rearranged alkyl halide (which reacts much faster than methyldi-*t*-butylcarbinyl chloride) and olefin, the total solid was stirred for 1 hr. in absolute ethanol to allow fractional solvolysis. The solvent was evaporated and the residue was vacuum sublimed at room temperature twice. Methyldi-*t*-butylcarbinyl chloride was obtained as pure white crystals, m.p. 86.5–87°, lit.[16] m.p. 68–70° dec. Thin layer chromatography in ethyl acetate–chloroform, chloroform, benzene, or *n*-hexane, developed with iodine, showed only one peak. The substance shows the same retention time before and after fractional solvolysis. If the purified substance is subjected to the conditions of its preparation from the alcohol, it can be recovered unchanged.

Equivalent Weight Determination.—An aliquot of methyldi-*t*-butylcarbinyl chloride was dissolved in excess base and back titrated with acid, giving equivalent weights in two determinations of 180 and 184.3 (calcd. 176.5).

2,3,3,4,4-Pentamethyl-2-chloropentane, dimethyltriptylcarbinyl chloride, was prepared from dimethyltriptylcarbinol in the same way as 2,2,3,4,4-pentamethyl-3-chloropentane. Purification was achieved by vacuum sublimation at room temperature. Contact with air caused decomposition; thus, for kinetic measurements direct transfer from the sublimation device to the conductance cell was necessary. Physical constants, except the n.m.r. spectrum, were not obtained.

Dideuteriosulfuric acid was prepared according to Brauer.[25]

Solvents.—Solvents for solvolysis were made up by weight methods[21] even though they are identified in the conventional terminology: *e.g.*, 80% aqueous ethanol refers to a solution that would be obtained by mixing four volumes of ethanol with one volume of water, both measured at 25°.

Kinetic Measurements and Product Studies.—The rates of solvolysis were followed conductometrically[21] and the results were processed by means of a least-squares program on the IBM 709 digital computer.

Products of Solvolysis.—An aliquot of the alkyl halide was dissolved in dioxane–water (about 2:1) and stirred in a closed flask for 48 hr. at room temperature. After completion of the reaction, the flask was connected to a sublimation device with a cold finger kept at −75°. The stopcock was then opened, and under vacuum the cold finger quickly became covered with a solid material. The sublimation was interrupted after a short time, and some of the condensed phase was dissolved in carbon tetrachloride and transferred into an n.m.r. tube. The n.m.r. spectrum did not show in either case any organic material besides dioxane and a small amount of the unfragmented olefins. Therefore, it can be concluded that no low-boiling fragments are formed during solvolysis.

N.m.r. spectra were taken with a Varian A-60 spectrometer. The observed shifts in δ (parts per million) from tetramethylsilane internal reference in carbon tetrachloride solution are given in Table I.

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[25] G. Brauer, "Handbuch der präprativen anorganischen Chemie," Vol. I, F. Enke, Stuttgart, 1960, p. 134.

The Syntheses and Some Reactions of ω-Isocyanatoalkanecarboxylic Acid Chlorides and Isocyanatobenzoyl Chlorides

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3-, 5-, and 6-isocyanatoalkanecarboxylic acid chlorides and *m*- and *p*-isocyanatobenzoyl chlorides were prepared by treatment of the corresponding amino acids or their hydrochlorides with phosgene and hydrogen chloride in dioxane. In the same reaction, 4-aminobutanoic acid and *o*-aminobenzoic acid gave 1-chloroformyl-5-chloro-2,3-dihydropyrrole and isatoic anhydride, respectively. *o*-Isocyanatobenzoyl chloride was obtained by treating isatoic anhydride with thionyl chloride or phosphorus pentachloride. These isocyanatocarboxylic acid chlorides reacted with excess primary and secondary amines, ethanol, and water at both groups, COCl and NCO. With 1 mole of amine or water, they reacted preferentially at the COCl site. In an equimolar reaction with ethanol, aliphatic isocyanatocarboxylic acid chlorides reacted preferentially at the COCl site, but without great selectivity as with amine. The aromatic compounds reacted preferentially with alcohols at the NCO site.

It has previously been reported[1] that 2-isocyanatoalkanecarboxylic acid chlorides were prepared in good yield when 2-aminoalkanecarboxylic acids were treated with phosgene and hydrogen chloride in dioxane, and that the COCl group of the 2-isocyanatocarboxylic acid chloride is more reactive than the NCO group as an electrophile. This investigation was undertaken to extend the previous work to the preparation and reaction of ω-isocyanatoalkanecarboxylic acid chlorides and isocyanatobenzoyl chlorides.

The formation of 3-isocyanatopropanoyl chloride and its 3-aryl-substituted derivatives have been reported without details or yield by Birkofer and Modic.[2] Steinbrunn produced 6-isocyanatohexanoyl chloride and *m*-isocyanatobenzoyl chloride from the corresponding amino acid chloride hydrochlorides and phosgene.[3] It has also been reported that aromatic isocyanatocarboxylic acid chlorides are obtained by treatment of aminobenzoic acids, aminonaphthoic acids or their derivatives with phosgene at 160–180°.[4] However, *o*-isocyanatobenzoyl chloride could not be obtained in these reactions.[3,4]

Our investigation of the reaction of amino acids with phosgene below 70° showed that introduction of hydrogen chloride afforded certain isocyanatocarboxylic acid chlorides in good yield and purity (see Table I). This pronounced effect of hydrogen chloride on the reaction was previously reported in an improved synthesis of 2-isocyanatoalkanecarboxylic acid chlorides from 2-amino acids.[1]

Isocyanatocarboxylic Acid Chlorides.—With aliphatic compounds, 3-aminopropanoic acid gave 3-isocyanatopropanoyl chloride (Ia) in 36% yield without added hydrogen chloride and 92% yield with added hydrogen chloride. Similarly, 6-aminohexanoic acid without added hydrogen chloride gave only a trace of 6-isocyanatohexanoyl chloride (Ic) but the yield was increased to 91% when hydrogen chloride was added. 4-Aminobutanoic acid, however, with hydrogen chloride gave the cyclic product 1-chloroformyl-5-chloro-2,3-dihydropyrrole (IIa) in 40% yield as reported by Steinbrunn,[3] while 5-aminopentanoic acid gave principally (over 65% yield) the 5-isocyanato-

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[1] Y. Iwakura, K. Uno, and S. Kang, *J. Org. Chem.*, **30**, 1158 (1965).

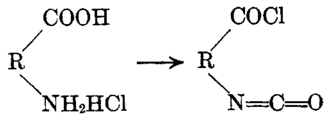
[2] L. Birkofer and R. Modic, *Ann.*, **628**, 162 (1959).

[3] G. Steinbrunn, German Patent 848,808 (1952).

[4] British Patent 752,105 (1956), assigned to the Farbenfabriken Bayer Aktiengesellschaft.

Table I

Isocyanatocarboxylic Acid Chlorides (Ia–f)

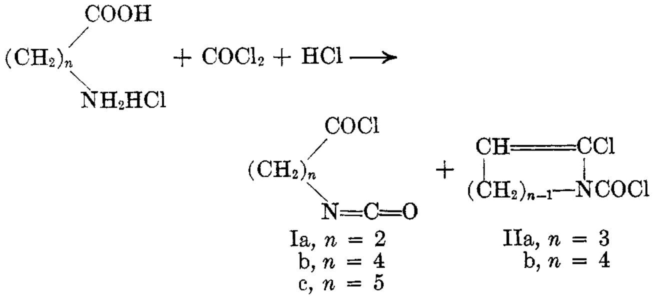


Compd.	R	M.p. or b.p. (mm.), °C.	Yield, %
Ia	$(CH_2)_2$	68 (10)	36[a]
Ia	$(CH_2)_2$	91–91.5 (24.5)	92
Ib	$(CH_2)_4$	79 (2)	66
Ic	$(CH_2)_5$		Trace[a]
Ic	$(CH_2)_5$	114 (6)	91
Id	p-C_6H_4	95–96 (1) 36–37	45
Ie	m-C_6H_4	100 (3)	19
If	o-C_6H_4		Trace[b]
If	o-C_6H_4	103–104 (5) 32	47[c]
If	o-C_6H_4	105 (6)	90[d]

[a] The reaction was carried out without introduction of hydrogen chloride. [b] Isatoic anhydride was produced in 96% yield. [c] Isatoic anhydride was treated with phosphorus pentachloride. [d] Isatoic anhydride was treated with thionyl chloride.

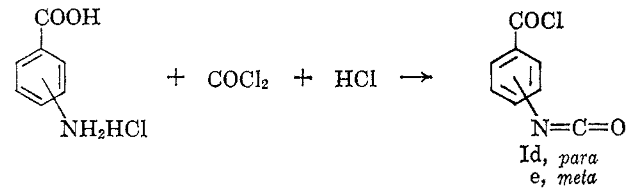
pentanoyl chloride (Ib) along with a small amount of 1-chloroformyl-2-chloro-2,3-dehydropiperidine (IIb).

With aromatic compounds, *p*- and *m*-aminobenzoic acid with phosgene in the presence of hydrogen chloride similarly gave isocyanatobenzoyl chlorides in yields of 45 and 19%, respectively. With the *ortho* isomer, however, reaction with phosgene gave the cyclic mixed anhydride, isatoic anhydride (III), in a yield over 96% with or without added hydrogen chloride. The latter was subsequently converted to *o*-isocyanatobenzoyl chloride (If) with thionyl chloride (90% yield) or with phosphorus pentachloride (47% yield) in the presence of a trace of pyridine. This reaction is parallel to the formation[5] of a 2-isocyanatoalkanecarboxylic acid chloride from Leuchs anhydride and thionyl chloride.

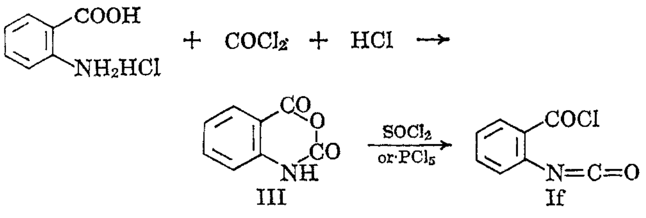


Ia, $n = 2$
b, $n = 4$
c, $n = 5$

IIa, $n = 3$
b, $n = 4$



Id, *para*
e, *meta*



III

If

From the remarkable effect of hydrogen chloride on the yield, it seems that these isocyanatocarboxylic acid chlorides are formed according to the scheme shown below. The isocyanate or carbamoyl chloride group produced by phosgenation of the amino group reacts with the carboxyl group to yield an intra- or intermolecular mixed anhydride, which is then converted to isocyanatocarboxylic acid chloride by cleavage to the amino acid chloride hydrochloride with hydrogen chloride followed by phosgenation. If the anhydride is especially stable, as in the case of the *ortho* aminobenzoyl isomer, the reaction stops at this stage without producing isocyanatocarboxylic acid chloride. This scheme is consistent with our observation that when hydrogen chloride was not introduced into the reaction mixture, only a trace of Ic was obtained and that the yield of Ia decreased remarkably as shown in Table I. This mechanism is essentially similar to that observed in 2-isocyanatoalkanecarboxylic acid chloride formation,[1] where the mixed anhydride can be isolated.

$$—NH_2 \text{ or } —NH_2HCl + COCl_2 \xrightarrow[—HCl]{}$$

$$—N{=}C{=}O \text{ or } —NHCOCl \xrightarrow[(-HCl)]{-COOH}$$

$$—NHCO—O—CO— \xrightarrow[-CO_2]{\text{excess HCl}}$$

$$—NH_2HCl + —COCl \xrightarrow[-HCl]{COCl_2}$$

$$—NHCOCl + —COCl \xrightarrow[—HCl]{} —N{=}C{=}O + —COCl$$

Reactions of Isocyanatocarboxylic Acid Chlorides.—Isocyanatocarboxylic acid chloride has two different reactive functional groups, NCO and COCl, and reacts with nucleophilic reagents to give various compounds.

Amines.—Compounds Ia–f reacted with a 2 molar or greater excess of amine at the both groups to give corresponding ureidoamides (IVa–f). In an equimolar reaction with a primary or secondary amine, however, they gave amides containing unreacted NCO group produced by preferential reaction at the COCl site or cyclic acylureas produced by a consecutive reaction of the unreacted group. With 1 mole of N-methylaniline in the presence of hydrogen chloride acceptor, Ic, Id, and If reacted to give N-methyl-6-isocyanatohexananilide (Va), N-methyl-*p*-, and -*o*-isocyanatobenzanilide (Vb and Vc), respectively. They were characterized by infrared spectra and their derivatives: N-methyl-6-(*p*-phenetylureido)hexananilide (VIa), N-methyl-*p*- and -*o*-ethoxycarbonylaminobenzanilide (VIb and VIc), and 4,4′-(N-methylcarbanilino)carbanilide (VII). In the presence of 1 equiv. of a tertiary amine, Ia and If reacted with 1 mole of aniline to give 2,4-dioxo-3-phenylhexahydropyrimidine (VIIIa) and 2,4-dioxo-3-phenyltetrahydroquinazoline (VIIIb), respectively.

Alcohol and Water.—Isocyanatocarboxylic acid chlorides reacted with excess of ethanol at the both groups, COCl and NCO, to give corresponding ethoxycarbonylaminocarboxylate (IXa–d). In the equimolar reaction with ethanol, aliphatic isocyanatocarboxylic acid chlorides (Ia and Ic) showed the tendency to favor ester formation at the COCl site, but without great selectivity as with an amine or as in the reaction of 2-isocyanatoacetyl chloride and ethanol.[1] The ethyl ω-isocyanatocarboxylates (Xa and Xb) were obtained

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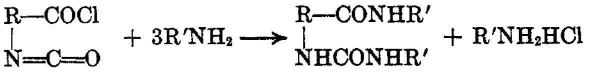
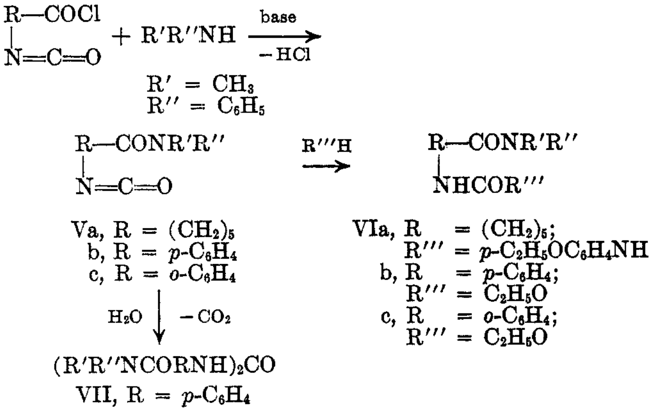
(5) W. Baird, E. G. Parry, and S. Robinson, British Patent 646,033 (1950).



$$\begin{matrix}\text{R—COCl}\\|\\\text{N=C=O}\end{matrix} + 3\text{R'NH}_2 \longrightarrow \begin{matrix}\text{R—CONHR'}\\|\\\text{NHCONHR'}\end{matrix} + \text{R'NH}_2\text{HCl}$$

IVa, R = $(CH_2)_2$; R' = *p*-$C_2H_5OC_6H_4$
b, R = $(CH_2)_4$; R' = C_6H_5
c, R = $(CH_2)_5$; R' = C_6H_5
d, R = *p*-C_6H_4; R' = *p*-$C_2H_5OC_6H_4$
e, R = *m*-C_6H_4; R' = C_6H_5
f, R = *o*-C_6H_4; R' = C_6H_5



$$\begin{matrix}\text{R—COCl}\\|\\\text{N=C=O}\end{matrix} + \text{R'R''NH} \xrightarrow[-\text{HCl}]{\text{base}}$$

R' = CH_3
R'' = C_6H_5

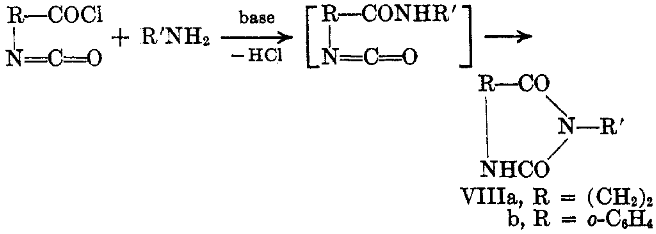
$$\begin{matrix}\text{R—CONR'R''}\\|\\\text{N=C=O}\end{matrix} \xrightarrow{\text{R'''H}} \begin{matrix}\text{R—CONR'R''}\\|\\\text{NHCOR'''}\end{matrix}$$

Va, R = $(CH_2)_5$
b, R = *p*-C_6H_4
c, R = *o*-C_6H_4

VIa, R = $(CH_2)_5$; R''' = *p*-$C_2H_5OC_6H_4NH$
b, R = *p*-C_6H_4; R''' = C_2H_5O
c, R = *o*-C_6H_4; R''' = C_2H_5O

$$\xrightarrow{H_2O\ \ -CO_2} (\text{R'R''NCORNH})_2\text{CO}$$

VII, R = *p*-C_6H_4

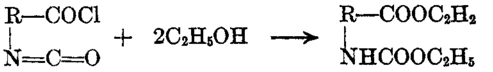


$$\begin{matrix}\text{R—COCl}\\|\\\text{N=C=O}\end{matrix} + \text{R'NH}_2 \xrightarrow[-\text{HCl}]{\text{base}} \left[\begin{matrix}\text{R—CONHR'}\\|\\\text{N=C=O}\end{matrix}\right] \longrightarrow$$

VIIIa, R = $(CH_2)_2$
b, R = *o*-C_6H_4

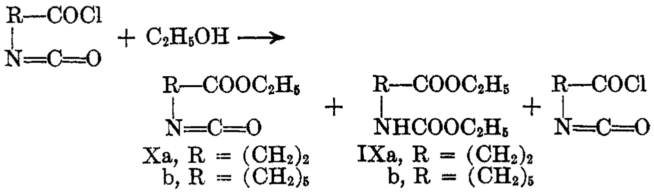
from the reaction at the COCl group together with the products (IXa and IXb) from reaction at the both sites along with unreacted starting materials (Ia and Ic).

Aromatic compounds isocyanatobenzoyl chlorides (Id and Ie), however, in contrast to their behavior with amines, reacted with 1 mole of ethanol, preferentially at the NCO group, to give ethoxycarbonylaminobenzoyl chlorides (XIa and XIb), which were characterized by the infrared spectra and by their derivatives with water (XIIa and XIIb) or aniline (XIII). This finding is also in contrast to the result of an equimolar reaction of 2-isocyanatoacetyl chloride and ethanol, where ethyl 2-isocyanatoacetate was obtained in 89% yield.[1]



$$\begin{matrix}\text{R—COCl}\\|\\\text{N=C=O}\end{matrix} + 2C_2H_5OH \longrightarrow \begin{matrix}\text{R—COOC}_2\text{H}_2\\|\\\text{NHCOOC}_2\text{H}_5\end{matrix}$$

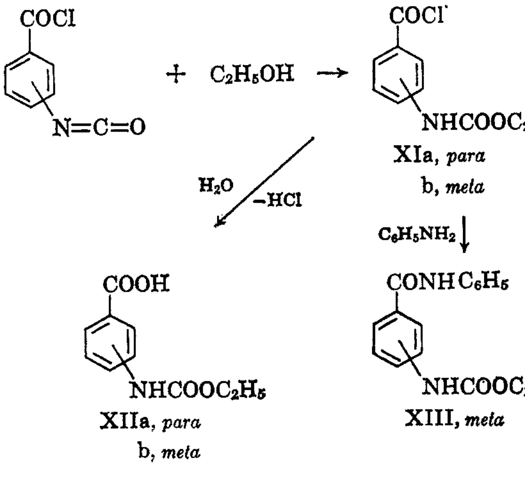
IXa, R = $(CH_2)_2$
b, R = $(CH_2)_5$
c, R = *p*-C_6H_4
d, R = *m*-C_6H_4



$$\begin{matrix}\text{R—COCl}\\|\\\text{N=C=O}\end{matrix} + C_2H_5OH \longrightarrow \begin{matrix}\text{R—COOC}_2\text{H}_5\\|\\\text{N=C=O}\end{matrix} + \begin{matrix}\text{R—COOC}_2\text{H}_5\\|\\\text{NHCOOC}_2\text{H}_5\end{matrix} + \begin{matrix}\text{R—COCl}\\|\\\text{N=C=O}\end{matrix}$$

Xa, R = $(CH_2)_2$
b, R = $(CH_2)_5$

IXa, R = $(CH_2)_2$
b, R = $(CH_2)_5$

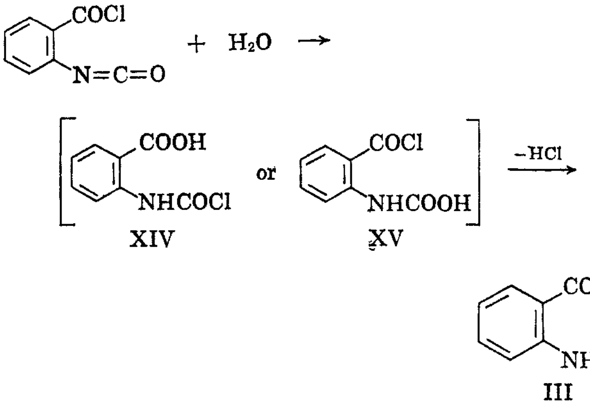


XIa, *para*
b, *meta*

XIIa, *para*
b, *meta*

XIII, *meta*

With 1 mole of water, *o*-isocyanatobenzoyl chloride (If) reacted to yield isatoic anhydride (III) in 86% yield similar to the formation of oxazolizine-2,5-dione from 2-isocyanatoacetyl chloride and water.[1] This formation of III seems to result from the consecutive intramolecular reaction of *o*-chloroformylaminobenzoic acid (XIV) or *o*-hydroxycarbonylaminobenzoyl chloride (XV) produced from If and water, but, considering the stability of XIV and XV, XIV may be reasonably favored as the intermediate.



XIV

XV

III

Experimental Section

3-Isocyanatopropanoyl Chloride (Ia) and 3-(*p*-Phenethylureido)propan-*p*-phenetidide (IVa).—Into a suspension of 20 g. of finely ground 3-aminopropanoic acid hydrochloride in 350 ml. of dry dioxane, a slow stream of phosgene was introduced at 70° with stirring. A clear solution was obtained after 6 hr. Treatment with phosgene was then stopped, and dry hydrogen chloride, which was produced by dropping 40 ml. of concentrated hydrochloric acid into 300 ml. of concentrated sulfuric acid, was introduced into the solution at 5–10°. After the solution stood overnight, a stream of phosgene was introduced again at 65–70° with stirring for 8.5 hr. The pale yellow solution obtained was concentrated *in vacuo* and the residual oil was distilled to yield 19.6 g. (92%) of 3-isocyanatopropanoyl chloride (Ia), b.p. 91–91.5° (24.5 mm.). The compound showed characteristic absorptions at 2275 (N=C=O) and 1790 cm.^{-1} (C=O). *Anal.* Calcd. for $C_4H_4ClNO_2$: N, 10.48. Found: N, 10.15.

Reaction with *p*-Phenetidine.—To a solution of 4.15 g. (0.03 mole) of *p*-phenetidine in 30 ml. of ether, a solution of 1.34 g. (0.01 mole) of Ia was added dropwise with stirring at room temperature. After 1 hr., the precipitates were filtered, washed with water, and dried. Recrystallization of the crude product from pyridine–dioxane (1:3) gave 3.42 g. of 3-(*p*-phenethylureido)propan-*p*-phenetidide (IVa), m.p. 246°. *Anal.* Calcd. for $C_{20}H_{25}N_3O_4$: N, 11.31. Found: N, 11.52.

1-Chloroformyl-5-chloro-3-dihydropyrrole (IIa).—A suspension of 20 g. of finely ground 4-aminobutanoic acid hydrochloride in 300 ml. of dioxane was treated with phosgene at 55–60° for 8 hr. followed by introduction of hydrogen chloride at 5–10° according to the procedure described above. After the second phosgenation of the solution at 55–60° for 11 hr. and then concentration under atmospheric pressure, the reaction mixture gave 13.7 g. of colorless liquid, b.p. 93–104° (2 mm.). This liquid was redistilled to give 9.6 g. (40%) of 1-chloroformyl-5-chloro-2,3-dihydropyrrole (IIa), b.p. 93–94° (2 mm.). The compound showed absorptions at 1810 and 1765 (C=O), and 1645 cm.^{-1} (C=C). *Anal.* Calcd. for $C_5H_5Cl_2NO$: C, 36.17; H, 3.04; N, 8.44. Found: C, 36.00; H, 3.26; N, 8.57.

1-Chloroformyl-2-chloro-2,3-dehydropiperidine (IIb), 5-Isocyanatopentanoyl Chloride (Ib), and 5-Phenylureidopentananilide (IVb).—A reaction mixture, obtained from 12 g. of 5-aminopentanoic acid hydrochloride, 41 g. of liquid phosgene, 27 g. of hydrogen chloride, and 200 ml. of dioxane following the above procedure, was maintained at 65° for 12 hr. under introduction of a thin stream of phosgene. After 1 day, concentration and then distillation of the reaction mixture gave colorless liquid boiling at 89–99° (4 mm.). From this liquid, 8.4 g. (66%) of 5-isocyanatopentanoyl chloride (Ib), b.p. 79° (2 mm.), and 2.3 g. of a mixture boiling at 82–89° (2 mm.) were obtained, and the latter proved to be a mixture of Ib and 1-chloroformyl-2-chloro-2,3-dehydropiperidine (IIb) by the infrared spectrum and chlorine content (*Anal.* Calcd. for Ib: Cl, 21.98. Calcd. for IIb: Cl, 39.44. Found: Cl, 26.70.). *Anal.* Calcd. for $C_6H_8ClNO_2$ (Ib): C, 44.59; H, 4.99; N, 8.66. Found: C, 44.32; H, 4.87; N, 8.25.

Reaction of Ib with excess aniline in ether gave 5-phenylureidopentananilide (IVb), m.p. 189.5–190° (methanol–water). *Anal.* Calcd. for $C_{18}H_{21}N_3O_2$: C, 69.43; H, 6.80; N, 13.50. Found: C, 69.54; H, 6.72; N, 13.41.

6-Isocyanatohexanoyl Chloride (Ic) and 6-Phenylureidohexananilide (IVc).—From 30 g. of finely ground 6-aminohexanoic acid hydrochloride, 28.6 g. (91%) of 6-isocyanatohexanoyl chloride (Ic), b.p. 114° (6 mm.), was obtained following the above procedure (the first phosgenation at 60° for 7 hr., introduction of hydrogen chloride at 5–10° for 4.5 hr., and the second phosgenation at 62° for 5 hr.). *Anal.* Calcd. for $C_7H_{10}ClNO_2$: C, 47.89; H, 5.74; N, 7.98. Found: C, 48.22; H, 5.91; N, 8.09.

Reaction of Ic with excess aniline gave 6-phenylureidohexananilide (IVc), m.p. 169° (methanol–water). *Anal.* Calcd. for $C_{19}H_{23}N_3O_2$: C, 70.13; H, 7.12; N, 12.91. Found: C, 70.42; H, 7.19; N, 13.16.

***p*-Isocyanatobenzoyl Chloride (Id), *p*-(*p*-Phenetylureido)-benz-*p*-phenetidide (IVd), and Ethyl *p*-Ethoxycarbonylaminobenzoate (IXc).**—According to the above procedure, 15 g. of finely ground *p*-aminobenzoic acid hydrochloride in 300 ml. of dioxane was treated in turn with phosgene (60°, 10.5 hr.), hydrogen chloride (5–10°), and phosgene (60–65°, 5 hr.). The resulting clear solution was concentrated *in vacuo*. To the concentrate, 20 ml. of toluene was added and refluxed for 30 min., and the insoluble solid was filtered off. After evaporation of solvent from the filtrate, the residue was distilled to yield 7.0 g. (45%) of *p*-isocyanatobenzoyl chloride (Id), b.p. 95–96° (1 mm.), m.p. 36–37°. The compound showed absorptions at 2275 (N═C═O), and 1775 and 1735 cm.$^{-1}$ (C═O).[6] *Anal.* Calcd. for $C_8H_4ClNO_2$: C, 52.89; H, 2.20; N, 7.71. Found: C, 52.78; H, 2.31; N, 7.76.

The reaction of Id with excess of *p*-phenetidine in ether gave *p*-(*p*-phenetylureido)benz-*p*-phenetidide (IVd), m.p. 291–293° (acetic acid), showing absorptions at 3325 and 3250 (NH), and 1660 and 1645 cm.$^{-1}$ (C═O). *Anal.* Calcd. for $C_{24}H_{25}N_3O_4$: C, 68.72; H, 6.01; N, 10.02. Found: C, 68.91; H, 6.25; N, 10.07.

The reaction with excess ethanol gave ethyl *p*-ethoxycarbonylaminobenzoate (IXc), m.p. 130–131° (ethanol–water), showing absorptions at 3300 (NH), 1725 (C═O of ester), and 1690 cm.$^{-1}$ (C═O of urethan). *Anal.* Calcd. for $C_{12}H_{15}NO_4$: C, 60.75; H, 6.37; N, 5.90. Found: C, 60.67; H, 6.21; N, 5.81.

***m*-Isocyanatobenzoyl Chloride (Ie), *m*-Phenylureidobenzanilide (IVe), and Ethyl *m*-Ethoxycarbonylaminobenzoate (IXd).**—Into a suspension of 15 g. of finely ground *m*-aminobenzoic acid hydrochloride in 900 ml. of dioxane, phosgene and hydrogen chloride were introduced at the same time at 60° with stirring. After 10 hr., the resulting clear solution was concentrated *in vacuo*, and the insoluble material which precipitated on adding petroleum ether (b.p. 30–70°) was removed by filtration. The filtrate gave 3.0 g. (19%) of *m*-isocyanatobenzoyl chloride (Ie), b.p. 100° (3 mm.), when distilled. The compound showed absorptions at 2275 (N═C═O), and 1760 (C═O), with a shoulder at 1725 cm.$^{-1}$. *Anal.* Calcd. for $C_8H_4ClN_2$: C, 52.89; H, 2.20; N, 7.71. Found: C, 52.70; H, 2.27; N, 7.75.

The reaction of Ie with excess of aniline in ether gave *m*-phenylureidobenzanilide (IVe), m.p. 235–236° (acetic acid), showing absorptions at 3300 (NH), and 1655 and 1640 cm.$^{-1}$ (C═O). *Anal.* Calcd. for $C_{20}H_{17}N_3O_2$: C, 72.49; H, 5.17; N, 12.68. Found: C, 72.22; H, 5.22; N, 12.46.

The reaction with excess of ethanol gave ethyl *m*-ethoxycarbonylaminobenzoate (IXd), m.p. 94–95° (ethanol–water), showing absorptions at 3350 (NH), 1720 (C═O of ester), and 1700 cm.$^{-1}$ (C═O of urethan). *Anal.* Calcd. for $C_{12}H_{15}NO_4$: C, 60.75; H, 6.37; N, 5.90. Found: C, 61.13; H, 6.67; N, 6.13.

Isatoic Anhydride (III) from *o*-Aminobenzoic Acid and Phosgene.—To a solution of 25 g. of *o*-aminobenzoic acid in 300 ml. of dioxane, 55 g. of liquid phosgene was added with stirring at room temperature, and the mixture was maintained at 40–45° for 2 hr. After it was allowed to stand at room temperature overnight, 29.3 g. of isatoic anhydride (III) was obtained in a pure state by filtration, and an additional 2.5 g. of III was obtained by evaporation of the filtrate (total yield, 100%). The compound melted at 242–243° dec. (lit.[7] m.p. 241–243° dec.), and showed at absorptions at 1765 and 1725 cm.$^{-1}$ (C═O).

***o*-Isocyanatobenzoyl Chloride (If) and *o*-Phenylureidobenzanilide (IVf).** A.—According to the procedure mentioned in the preparation of Ie, the reaction was carried out at 65–70° for 19 hr. using 15 g. of *o*-aminobenzoic acid hydrochloride and 380 ml. of dioxane. But, from the reaction mixture, 13.5 g. (96%) of III was obtained along with a trace of *o*-isocyanatobenzoyl chloride (If), which was characterized by the infrared spectrum.

B.—A mixture of 13.1 g. of finely ground isatoic anhydride (III) and 17.0 g. of phosphorus pentachloride in 60.0 g. of phosphorus oxychloride was stirred at 65–75° for 35 hr. in the presence of a trace of pyridine. The resulting clear solution was concentrated *in vacuo*, and to the residue was added 50 ml. of benzene. After 1 day, the precipitates formed were removed by filtration and the filtrate was distilled to yield 6.8 g. (47%) of *o*-isocyanatobenzoyl chloride (If), b.p. 103–104° (5 mm.), m.p. 32°. The compound showed absorptions at 2300 (N═C═O), and 1775 and 1735 cm.$^{-1}$ (C═O). *Anal.* Calcd. for $C_8H_4ClNO_2$: C, 52.89; H, 2.20; N, 7.71. Found: C, 52.62; H, 2.35; N, 7.62.

C.—A mixture of 12.3 g. of III and 70 g. of thionyl chloride was refluxed in the presence of a trace of pyridine for 35 hr. The resulting clear reaction mixture was concentrated *in vacuo*, and from the residue was filtered a small amount of insoluble material which formed on adding 50 ml. of benzene. Distillation of the filtrate gave 12.0 g. (90%) of If, b.p. 105° (6 mm.). *Anal.* Calcd. for $C_8H_4ClNO_2$: Cl, 19.55. Found: Cl, 19.54.

The reaction of If with excess of aniline gave *o*-phenylureidobenzanilide (IVf), m.p. 211–212° (acetic acid–water). *Anal.* Calcd. for $C_{20}H_{17}N_3O_2$: C, 72.49; H, 5.17; N, 12.68. Found: C, 72.36; H, 5.25; N, 12.44.

N-Methyl-6-isocyanatohexananilide (Va) and N-Methyl-6-(*p*-phenethylureido)hexananilide (VIa).—To a solution of 1.755 g. (0.01 mole) of 6-isocyanatohexanoyl chloride (Ic) in 20 ml. of ether, a solution of 2.140 g. (0.02 mole) of N-methylaniline in 40 ml. of ether was added dropwise at 5° over a period of 50 min. with stirring, and after 40 min., N-methylaniline hydrochloride was filtered off. Removal of ether from the filtrate *in vacuo* gave N-methyl-6-isocyanatohexananilide (Va) showing absorptions at 2275 (N═C═O) and 1660 cm.$^{-1}$ (C═O). By treatment with 1.370 g. (0.01 mole) of *p*-phenetidine in ether, Va further gave 3.50 g. (92%) of N-methyl-6-(*p*-phenetylureido)hexananilide (VIa), m.p. 109–110° (acetone–water). The compound showed absorptions at 3350 (NH), and 1690 and 1630 cm.$^{-1}$ (C═O). *Anal.* Calcd. for $C_{22}H_{29}N_3O_3$: N, 10.96. Found: N, 10.88.

N-Methyl-*p*-isocyanatobenzanilide (Vb) and N-Methyl-*p*-ethoxycarbonylaminobenzanilide (VIb).—Following the above procedure, N-methyl-*p*-isocyanatobenzanilide (Vb) was obtained from 1.8150 g. of *p*-isocyanatobenzoyl chloride (Id), 1.0715 g. of N-methylaniline, and 1.1153 g. of triethylamine. The compound showed absorptions at 2275 (N═C═O) and 1640 cm.$^{-1}$ (C═O). By the reaction with 0.5 g. of ethanol in the presence of a trace of triethylamine in ether, VIb obtained above gave 2.7 g. (92%) of N-methyl-*p*-ethoxycarbonylaminobenzanilide (VIb), m.p. 170–173° (methanol–water). The compound showed absorptions at 3300 (NH), 1730 (C═O of urethan), and 1625 cm.$^{-1}$ (C═O of amide). *Anal.* Calcd. for $C_{17}H_{18}N_2O_3$: C, 58.50; H, 3.09; N, 8.59. Found: C, 58.59; H, 3.14; N, 8.81.

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[6] It is described that benzoyl chloride absorbs at 1773 and 1736 cm.$^{-1}$: L. J. Bellamy, "The Infrared Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, N. Y., 1958, p. 126.

[7] R. H. Clark and E. C. Wagner, *J. Org. Chem.*, **9**, 60 (1944).

N-Methyl-*o*-isocyanatobenzanilide (Vc) and N-Methyl-*o*-ethoxycarbonylaminobenzanilide (VIc).—Following the procedure as mentioned above, N-methyl-*o*-isocyanatobenzanilide (Vc) was obtained from a solution of 2.1726 g. of *o*-isocyanatobenzoyl chloride (If) in 40 ml. of ether and a mixture of 1.2833 g. of N-methylaniline and 2.2212 g. of tri-*n*-butylamine in 40 ml. of ether. The product showed absorptions at 2300 (N=C=O) and 1645 cm.$^{-1}$ (C=O). Then the product was treated with excess ethanol in 80 ml. of *n*-hexane containing a trace of triethylamine, and the reaction mixture was evaporated. From the resulting solid, 3.3 g. of crude N-methyl-*o*-ethoxycarbonylaminobenzanilide (VIc) was obtained by washing with dilute hydrochloric acid. It was recrystallized to give 3.2 g. (90%) of pure VIc, m.p. 93.5–95.5° (ethanol–water), showing absorptions at 3350 (NH), 1730 (C=O of urethan), and 1635 cm.$^{-1}$ (C=O of amide). *Anal.* Calcd. for $C_{17}H_{18}N_2O_3$: C, 68.44; H, 6.08; N, 9.39. Found: C, 68.70; H, 6.13; N, 9.73.

2,4-Dioxo-3-phenylhexahydropyrimidine (VIIIa).—To a solution of 1.3887 g. of 3-isocyanatopropanoyl chloride (Ia) in 30 ml. of toluene, a solution of 0.9629 g. of aniline and 1.0615 g. of triethylamine in 20 ml. of toluene was added dropwise at 0° over a period of 70 min. with stirring, and the dropping funnel was rinsed with 10 ml. of toluene. After an ice bath was removed, the reaction mixture was stirred for 1 additional hr. at room temperature followed by heating at reflux (120°) for 2 hr. Toluene was evaporated *in vacuo* and the residual solid was washed with water to remove triethylamine hydrochloride. The resulting crude product (1.8 g., 91%), m.p. 213–225°, was recrystallized to give 1.7 g. (86%) of pure 2,4-dioxo-3-phenylhexahydropyrimidine (VIIIa), m.p. 225° (methanol–water). The compound showed absorptions at 1725 and 1680 cm.$^{-1}$ (C=O). *Anal.* Calcd. for $C_{10}H_{10}N_2O_2$: 63.15; H, 5.30; N, 14.73. Found: C, 63.35; H, 5.27; N, 14.70.

2,4-Dioxo-3-phenyltetrahydroquinazoline (VIIIb).—To a solution of 1.8181 g. of *o*-isocyanatobenzoyl chloride (If) in 20 ml. of toluene, a mixture of 0.9288 g. of aniline and 1.6713 g. of tri-*n*-butylamine in 30 ml. of toluene was added dropwise at 0° over a period of 15 min., and the dropping funnel was rinsed with an additional 5 ml. of toluene. The reaction mixture was maintained at this temperature for 1 hr. and then allowed to stand at room temperature overnight. After heating at 100° for 7 hr., it was evaporated *in vacuo*. The obtained solid was washed with water and the resulting crude product was recrystallized to give 2.2 g. (93%) of 2,4-dioxo-3-phenyltetrahydroquinazoline (VIIIb), m.p. 274–275° (methanol-water). The compound showed absorptions at 1725 and 1665 cm.$^{-1}$ (C=O). *Anal.* Calcd. for $C_{14}H_{10}N_2O_2$: C, 70.58; H, 4.23; N, 11.76. Found: C, 70.29; H, 4.33; N, 11.63.

4,4′-(N-Methylcarbanilino)carbanilide (VII).—To a solution of 3.6300 g. of *p*-isocyanatobenzoyl chloride (Id) in 50 ml. of ether, a solution of 2.1453 g. of N-methylaniline and 3.7040 g. of tri-*n*-butylamine in 45 ml. of ether was added dropwise at 5–7° over a period of 1 hr. with stirring. After 1 hr., 3 ml. of water was added to the reaction mixture at room temperature with efficient stirring, and it was allowed to stand overnight. The solvent was evaporated and the residual solid was washed with dilute hydrochloric acid. The resulting crude product (4.8 g., 100%, m.p. 252–254°) was recrystallized to give 4.6 g. (96%) of pure 4,4′-(N-methylcarbanilino)carbanilide (VII), m.p. 282–283° (acetic acid–water). The compound showed absorptions at 1695 and 1635 cm.$^{-1}$ (C=O). *Anal.* Calcd. for $C_{29}H_{26}N_4O_3$: C, 72.78; H, 5.48; N, 11.71. Found: C, 72.53; H, 5.55; N, 11.54.

Ethyl 3-Isocyanatopropanoate (Xa) and Ethyl 3-Ethoxycarbonylaminopropanoate (IXa).—To a solution of 5.3413 g. of 3-isocyanatopropanoyl chloride (Ia) in 30 ml. of toluene, a solution of 1.8400 g. of ethanol in 30 ml. of toluene was added dropwise over a period of 50 min. at room temperature with stirring. After 1 day, toluene was removed from the reaction mixture by distillation at atmospheric pressure and then *in vacuo*. The residual oil was distilled to yield 2.5 g. of a mixture of ethyl 3-isocyanatopropanoate (Xa) and Ia which was characterized by infrared spectrum and elementary analysis, and 1.6 g. of ethyl 3-ethoxycarbonylaminopropanoate (IXa), b.p. 105–106° (3 mm.). The compound showed absorptions at 3350 (NH), 1735 (C=O of ester), and 1705 cm.$^{-1}$ (C=O of urethan). *Anal.* Calcd. for $C_8H_{15}NO_4$: C, 50.78; H, 7.99; N, 7.40. Found: C, 50.58; H, 8.04; N, 7.13.

Ethyl 6-Isocyanatohexanoate (Xb) and Ethyl 6-Ethoxycarbonylaminohexanoate (IXb).—According to the above procedure, 5.3002 g. of 6-isocyanatohexanoyl chloride (Ic) in 20 ml. of ether was treated with 1.3892 g. of ethanol in 30 ml. of ether. From the reaction mixture, a mixture of ethyl 6-isocyanatohexanoate (Xb) and unreacted Ic was obtained along with 1.4 g. of ethyl 6-ethoxycarbonylaminohexanoate (IXb), b.p. 131° (0.4 mm.). The former was characterized by its infrared spectrum. The latter showed absorptions at 3350 (NH), 1735 (C=O of ester), and 1700 cm.$^{-1}$ (C=O of urethan). *Anal.* Calcd. for $C_{11}H_{21}NO_4$: C, 57.12; H, 9.15; N, 6.06. Found: C, 56.98; H, 9.08; N, 6.30.

***p*-Ethoxycarbonylaminobenzoyl Chloride (XIa) and *p*-Ethoxycarbonylaminobenzoic Acid (XIIa).**—To a solution of 3.5151 g. of *p*-isocyanatobenzoyl chloride (Id) in 30 ml. of toluene, a solution of 0.8898 g. of ethanol in 20 ml. of toluene was added dropwise over a period of 20 min. at 7° with stirring. After a short time, white powder precipitated, and it was identified as *p*-ethoxycarbonylaminobenzoyl chloride (XIa) by its infrared spectrum (3350 for NH and a broad peak at 1720 cm.$^{-1}$ for C=O). To the reaction mixture, a mixture of 1 ml. of water and 20 ml. of dioxane was added at room temperature with stirring. After 1 day, the solvents were evaporated *in vacuo*, and the residual solid was washed with water. The obtained crude product was recrystallized from benzene to give 5.4 g. (96%) of *p*-ethoxycarbonylaminobenzoic acid, m.p. 200–201°. The compound showed absorptions at 1705 and 1690 cm.$^{-1}$ (C=O). *Anal.* Calcd. for $C_{10}H_{11}NO_4$: C, 57.41; H, 5.30; N, 6.70. Found: C, 57.77; H, 5.34; N, 6.75.

***m*-Ethoxycarbonylaminobenzoyl Chloride (XIb) and *m*-Ethoxycarbonylaminobenzoic Acid (XIIb).**—According to the above procedure, 3.6566 g. of *m*-isocyanatobenzoyl chloride (Ie) in 40 ml. of ether was treated with 0.9255 g. of ethanol in 30 ml. of ether at 5–10°. The resulting solution of *m*-ethoxycarbonylaminobenzoyl chloride (XIb), which was characterized by the infrared spectrum, was further treated with a mixture of 10 ml. of dilute hydrochloric acid and 40 ml. of dioxane at room temperature. After 5 hr., the solvents were evaporated and the residual solid was washed with water. The obtained crude product was recrystallized from benzene to give 3.6 g. (86%) of *m*-ethoxycarbonylaminobenzoic acid (XIIb), m.p. 189–190°, showing absorptions at 3300 (NH) and 1695 cm.$^{-1}$ (C=O). *Anal.* Calcd. for $C_{10}H_{11}NO_4$: C, 57.41; H, 5.30; N, 6.70. Found: C, 57.31; H, 5.30; N, 6.86.

***m*-Ethoxycarbonylaminobenzanilide (XIII).**—To a solution of 3.6561 g. of *m*-isocyanatobenzoyl chloride (Ie) in 50 ml. of ether, 0.9234 g. of ethanol and 3.7018 g. of tri-*n*-butylamine in 50 ml. of ether were added dropwise over a period of 1 hr. at 0–5° with stirring. After standing for 2 hr., the reaction mixture was treated with 1.8673 g. of aniline in 30 ml. of ether at room temperature and allowed to stand overnight. Precipitated crystals were collected on a suction filter and washed with water to remove tri-*n*-butylamine hydrochloride. The resulting crude product was recrystallized to give 5.3 g. (93%) of *m*-ethoxycarbonylaminobenzanilide (XIII), m.p. 159–160° (ethanol-water), showing absorptions at 3320 (NH), 1700 (C=O of urethan), and 1650 cm.$^{-1}$ (C=O of amide). *Anal.* Calcd. for $C_{16}H_{16}N_2O_3$: C, 67.59; H, 5.67; N, 9.85. Found: C, 67.88; H, 5.94; N, 9.91.

Isatoic Anhydride (III) from *o*-Isocyanatobenzoyl Chloride (If) and Water.—To a solution of 1.8200 g. of *o*-isocyanatobenzoyl chloride (If) in 20 ml. of toluene, 0.1792 g. of water in 20 ml. of dioxane was added dropwise at 0–5° with stirring. After the reaction mixture was allowed to stand overnight at room temperature, precipitating crystals were collected by filtration and recrystallized from ethanol to yield 1.4 g. (86%) of isatoic anhydride, m.p. 243° dec., undepressed by admixture with an authentic sample. The infrared spectrum was identical with that of an authentic sample. *Anal.* Calcd. for $C_8H_5NO_3$: C, 58.90; H, 3.09; N, 8.59. Found: C, 58.59; H, 3.14; N, 8.81.