature did not exceed 0°. Potassium chloride was removed by filtration, the filtrate was concentrated to about 40 ml., and chilled overnight in the refrigerator. The crystalline acid was collected and dried, yield 10.5 g. (39%), m.p. 110–123°. On several occasions the product had partially polymerized at this point. The monomeric material could be separated by extraction with warm acetonitrile. Two recrystallizations from acetonitrile raised the melting point to 130–132°.

Anal. Calcd. for $C_8H_7NO_3$: C, 46.5; H, 5.43; N, 10.8. Found: C, 46.0; H, 5.4; N, 11.4.

Ethyl acrylamidoacetamidoacetate. (a) Four grams of acrylamidoacetic acid (0.03 mole) and 6 ml. of carbethoxymethyl isocyanate (0.04 mole) were combined and kept at 60°. After a few minutes, evolution of carbon dioxide was brisk and solution occurred. On further heating, the solution solidified and was then treated with ether and the solid

(2) J. C. Sheehan and G. P. Hess, *J. Am. Chem. Soc.*, **77**, 1067 (1955).

collected and dried, yield 2.6 g. (42%). Recrystallization from hot water gave pale yellow leaflets melting at 149–150°. A mixed melting point with *N,N'*-dicarbethoxymethylurea (m.p. 147–148°) was depressed to 125–131°.

Anal. Calcd. for $C_9H_{14}N_2O_4$: C, 50.5; H, 6.55; N, 13.1. Found: C, 50.8; H, 7.0; N, 12.9.

(b) A solution of 10.6 g. (0.01 mole) of ethyl glycinate (freshly distilled) and 21.0 g. (0.1 mole) of dicyclohexylcarbodiimide in 50 ml. of ethanol was treated with 13.0 g. (0.1 mole) of acrylamidoacetic acid dissolved in a little ethanol. After shaking 30 min., the mixture was filtered and the solid washed with ethanol. The filtrate was evaporated to dryness, yielding 1.5 g. of impure material which was not worked up. The solid was repeatedly extracted with hot acetonitrile, the combined extracts were concentrated and chilled, yielding 12.3 g. (58%) of colorless crystals, m.p. 148–150°. A mixed melting point with the product obtained in (a) was not depressed.

Poly(ethyl acrylamidoacetate). A solution of 10.0 g. (0.047 mole) of ethyl acrylamidoacetate in 30 ml. of water was treated with a trace of ammonium persulfate and kept at 60° for 2 hr. The soft white cake was separated and squeezed dry. It was soluble in alcohol and other organic solvents in the freshly prepared state but drying rendered it insoluble.

Ammonolysis of this product with aqueous ammonia at room temperature gave a polymer which showed thermally reversible gelation.

Saponification of the polymeric ester with dilute sodium hydroxide at room temperature yielded the acid which also showed gelation properties.

Poly(ethyl acrylamidoacetamidoacetate). Ethyl acrylamidoacetamidoacetate in aqueous solution gave a soft spongy polymer when heated with a trace of potassium persulfate. This material could be converted to the acid as in the previous example, but it did not show gelation properties.

Poly(vinyl carbazymethylcarbamate). A suspension of 50 g. of polyvinyl alcohol (Elvanol 71–30) in 500 ml. of pyridine was treated with 180 g. of carbethoxymethyl isocyanate and stirred on the steam-bath for 1 hr. The resulting solution was poured into a large volume of cold water and the rubbery precipitate washed. The ester was converted to the acid by stirring at 25° with a solution of 45 g. of sodium hydroxide in 800 ml. of water. This operation produced an almost clear solution from which the product was isolated by precipitation in dilute hydrochloric acid. The product was purified by solution in methanol and precipitation in acetone.

Treatment of this material with carbethoxymethyl isocyanate in dimethylformamide solution at 150° gave a cross-linked product.

RESEARCH LABORATORIES
EASTMAN KODAK Co.
ROCHESTER 4, N. Y.

Decarbonylation of 3-Indoleglyoxalyl Chloride

PAUL E. PETERSON, JOHN P. WOLF III,
AND CARL NIEMANN

Received July 15, 1957

The observation that 3-indoleglyoxalyl chloride may be prepared in excellent yield by the reaction of indole with oxalyl chloride¹ and that *p*-dimethylaminobenzoyl chloride, the expected product from the decarbonylation of *p*-dimethylaminophenylgly-

oxalyl chloride, may be obtained by the reaction of dimethylaniline with oxalyl chloride² led us to investigate the possibility of using 3-indoleglyoxalyl chloride as an intermediate in the preparation of 3-indolecarbonyl chloride.

When a solution of 3-indoleglyoxalyl chloride in tetrachloroethane was heated to 115–120°, carbon monoxide was evolved and when hexane was added to the cooled reaction mixture a precipitate was obtained. Fractional recrystallization of this precipitate from a mixture of benzene and hexane gave 3-indolecarbonyl chloride in yields of 16–23% based upon indole. The acid chloride was identified by hydrolysis to the known 3-indolecarboxylic acid³ and by alcoholysis to the known methyl and ethyl 3-indolecarboxylates.^{3,4}

Because of the ease with which indole can be transformed into 3-indolecarbonyl chloride, the relatively low yield of *ca.* 20% is not too disturbing. However, in order to understand the reasons for the low yield, the crude reaction product was analyzed and it was observed that it contained but *ca.* 25% of the expected amount of chlorine. When an infrared spectrum of the crude reaction product disclosed the presence of two carbonyl peaks, *i.e.*, one at *ca.* 1750 cm^{-1} and the other at *ca.* 1690 cm^{-1} , and when it was found that alkaline hydrolysis of the same material gave, after acidification, 3-indolecarboxylic acid in yields of *ca.* 95%, it became evident⁵ that the crude reaction product was a mixture containing *ca.* 25% of the expected 3-indolecarbonyl chloride with the remainder being principally a polymeric amide arising from the reaction of the acid chloride with itself. All attempts to limit the formation of this latter substance, except by the impractical procedure of conducting the reaction under conditions of extreme dilution, were unsuccessful. The remaining alternative of hydrolyzing the polymeric amide to 3-indolecarboxylic acid and then attempting to convert this substance to the acid chloride was also considered impractical because of the availability of both indole and oxalyl chloride and the ease of obtaining the desired acid chloride from the crude reaction product.

Since our interest in 3-indolecarbonyl chloride was generated by its anticipated use in the acylation of α -amino acid derivatives, it was gratifying to find that 3-indolecarboxanilide, 3-indolecarbox-*p*-toluide, 3-indolecarbonylglycine ethyl ester, and 3-indolecarbonyl-L-phenylalanine methyl ester could be prepared in 30–50% yields from the acid chloride and the amine using conventional procedures.

(2) H. Staudinger and H. Stockmann, *Ber.*, **42**, 3485 (1909).

(3) R. Majima, *Ber.*, **55**, 3865 (1922).

(4) C. Zahi and A. Ferratini, *Ber.*, **23**, 2297 (1890).

(5) L. J. Bellamy, *Infra-red Spectra of Complex Molecules*, John Wiley and Sons, New York, N. Y. (1954).

(1) M. E. Specter and W. C. Anthony, *J. Am. Chem. Soc.*, **76**, 6208 (1954).