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Synthesis of *N*-Carboalkoxy-ϵ-Aminocaproic Acid Esters

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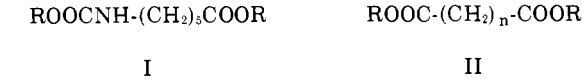
Two procedures for the synthesis of *N*-carboalkoxy-ϵ-aminocaproates starting with ϵ-caprolactam are described. The first method involves hydrolysis, treatment with a chloroformate, and esterification. The second procedure involves alcoholysis, phosgenation, and treatment with an alcohol. Physical properties of the compounds and their intermediates are listed.

STRUCTURAL SIMILARITY between *N*-carboalkoxy-ϵ-aminocaproic acid esters (I) and diesters of aliphatic dicarboxylic acids (II), prompted the synthesis of a variety of such urethane-esters and the evaluation of them in areas where the diesters find wide applications—plasticizers, synthetic lubricants, polymer intermediates.



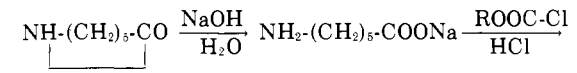
I II

The higher homologues of the urethane-esters were effective plasticizers for poly(vinyl chloride) resins and exhibited little tendency towards migration. Polymers containing both urea and amide linkages were prepared by condensing a urethane-ester with an aliphatic diamine.

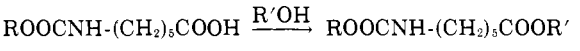
Treibs and Hauptmann (*4*) prepared methyl *N*-carbomethoxy-ϵ-aminocaproate via a Hofmann degradation by treating 6-carbomethoxyhexanoic acid amide with bromine and alkali in the presence of methanol. Adamson and Kenner (*1*) synthesized ethyl *N*-carboethoxy-ϵ-aminocaproate from ethyl-ϵ-aminocaproate. The disadvantage of the latter method is that a relatively unstable intermediate (the free amino ester) must be used.

Two convenient methods for the synthesis of the *N*-carboalkoxy-ϵ-aminocaproates starting with ϵ-caprolactam were developed.

Chloroformate Method.



III IV

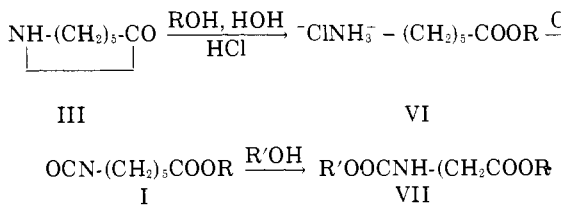


V I

Refluxing ϵ-caprolactam (III) with an aqueous solution of sodium hydroxide effects the ring opening (IV), following which an alkyl chloroformate is added at room temperature. Upon acidification, the *N*-carboalkoxy-ϵ-aminocaproic acid (V) is obtained. The latter is esterified with an alcohol in the usual manner to give the *N*-carboalkoxy-ϵ-aminocaproic acid ester (I).

Table I lists a variety of urethane acids prepared by this method.

Isocyanate Method.



III VI

I VII

Refluxing ϵ-caprolactam (III) with an excess of alcohol and the theoretical amount of water while passing in gaseous hydrogen chloride effects the ring opening. The water and excess alcohol are removed by distillation at reduced pressure, following which the amino ester hydrochloride (VI) is converted to the isocyanate (VII) by phosgenation in an inert solvent. Condensation of the isocyanate ester with an alcohol yielded the corresponding urethane ester (I).

Hydrolyzing ϵ-caprolactam by refluxing with hydrochloric acid yields ϵ-aminocaproic acid hydrochloride (2), which, on heating with an alcohol, gives the corresponding ϵ-aminocaproic acid ester hydrochloride. Excellent yields are obtained when the alcohol used is methanol (3), ethanol, or propanol. However, attempts to prepare the butyl or higher amino ester hydrochloride homologs via this method always resulted in the formation of a product which was unsuitable for phosgenation.

Phosgenation of the amino ester hydrochlorides is best carried out by refluxing in toluene or chlorobenzene. Table III lists the alkyl-ϵ-isocyanatocaproates prepared by this method.

Table IV lists a series of alkyl-*N*-carboalkoxy-ϵ-aminocaproates prepared by reacting alkyl-6-isocyanatocaproates with alcohols. The reaction proceeds smoothly by heating the isocyanato ester with the alcohol and using a tertiary amine as a catalyst.

PROCEDURE

N-Carboalkoxy-ϵ-aminocaproic acids. A solution of 0.5 mole of ϵ-caprolactam in 300 ml. of water containing 1.0 mole of sodium hydroxide was agitated and refluxed for four hours. After the mixture was cooled to room temperature, 0.5 mole of an alkyl chloroformate was added dropwise while maintaining the temperature below 20° C. After being stirred at room temperature for 16 hours, the solution was acidified with dilute hydrochloric acid (1:1 by volume). The product was filtered, washed free of acid with distilled water and dried in vacuo at room temperature. The product was pure enough for further use.

Alkyl-ϵ-isocyanatocaproates. A solution consisting of 0.5 mole of ϵ-caprolactam, 0.7 mole of an alcohol, and 0.5 mole of water was refluxed for six hours while a steady stream of hydrogen chloride was passed in. Toluene, 50 ml., was added and the water removed by an azeotropic distillation through a Dean-Stark trap. The excess alcohol was distilled at reduced pressure leaving behind the alkyl-ϵ-aminocaproate hydrochloride which was suitable for phosgenation.

The hydrochloride was suspended in 200 ml. of toluene and refluxed. Phosgene was bubbled through the mixture at a vigorous rate until no more hydrogen chloride was evolved and the mixture became homogeneous. After being purged with dry nitrogen to remove excess phosgene, the solution was stripped of toluene at reduced pressure and the residue distilled under vacuum to yield the alkyl-6-isocyanatocaproate.

Alkyl-*N*-carboalkoxy-ϵ-aminocaproates. A solution of 0.25 mole of an *N*-carboalkoxy-ϵ-aminocaproic acid, 1.0 mole of an alcohol, 200 ml. of toluene, and 1 gram of *p*-toluene sulfonic acid was refluxed for 18 hours while water formed during the reaction was removed through a Dean-Stark trap. The reaction mixture was filtered. The filtrate was washed with four 50-ml. portions of distilled water, with four 50-ml. portions of a 5% aqueous sodium carbonate solution, again with four 50-ml. portions of water and then dried over anhydrous sodium sulfate. The toluene and excess alcohol were removed by distillation and the alkyl-*N*-carboalkoxy-ϵ-aminocaproate was isolated by fractionation under vacuum.

Another method of preparation is to treat a solution of 0.1 mole of an alkyl-6-isocyanatocaproate and 0.3 mole of an alcohol in 100 ml. of toluene with 2 ml. of triethylamine and reflux for 16 hours. The toluene and excess alcohol are removed by distillation, and the product is isolated and purified by fractionation at reduced pressure.

Table I. *N*-Carboalkoxy-ϵ-Aminocaproic Acids

(ROOCNH-$(CH_2)_5$-COOH)

R, Alkyl	Yield, %	M.P., ° C.	Nitrogen, % Calcd.	Found
Ethyl	77	...[b]	...	...
n-Propyl	88	57–58	6.45	6.3
n-Butyl	97	51–52	6.06	5.9
n-Pentyl	92	43–44	5.7	5.6
n-Hexyl	95	49–50	5.4	5.4

[a] Melting points are uncorrected. [b] Liquid at room temperature.

Table II. Alkyl-*N*-Carboalkoxy-ϵ-Aminocaproates

(ROOCNH-$(CH_2)_5$COOR)

Product R	Product R′	Yield, %	B.P., ° C./mm. Hg	Nitrogen Calcd.	Found
Ethyl	Ethyl	82	136–142/2	6.06	5.9
Ethyl	*n*-Butyl	94	152–155/2	5.4	5.2
Ethyl	2-Ethylhexyl	87	172–176/2	4.4	4.5
n-Propyl	*n*-Butyl	..	182–183/2	5.1	5.1
n-Propyl	2-Ethylhexyl	..	218–219/4	4.3	4.3
n-Butyl	*n*-Butyl	84	200–202/4	4.9	4.9
n-Butyl	2-Ethylhexyl	74	204–207/2	4.1	4.2
n-Pentyl	*n*-Butyl	72	181–184/2	4.7	4.8
n-Pentyl	2-Ethylhexyl	70	228–230/5	3.9	4.05
n-Hexyl	*n*-Butyl	69	201–204/3	4.4	4.5
n-Hexyl	2-Ethylhexyl	70	208–210/2	3.8	3.9

Table III. Alkyl-ϵ-Isocyanatocaproates

(OCN-$(CH_2)_5$-COOR)

R Alkyl Group	Yield, %	B.P., ° C./mm. Hg	%-NCO Calcd.	Found
Methyl	88	111–112/6	24.6	24.6
Ethyl	76	96–98/2	22.6	22.6
n-Butyl	57	135–136/7	19.4	19.4
n-Octyl	56	181–189/8–9	15.6	15.6
2-Ethylhexyl	73	172–173/6	15.6	15.5
n-Decyl	51	200–205/10	14.1	13.6
n-Dodecyl	60	215–221/7	12.9	12.8

Table IV. Alkyl-*N*-Carboalkoxy-ϵ-Aminocaproates

(ROOCNH-$(CH_2)_5$COOR′)

Product R	Product R′	Yield, %	B.P., ° C./mm. Hg	Nitrogen Calcd.	Found
Methyl	Methyl	88	164–165/9	6.9	6.4
n-Butyl	*n*-Butyl	80	200–202/4	4.9	4.9
n-Octyl	*n*-Octyl	63	200–205/2–3	3.5	3.6
2-Ethylhexyl	2-Ethylhexyl	69	190–200/2–3	3.5	3.6

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