

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 chloride<sup>1</sup> 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 chloride<sup>2</sup> 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 acid<sup>3</sup> and by alcoholysis to the known methyl and ethyl 3-indolecarboxylates.<sup>3,4</sup>

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  $\text{cm}^{-1}$  and the other at *ca.* 1690  $\text{cm}^{-1}$ , 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 evident<sup>5</sup> 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  $\alpha$ -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).

EXPERIMENTAL<sup>6,7</sup>

**3-Indolecarbonyl chloride.** The 3-indoleglyoxalyl chloride obtained from the reaction of 10 g. of indole with 10 ml. of oxalyl chloride in 100 ml. of ether<sup>1</sup> was dissolved in 150 ml. of tetrachloroethane and the solution heated to 115–120°. After the rapid evolution of carbon monoxide had ceased, the deep brown solution was rapidly cooled to room temperature, 450 ml. of hexane added to precipitate the crude reaction product, the latter collected, washed with hexane, and dried in a stream of dry air to give ca. 10 g. of crude reaction product in the form of a brownish yellow powder. Analysis of a representative product gave Cl, 4.7%; calcd. for 3-indolecarbonyl chloride, 11.1%. An infrared spectrum, determined in solid KBr, exhibited two peaks of ca. equal intensity, one at ca. 1750 cm.<sup>-1</sup> and the other at ca. 1690 cm.<sup>-1</sup> The crude reaction product was dissolved in boiling benzene, the solution filtered, 25 ml. of hexane added to the hot solution, the dark brown precipitate which appeared on cooling discarded, an additional 5 ml. of hexane added to the filtrate, the brown precipitate again discarded, 75 ml. of hexane added to the now light yellow solution to give after collection by filtration and drying 2.5–3.5 g., (16–23% based upon indole) of 3-indolecarbonyl chloride in the form of yellow crystals.

Hydrolysis of the above acid chloride in the presence of 1M aqueous sodium bicarbonate gave, after acidification, 3-indolecarboxylic acid, m.p. 217–219° dec. (lit.<sup>3</sup> m.p. 218–220).

The crude reaction product, 10.61 g., was suspended in 60 ml. of aqueous 1M sodium bicarbonate, the insoluble residue collected and the solution acidified to give 1.17 g. (11%) of 3-indolecarboxylic acid, m.p. 217–219° with dec. The insoluble residue was dissolved in 60 ml. of 1M aqueous sodium hydroxide, the solution filtered and the filtrate acidified to give 6.17 g. (58%) of 3-indolecarboxylic acid, m.p. 214–217° dec. Hydrolysis of the crude reaction product with 1M aqueous sodium hydroxide under more drastic conditions gave, after acidification, ca. 95% of the above carboxylic acid.

To a filtered solution of 3 g. of the crude reaction product in 25 ml. of anhydrous methanol, was added 30 ml. of water. The solid product which formed was recrystallized from aqueous methanol to give ca. 1 g. of methyl 3-indolecarboxylate, m.p. 144–145.6° (lit.<sup>4</sup> m.p. 147–148°).

The similar reaction of 3 g. of the crude reaction product with 25 ml. of absolute ethanol gave, after three recrystallizations from aqueous ethanol, ca. 1 g. of ethyl 3-indolecarboxylate, m.p. 119–123° (lit.<sup>3</sup> m.p. 118–120°).

**3-Indolecarboxanilide.** Recrystallized 3-indolecarbonyl chloride was added to an excess of aniline in anhydrous ethyl acetate, the ethyl acetate solution washed with aqueous hydrochloric acid, aqueous sodium hydroxide and water and then dried. The addition of hexane to the dry ethyl acetate solution gave 3-indolecarboxanilide, m.p. 175.5–176.2° after recrystallization from aqueous ethanol.

*Anal.* Calcd. for C<sub>15</sub>H<sub>12</sub>ON<sub>2</sub> (236): C, 76.3; H, 5.1; N, 11.9. Found: C, 76.4; H, 5.2; N, 11.8.

**3-Indolecarbox-*p*-toluide.** The reaction of the recrystallized acid chloride with *p*-toluidine as described above for the corresponding anilide gave 3-indolecarbox-*p*-toluide, m.p. 200.9–201.1°, after recrystallization from aqueous ethanol.

*Anal.* Calcd. for C<sub>16</sub>H<sub>14</sub>ON<sub>2</sub> (250): C, 76.8; H, 5.6; N, 11.2. Found: C, 76.9; H, 5.7; N, 10.8.

**3-Indolecarbonylglycine ethyl ester.** A solution of 1.55 g. of glycine ethyl ester hydrochloride in 5 ml. of water containing 3.18 g. of potassium carbonate was placed in a separatory funnel containing 60 ml. of ethyl acetate. Two grams of recrystallized 3-indolecarbonyl chloride in 30 ml. of ethyl acetate was added to the reaction mixture which was then shaken for 10 min. The ethyl acetate phase was separated,

washed with water, dried, and the solvent removed to give 0.84 g. (30%) of 3-indolecarbonylglycine ethyl ester, m.p. 159–160°, after recrystallization from aqueous ethanol.

*Anal.* Calcd. for C<sub>13</sub>H<sub>14</sub>O<sub>3</sub>N<sub>2</sub> (246): C, 63.4; H, 5.7; N, 11.4. Found: C, 63.5; H, 5.7; N, 11.6.

**3-Indolecarbonyl-L-phenylalanine methyl ester.** The reaction of 2 g. of 3-indolecarbonyl chloride, 3.2 g. of L-phenylalanine methyl ester hydrochloride and 4.18 g. of potassium carbonate was conducted as described for the glycine analog. The oily product recovered from the ethyl acetate phase was dissolved in methanol and this solution was brought to the cloud point by the addition of water. After standing for 20 hr. at 4°, the product was collected and recrystallized from aqueous methanol to give 1.08 g. (30%) of 3-indolecarbonyl-L-phenylalanine methyl ester, m.p. 133–134°.

*Anal.* Calcd. for C<sub>19</sub>H<sub>18</sub>O<sub>3</sub>N<sub>2</sub> (322): C, 70.8; H, 5.6; N, 8.7. Found: C, 70.8; H, 5.6; N, 8.7.

This investigation was supported in part by a grant from the National Institutes of Health, U. S. Public Health Service.

CONTRIBUTION No. 2222 FROM THE GATES  
AND CRELLIN LABORATORIES OF CHEMISTRY  
CALIFORNIA INSTITUTE OF TECHNOLOGY  
PASADENA 4, CALIF.

Glycolamide Esters of Acylated  $\alpha$ -Amino Acids

RICHARD J. KERR AND CARL NIEMANN

Received August 5, 1957

It is common knowledge that a number of acylated  $\alpha$ -amino acid alkyl esters are hydrolyzed in the presence of the pancreatic proteases. However, their use as specific substrates in studies with the above enzymes frequently is limited by their relatively low solubility in water.

In the course of a search for a class of neutral water soluble acylated  $\alpha$ -amino acid esters capable of functioning as specific substrates for  $\alpha$ -chymotrypsin, it was observed that benzoylglycolamide, prepared by the condensation of sodium benzoate and chloracetamide, was sufficiently soluble in water to permit the preparation of 0.1 M solutions. While the very water soluble acetyl-DL-phenylalanine glycolamide ester could be prepared in an analogous manner, it was clear that a more satisfactory synthesis was required.

When acetyl-DL and L-phenylalanine were employed as representative examples, it was found that reaction of the corresponding cyanomethyl esters<sup>1</sup> with an excess of hydrogen chloride and one mole equivalent of methanol in benzene, followed by removal of the benzene by distillation at atmospheric pressure, gave the desired acetyl-DL- and L-phenylalanine glycolamide esters in good yields. McElvain and Nelson<sup>2</sup> have noted that imidoes-

(1) R. Schwyzer, M. Feurer, B. Iselin, and H. Kagi, *Helv. Chim. Acta*, **38**, 80 (1955).

(2) S. M. McElvain and J. N. Nelson, *J. Am. Chem. Soc.*, **64**, 1825 (1942).

(6) All melting points are corrected.

(7) Microanalyses by Dr. A. Elek.