trast to the only reported[6] preparation of chloroacetyl chloride free of dichloroacetyl chloride from ketene and chlorine. In this case chlorine reacted in the vapor phase with an 80% or greater excess of ketene.

Chloroacetyl chloride was tried as the solvent in a number of runs. In all cases, dichloroacetyl chloride was produced as evidence by the isolation of acetyl chloride from the reaction mixture.

### EXPERIMENTAL[7]

*Ketene source.* The ketene used was prepared by the pyrolysis of acetic anhydride[8] in a modification of the apparatus described by Fisher, *et al.*[9] In the present apparatus the acetic anhydride was fed to the evaporator from a reservoir under nitrogen pressure through a Fisher and Porter "Tri-Flat Flowrater Meter" (tube No. 02F). The rate of flow was controlled with a suitable needle valve. The evaporator, connecting to the top of the cracker and tilting a few degrees from the horizontal was constructed of 14 mm. Pyrex tubing 53 cm. long with a 38-cm. heated section. Heat was supplied by a winding of Nichrome ribbon. Operating temperatures were as described by Fisher *et al.*

*Reaction of chlorine in ketene.* The reactor or flask was charged with the solvent, cooled to the desired temperature and ketene and chlorine were introduced for the specified time. In the reactor the chlorine entered the mixture from the bottom through a 2-mm. capillary. A sintered glass disperser was used in the runs conducted in the 500-ml. flask. In both cases ketene was introduced through a hollow stirrer (Ace Glass "Mini-Lab" stirrers modified to fit a 34/45 standard taper joint).

At the completion of the run the mixture was distilled through a 10-in. helix-packed column. When sulfur dioxide was used as solvent it was first removed through an ice-cooled condenser. Three fractions were taken during the distillation—low boiler (mostly acetyl chloride), b.p. up to 103°; product fraction (chloroacetyl chloride and dichloroacetyl chloride), b.p. 103–107°; and high boilers, b.p. above 107°.

*Analysis.* The product fraction was analyzed either by determining its neutral equivalent and calculating its chloroacetyl chloride content, assuming that only chloroacetyl chloride and dichloroacetyl chloride were present or by hydrolyzing the dichloroacetyl chloride to oxalic acid and titrating with permanganate. The former was used as a screening analyses; when the dichloroacetyl chloride content was indicated to be low it was determined directly by the latter procedure.

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[6] R. N. Lacey and A. E. Blades, Brit. Pat. **735,902** (to Distillers Co.) Aug. 31, 1955.

[7] Analyses were conducted by Mrs. Geneva Kratzer and Mrs. Dawn Knight.

[8] When ketene prepared from acetone was employed large quantities of sulfuryl chloride and residue were obtained which resulted in a low yield of chloroacetyl chloride. Apparently some by-products in this ketene stream catalyzed the combination of chlorine and sulfur dioxide. The chloroacetyl chloride produced contained only a small amount of dichloroacetyl chloride, however.

[9] G. J. Fisher, A. F. MacLean, and A. W. Schnizer, *J. Org. Chem.*, **18**, 1055 (1953).

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## Mixed Anhydrides of *S*-Phenylthiocarbonic Acid and Carboxylic Acids

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In a previous communication[1] it was suggested that an intermediate mixed anhydride of *S*-phenylthiocarbonic acid, *i.e.*, $C_6H_5SCO_2H$, and *N,N'*-carbonyl-bis-DL-phenylalanine was formed and was responsible for the observation that an unlimited amount of *S*-phenylthiocarbonyl chloride could be hydrolyzed in a biphasic aqueous system initially containing the relatively water-insoluble acid chloride, an unlimited amount of base and a relatively small amount of DL-phenylalanine whereas when the latter compound was absent, or was replaced by a simple amine, the excess *S*-phenylthiocarbonyl chloride was hydrolyzed either very slowly or not at all.

In order to provide more direct evidence that a mixed anhydride could arise by the reaction of *S*-phenylthiocarbonyl chloride with a carboxylic acid in the presence of a base, an attempt was made to demonstrate mixed anhydride formation by allowing the acid chloride to react with acetic acid in the presence of aqueous ethanolic triethylamine and subsequently adding aniline to the reaction mixture to obtain the expected acetanilide. However, the only amide isolated was *N,S*-diphenylthiocarbamate which could have been formed by the reaction of aniline with the acid chloride.[1] Since it was presumed that any mixed anhydride that may have been formed had been hydrolyzed prior to the addition of the amine, the above reaction was then conducted in anhydrous dioxane. Under these conditions, the principle reaction product was found to be acetanilide, thus demonstrating that a mixed anhydride of *S*-phenylthiocarbonic acid and acetic acid had been formed and that its principle reaction product when treated with aniline is acetanilide. A similar experiment conducted with hippuric acid and aniline gave hippurylanilide.

While the above experiments demonstrate the existence of mixed anhydrides of *S*-phenylthiocarbonic acid and carboxylic acids and thus generalize the observation made previously with *N,N'*-carbonyl-bis-DL phenylalanine[1] to include all carboxylic acids, it should be noted that the other suggestion made earlier[1] that such mixed anhydrides may be useful as intermediates in the synthesis of derivatives of carboxylic acids has lost much of its force. While further investigation could result in improved conditions for the preparation of mixed anhydrides of *S*-phenylthiocarbonic acid and carboxylic acids, the experience gained in this investigation has shown that such mixed anhy-

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[1] D. G. Crosby and C. Niemann, *J. Am. Chem. Soc.*, **76**, 4458 (1954).

drides are inferior to those derived from the alkylchlorocarbonates[2,3] largely because of the difficulty of freeing the derivatives from the other reaction product, *i.e.*, thiophenol.

### EXPERIMENTAL[4]

*Acetanilide.* *S*-Phenylthiocarbonyl chloride, 1.58 g. (0.009 mole), was added over a 15-min. period to a vigorously stirred solution of 0.6 g. (0.01 mole) of glacial acetic acid and 1.01 g. (0.01 mole) of triethylamine in 20 ml. of water and 15 ml. of ethanol. After 2 hr. at room temperature, 0.93 g. (0.01 mole) of redistilled aniline was added drop-wise whereupon a precipitate formed. The precipitate was collected, washed with 2*N* aqueous hydrochloric acid, dried, and recrystallized from aqueous ethanol to give *N,S*-diphenylthiocarbamate, m.p. 126.5–127.7°. Lit.[1], m.p. 125.6–127.6°.

Repetition of the above experiment in anhydrous dioxane, with the first stage being conducted at 0°, gave, after the addition of the aniline, a yellow solid which was washed with 3*N* aqueous sodium carbonate, 2*N* aqueous hydrochloric acid, water, dried, and recrystallized from 60–70° ligroin to give 0.6 g. (44%) of acetanilide, m.p. 112.9–113.9°.

*Hippurylanilide.* To a cooled stirred solution of 1.79 g. (0.01 mole) of hippuric acid and 1.01 g. (0.01 mole) of triethylamine in 25 ml. of anhydrous dioxane was added, at 0°, 1.73 g. (0.01 mole) of *S*-phenylthiocarbonyl chloride and an additional 15 ml. of dioxane. After 15 min., 0.93 g. (0.01 mole) of redistilled aniline was added and the stirring continued for 90 min. at room temperature. The reaction mixture was then poured into 100 ml. of ice cold 0.3*N* aqueous hydrochloric acid, the precipitate collected by filtration and washed with 200 ml. of 2*N* aqueous hydrochloric acid and 200 ml. of water. The residue which still had a strong odor of thiophenol was stirred for 15 min. with 100 ml. of 10% aqueous sodium hydroxide, the precipitate collected, washed with aqueous acid and water, and finally recrystallized from aqueous ethanol to give 0.43 g. (17%) of hippurylanilide, m.p. 211.5–212.5°. Lit.,[5] m.p. 208.5°.

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[2] J. R. Vaughan, Jr., *J. Am. Chem. Soc.*, **73**, 3547 (1951).

[3] W. Grassmann and E. Wünsch, *Fortschr. Chem. org. Naturstoffe*, **13**, 444 (1956).

[4] All melting points are corrected.

[5] T. Curtius, *J. prakt. Chem.*, **52**, 243 (1895).

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## α-*N*-Trichloroacetyl-L-tyrosinamide

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The low yield reported for the preparation of trichloroacetyl-DL-alanine by reaction of the amino acid with trichloroacetyl chloride in the presence of aqueous sodium hydroxide at 0°,[1] presumably because of the rapid hydrolysis of the acid chloride under the above reaction conditions,[2] and the difficulty of achieving a satisfactory selective hydrolysis of *O*,α-*N*-di-trichloroacetyl-L-tyrosinamide, obtained by reaction of trichloroacetyl chloride and triethylamine with L-tyrosinamide in anhydrous tetrahydrofuran, to α-*N*-trichloroacetyl-L-tyrosinamide led us to attempt the direct α-*N*-acylation of L-tyrosinamide with ethyl trichloroacetate in a nonaqueous medium. The reaction of L-tyrosinamide with 1.2 equivalents of ethyl trichloroacetate in anhydrous ethyl acetate at the refluxing temperature of the reaction mixture gave the desired product in a 65% yield. When the reaction was attempted in anhydrous acetone, a reaction product containing no chlorine was obtained. On the basis of an elementary analysis, it appeared to be a condensation product resulting from the reaction of 1 mole of L-tyrosinamide with 1 mole of acetone with the loss of 1 mole of water.

### EXPERIMENTAL[3,4]

*α-N-Trichloroacetyl-L-tyrosinamide.* L-Tyrosinamide, prepared by ammonolysis of the corresponding ester, was placed in the extraction thimble of a Soxhlet extraction apparatus and transferred, by dissolution in ethyl acetate, in the course of 1 hr. to the boiler of the extraction apparatus which was charged with 1.2 equivalents of ethyl trichloroacetate present as a 20% solution in anhydrous ethyl acetate. The reaction mixture was cooled to give 65% of a crude product, m.p. 158–160°, which was successively recrystallized from chlorobenzene, methanol, aqueous methanol, and a mixture of anhydrous ethanol and benzene to give α-*N*-trichloroacetyl-L-tyrosinamide, m.p. 160–161°, $[\alpha]^{25}_{D}$ + 30.5° (in 30% ethanol).

*Anal.* Calcd. for $C_{11}H_{11}O_3N_2Cl_3$ (325.5): C, 41.9; H, 3.4; N, 8.9; Cl, 33.8. Found: C, 41.8; H, 3.4; N, 8.9; Cl, 33.7.

The presence of a phenolic hydroxyl group in the above compound was indicated by a positive test with the Folin-Denis[5] reagent and by a comparison of its infrared spectrum, in solid KBr, with that of an authentic sample of α-*N*-acetyl-L-tyrosinamide and of α-*N*-acetyl-D-phenylalaninamide in the same medium.

When the above reaction was attempted with acetone as the solvent, a crystalline product, m.p. 184–185°, separated from the hot reaction mixture. This material, $[\alpha]^{25}_{D}$ −18.2° (in 30% ethanol) contained no chlorine and on the basis of an elementary analysis, appeared to be a condensation product resulting from the reaction of 1 mole of L-tyrosinamide with 1 mole of acetone with the loss of 1 mole of water.

*Anal.* Calcd. for $C_{12}H_{16}O_2N_2$ (220): C, 65.5; H, 7.3; N, 12.7. Found: C, 65.2; H, 7.4; N, 12.3.

Contribution No. 2220 from the Gates and Crellin
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[1] W. S. Fones, *J. Org. Chem.*, **17**, 1661 (1952).

[2] N. O. V. Sonntag, *Chem. Revs.*, **52**, 237 (1953).

[3] All melting points are corrected.

[4] Microanalyses by Dr. Adalbert Elek.

[5] O. Folin and W. Denis, *J. Biol. Chem.*, **12**, 239 (1912).