of δ-aminovaleric acid-δ-C^{14} obtained was 0.55 g. This represents a yield of 59% after taking into account the recovered cyanide. After trituration with a little cold absolute ethanol, 25 ml. of acetone was added and the product was obtained by filtration. Paper chromatography both with collidine–lutidine–water and phenol–water yielded only one ninhydrin reactive spot which corresponded in each case to that obtained with authentic δ-aminovaleric acid (Eastman Kodak Co.). From the radioactive preparation only one radioactive spot was obtained which coincided exactly with the ninhydrin reactive spot of δ-aminovaleric acid. The product was halogen free and melted at 155–156° (reported for δ-aminovaleric acid, 156°).

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Polyphosphoric Acid as a Reagent in Organic Chemistry. V. Conversion of Acids to Substituted Amides; Further Observations on the Lossen Reaction

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In an earlier paper[2] it was postulated that the reaction of hydroxylamine with aromatic carboxylic acids in the presence of polyphosphoric acid proceeds to the amine by way of an intermediate hydroxamic acid. In agreement with this postulate it has been found that carboxylic acids react with weakly basic amines under similar conditions to yield the corresponding amides.

The yields of substituted amides formed from benzoic acid and various amines increase markedly as the basic strength of the amine decreases (Table I). Thus aniline was found to be unreactive while 2,4-dinitroaniline reacts almost quantitatively. The reaction is not limited to aromatic acids since acetic acid and 2,4-dinitroaniline give a 92% yield of 2,4-dinitroacetanilide.

The acylation of *p*-nitroaniline with various carboxylic acids was investigated. In these reactions, the ease of amide formation appears to increase as acid strength decreases. However, as shown in Table I, the correlation is not so clearly defined as that pertaining to the basic strength of the amines. Of the nitrobenzoic acids only the *meta* isomer reacts to give the amide and the yield is very low (8%). Neither *o*-nitrobenzoic acid nor the para isomer reacts with 2,4-dinitroaniline.

Further attempts were made to extend the amine synthesis[2] to aliphatic acids. With slightly modified conditions it was found that aliphatic acids do react with hydroxylamine to give low yields of the expected amines. *n*-Amylamine and cyclohexylamine were obtained in yields of 25 and 36%, respectively. The reaction, in contrast with that of aromatic acids, is difficult to control and gives considerable amounts of dark ether-insoluble oil.

Experimental

Table I gives the yields of crude amides obtained. The melting points are given as an indication of purity.

A. **Amide Formation.**—The preparation of *p*-nitroacetanilide is typical of the method used.

TABLE I

Acid	Amine	Amide Yield, %	M.p., °C.	Reported m.p., °C.
Benzoic	Methoxyamine	0		
Benzoic	Aniline	0		
Benzoic	*o*-Chloroaniline	39	98–99	99
Benzoic	*p*-Nitroaniline	54	196–197	199
Benzoic	*o*-Nitroaniline	71	90–92	94
Benzoic	2,4-Dinitroaniline	98	196–200	200–202
Acetic	2,4-Dinitroaniline	92	119–120	121
Acetic	*p*-Nitroaniline	67[a]	213–214	214
o-Chlorobenzoic	*p*-Nitroaniline	64	180–182	180
p-Toluic	*p*-Nitroaniline	60	201–203	206.5
m-Nitrobenzoic	*p*-Nitroaniline	8[b]	248–249	249
o-Nitrobenzoic	*p*-Nitroaniline	0		
p-Nitrobenzoic	*p*-Nitroaniline	0		
Monochloroacetic	*p*-Nitroaniline	7[b]	184–185	185
o-Nitrobenzoic	2,4-Dinitroaniline	0		
p-Nitrobenzoic	2,4-Dinitroaniline	0		

[a] Recrystallized from a mixture of dimethylformamide and water. [b] Recrystallized from ethanol.

To a mixture of 3.5 g. of acetic acid and 4.0 g. of *p*-nitroaniline in a three-necked flask, fitted with a reflux condenser and stirrer, was added 70 g. of polyphosphoric acid. The flask was placed in an oil-bath and the temperature was raised to 160° in the course of 20 minutes. The mixture was then hydrolyzed by pouring it over 200 g. of crushed ice. The precipitated amide was filtered off, washed with water and then recrystallized from a mixture of dimethylformamide and water. The *p*-nitroacetanilide was obtained in the form of fluffy white crystals melting at 213–214°. The yield was 3.5 g. (67%).

B. **Amine Synthesis.**—*n*-Amylamine and cyclohexylamine were prepared by essentially the same procedure.

A mixture of 7.0 g. of hydroxylamine hydrochloride and 85 g. of polyphosphoric acid was placed in a three-necked flask fitted with a reflux condenser and a stirrer. The mixture was heated to 135°, held at that temperature until the evolution of hydrogen chloride had ceased and then 10.0 g. of cyclohexanecarboxylic acid was added. The vigorous evolution of carbon dioxide which occurred was complete in about ten minutes. The mixture was hydrolyzed by pouring it over 200 g. of crushed ice and the resulting brown solution was made strongly basic with potassium hydroxide. This caused the separation of a brownish-black oil. The mixture was then extracted continuously with ether for 15 hours. The extract was dried over potassium hydroxide and then distilled through a Holtzmann column. The fraction boiling at 136° was collected. The yield was 2.8 g. (36%). The identity of the amine was confirmed by its conversion to the corresponding phenylthiourea, melting point 148°.

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[1] Visking Corporation Fellow, 1953-1954.

[2] H. R. Snyder, C. T. Elston and D. B. Kellom, THIS JOURNAL, **75**, 2014 (1953).

Polyphosphoric Acid as a Reagent in Organic Chemistry. VI.[1] The Hydrolysis of Nitriles to Amides

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The use of 100% phosphoric acid in the hydrolysis of nitriles to acids has been known for some time.[3] Recently, however, the effectiveness of polyphosphoric acid in the Beckmann rearrangement[4] and in the acylation of amines[1] indicated the rather exceptional stability of amides in this reagent. The reaction of polyphosphoric acid with various nitriles was therefore investigated.

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[1] For the preceding paper, see H. R. Snyder and C. T. Elston, THIS JOURNAL, **76**, 3039 (1954).

[2] Visking Corporation Fellow.

[3] G. Berger and S. C. J. Olivier, *Rec. trav. chim.*, **46**, 600 (1927).

[4] E. C. Horning, V. L. Stromberg and H. A. Lloyd, THIS JOURNAL, **74**, 5153 (1952).