

p-Oxybenzylidene Anthranilic Acid.—*p*-Oxybenzylidene anthranilic acid was made in alcoholic solution in the same way as the *p*-nitro compound. This substance crystallized out in the form of lemon-yellow needles. Soluble in the ordinary organic solvents. Melting point, 207°.

Calculated for $C_{14}H_{11}NO_3$: N, 5.80. Found, 5.98.

Acetyl-p-oxyphenylacetodihydrobenzmetoxazine.—This compound was made in exactly the same way as the preceding oxazines. In this case the hydrogen of the hydroxyl group is replaced by acetyl. Recrystallized from methyl alcohol, it yields colorless prisms. Melting point, 148°.

Calculated for $C_{18}H_{15}NO_3$: N, 4.31; C, 66.46; H, 4.61.

Found: N, 4.68; C, 66.11; H, 4.94.

Salicylidene Anthranilic Acid.—Salicylidene anthranilic acid was prepared in a manner analogous to that of the other benzylidene products. Orange-red crystals from alcohol. Soluble in ordinary organic solvents. Melting point, 195°.

Calculated for $C_{14}H_{11}NO_3$: N, 5.81. Found, 6.03.

Acetyl-o-oxyphenylacetodihydrobenzmetoxazine.—This compound was prepared from salicylidene anthranilic acid in the same way as the preceding oxazines. Colorless crystals from methyl alcohol. Melting point, 162°.

Calculated for $C_{18}H_{15}NO_3$: N, 4.31; C, 66.46; H, 4.61.

Found: N, 4.64; C, 65.85; H, 4.75.

Vanillylidene Anthranilic Acid.—Equimolecular solutions of anthranilic acid and vanillin in benzene were mixed. On standing, lemon-yellow needles crystallized out. Recrystallization from boiling benzene yielded a product melting at 170°.

Calculated for $C_{16}H_{13}NO_4$: N, 5.16. Found, 5.01.

3-Methoxy-4-oxyphenylacetodihydrobenzmetoxazine.—This compound was prepared from vanillylidene anthranilic acid and acetic anhydride in the same manner as the preceding oxazines. Light straw-colored crystals, melting at 184°.

Calculated for $C_{19}H_{17}NO_6$: N, 3.94; C, 64.22; H, 4.78.

Found: N, 4.19; C, 63.94; H, 5.02.

Condensation products from other benzylidene anthranilic acids are being prepared and will be described in a succeeding paper.

BOULDER, COLORADO.

[CONTRIBUTIONS FROM THE SHEFFIELD LABORATORY OF YALE UNIVERSITY.]

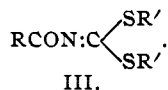
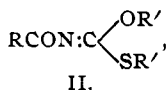
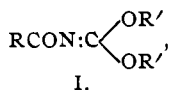
THE ACTION OF ALCOHOLATES AND AMINES ON BENZOYLISOCYANCHLORIDE.

BY TREAT B. JOHNSON AND LEWIS H. CHERNOFF.

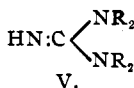
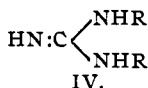
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Of the three classes of acylimidocarbonates, I, II and III, only the

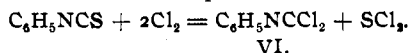
acylimidothio-, II, and acylimidodithiocarbonates, III, have been studied.¹ No representative of class I—*acylimidocarbonates*—so far as the writer is aware, has been described in the literature. We shall describe, in this paper, a method of preparing esters of this type and also a new method of synthesizing symmetrically substituted di- and tetraalkyl guanidines, IV and V.



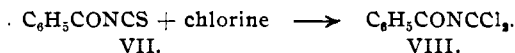
(RCO = benzoyl and R' = alkyl.)



Mustard oils, R.NCS, are attacked by chlorine, with replacement of the sulfur atom by the halogen, forming isocyanchlorides and sulfur chloride. Sell and Zierold,² for example, showed that phenylisothiocyanate reacts smoothly with this halogen in chloroform solution giving phenylisocyanchloride, VI, and represented the reaction as follows:



This same chloride, VI, and the corresponding bromide have also been prepared by Nef³ by the addition of chlorine and bromine respectively to phenylisocyanide. Johnson and Menge,⁴ in 1904, examined the behavior of chlorine towards acylisothiocyanates and showed that they react in a similar manner with chlorine, as phenylmustard oil, forming acylisocyanchlorides. They prepared in this manner, benzoylisocyanchloride, VIII, from benzoylrhodanide, VII. So far as the writer is aware, this chloride is the only representative of this new class of compounds, which has been described in the literature.



Owing to the pressure of other work, the writer has not been able, until recently, to study the chemical properties of this interesting compound. The chloride was originally prepared by the chlorination of benzoylisothiocyanate, VII, in chloroform. We now find that it can be obtained more easily and in greater yields by chlorinating the isothiocyanate in carbontetrachloride solution. The chloride is apparently more unstable than the arylisocyanchlorides. It is decomposed by water with formation of hydrochloric acid, benzamide and benzoic acid. How-

¹ Wheeler and Johnson, THIS JOURNAL, 24, 190; 27, 218; 26, 408.

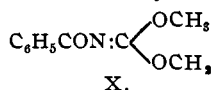
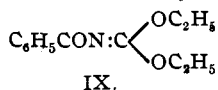
² Ber., 7, 1228 (1874).

³ Ann., 270, 282. Lengfeld and Stieglitz, Am. Chem. J., 17, 100.

⁴ Am. Chem. J., 32, 358.

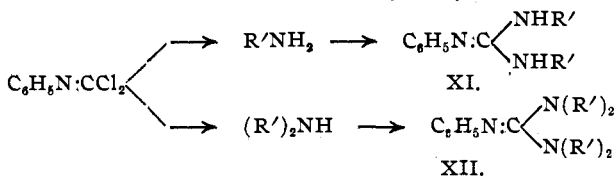
ever, if protected from moisture in tightly stoppered bottles, it can be preserved for months without decomposition.

Benzoylisocyanchloride, VIII, combines with sodium alcoholates, forming representatives of the hitherto unknown class of *acylimidocarbonates*, I. We have prepared for examination only two members of this series, *viz.*, diethyl- and dimethylbenzoylimidocarbonates, IX and X. They were formed by the action of sodium ethylate and sodium

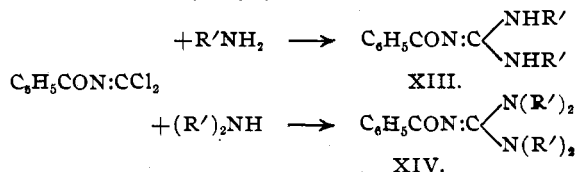


methylate respectively on the chloride. These esters were obtained as colorless oils of remarkable stability and could be distilled without decomposition. They undergo hydrolysis when warmed with alkali and hydrochloric acid, forming benzoic acid. The most characteristic property of this type of compounds was their remarkable stability when heated with organic bases. The acylimidothio- and acylimidodithiocarbonates, II and III, combine easily with amines, forming acylpseudoureas and acylpseudothioureas, respectively, with evolution of mercaptans.¹ Diethyl benzoylimidocarbonate, on the other hand, showed no tendency to react with aniline when heated with this reagent at 160°. There was no evidence of the formation of benzoylphenylpseudoethylurea. The same inertness was also manifested when the ester was heated with phenylhydrazine.

Phenylisocyanchloride reacts with amines giving tri- and penta-substituted guanidines,² XI and XII. Benzoylisocyanchloride reacts with



bases, in a perfectly similar manner, forming practically quantitative yields of the corresponding acylguanidines as follows:

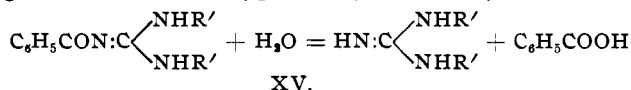


These acylguanidines, XIII and XIV, possess basic properties and form stable salts with mineral acids. When digested with alkali they undergo hydrolysis with formation of the free guanidines, XV, and benzoic acid.

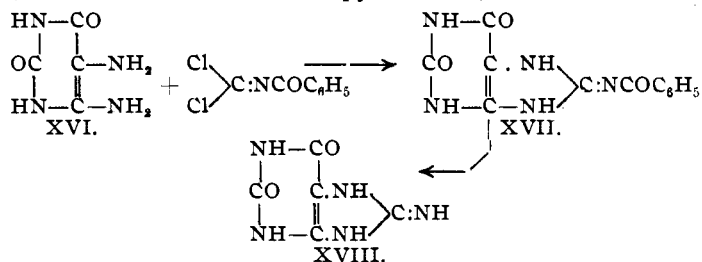
¹ Wheeler and Johnson, *loc. cit.*

² *Loc. cit.*

In fact, the yield of the guanidine base is excellent and with an accessible chloride like benzoylisocyanchloride we have a new simple method of preparing guanidines of these types easily and in any amount desired.



Benzoylisocyanchloride should be of value for the synthesis of 8-aminopurines, XVIII, from orthodiaminopyrimidines, XVI.



Experimental Part.

The benzoylisothiocyanate,¹ $\text{C}_6\text{H}_5\text{CONCS}$, which was used in this investigation, was prepared by the action of benzoylchloride on lead thiocyanate. The lead salt was made by dissolving lead acetate in water and then precipitating the thiocyanate by addition of the required amount of potassium thiocyanate. After filtering and washing with water and alcohol, the salt was then thoroughly dried in a desiccator over concentrated sulfuric acid. For the preparation of the rhodanide, 65 grams of the thiocyanate were suspended in 100 cc. of dry benzene, 55 grams of benzoylchloride added and the mixture was digested in an oil bath at $110-120^\circ$ for one hour. The yield of rhodanide is diminished by too long digestion and by heating at a higher temperature. After cooling, the lead chloride and excess of lead thiocyanate were separated by filtration, the excess of benzene evaporated in a partial vacuum and the rhodanide then purified by distillation under diminished pressure. The yield of pure rhodanide was 30 grams.

Benzoylisocyanchloride, $\text{C}_6\text{H}_5\text{CONCCl}_2$.—This compound has been described in a previous publication from this laboratory.² It was prepared by the action of chlorine on benzoylisothiocyanate in chloroform solution. We now find that it is formed far more smoothly by chlorination of the isothiocyanate when dissolved in carbontetrachloride. Thirty grams of benzoylisothiocyanate are dissolved in at least 3 volumes of anhydrous carbontetrachloride and the flask connected by a 3-way tube with a return condenser. The flask is then connected with a chlorine bomb and chlorine passed into the solution at 0° for 4 hours and the

¹ Miquel, *Ann. chim. phys.*, [5] 11, 300.

² Johnson and Menge, *loc. cit.*

solution then allowed to stand for 2-3 days. Under these conditions a red liquid is obtained in which is usually suspended a small amount of amorphous material. After filtering, the excess of carbontetrachloride and sulfur chloride is then evaporated in a vacuum and the isocyanchloride finally purified by distillation under diminished pressure. The yield was 25.0 grams. This yield, however, is greatly diminished if precautions are not taken throughout the experiment to exclude all moisture. The chloride obtained in 4 different experiments distilled as follows: 150-160° at 20-30 mm., 170-175° at 53 mm., 178-185° at 56 mm. and 115-121° at 20 mm.

Diethyl Benzoylimidocarbonate, $C_6H_5CON : C \begin{cases} OC_2H_5 \\ OC_2H_5 \end{cases}$.—This ester was

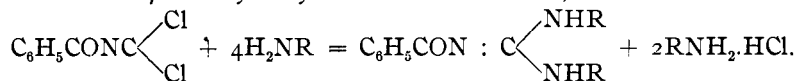
prepared by the action of benzoylisocyanchloride on sodium ethylate. Four and six-tenths grams of sodium were converted into dry sodium ethylate and the latter suspended in 200-300 cc. of anhydrous ether. The required amount of benzoylisocyanchloride was then carefully added and the mixture digested on the steam bath until the pungent odor of the isocyanchloride entirely disappeared (6-8 hours). After filtering from sodium chloride, the ether was evaporated and the carbonate distilled under diminished pressure. It boiled at 93-100° under 20 mm. pressure and at 110-120° under 32 mm. pressure. Analysis (Kjeldahl):

Calculated for $C_{12}H_{16}O_4N$: N, 6.31. Found, 6.5.

Dimethyl Benzoylimidocarbonate, $C_6H_5CON : C(OCH_3)_2$, was prepared in a similar manner as the above ethyl ester by the action of the isocyanchloride on dry sodiummethylate. It was obtained as a colorless oil, which distilled at 95-102° at 20 mm. pressure.

Hydrolysis of Diethyl Benzoylimidocarbonate with Alkali.—One gram of the ester was warmed, on the steam bath, with 50 cc. of a 10% potassium hydroxide solution until it dissolved. After cooling and acidifying with hydrochloric acid, pure benzoic acid separated and melted at 120°.

The Action of Benzoylisocyanchloride on Amines,



—This chloride reacts violently with bases forming the benzoyl derivatives of dialkyl guanidines. Dilution of the reagents with an inert solvent is necessary in order to obtain smooth reactions. The general procedure was to dissolve the base in dry benzene and then add this solution cautiously to a benzene solution of the chloride. There was usually an immediate reaction, with evolution of much heat and the free acylguanidine and, in some cases, its hydrochloride separated at once in crystalline form. After digestion for 2-3 hours to complete the reaction the benzene

was evaporated and the compound purified by recrystallization from a suitable solvent.

1,3-Diphenyl-2-benzoylguanidine, $C_6H_5CON : C(NHC_6H_5)_2$.—This compound was prepared by dissolving 9.2 grams of aniline in 30 cc. of benzene and adding slowly to a solution of 5.0 grams of benzoylisocyanchloride in 50 cc. of benzene. After warming 4.5 hours on the steam bath and cooling, an insoluble, colorless, crystalline substance was obtained. This was identified as a mixture of aniline hydrochloride and the hydrochloride of the acylguanidine. This material was washed with cold water to remove the aniline hydrochloride and the hydrochloride of the acylguanidine purified by crystallization from 95% alcohol. It separated, on cooling, in needles, which melted at 212° with decomposition.

Nitrogen (Kjeldahl)—Calculated for $C_{20}H_{17}ON_3 \cdot HCl$: N, 11.90. Found, 11.70.

The benzene filtrate above was concentrated and cooled, when the free guanidine deposited. It dissolved in boiling 95% alcohol and separated on cooling in prisms, which melted at 104° to an oil. Analysis (Kjeldahl):

Calculated for $C_{20}H_{17}ON_3$: N, 13.33. Found, 13.30.

Hydrolysis of 1,3-Diphenyl-2-benzoylguanidine.—This guanidine is very stable in the presence of hydrochloric acid. Three grams of the base were digested with 50 cc. of dilute hydrochloric acid for 2 hours and the solution then evaporated to dryness. On crystallizing the residue from 95% alcohol the hydrochloride of the unaltered benzoylguanidine was obtained and it melted at $209-210^\circ$ with effervescence. One and five-tenths grams of the benzoylguanidine were digested with 50 cc. of a 15% solution of potassium hydroxide for 2 hours and the solution then evaporated to dryness. The residue obtained was then triturated with cold water to remove the alkali and the undissolved material purified by crystallization from boiling 95% alcohol. On cooling, diphenylguanidine separated and melted at $146-148^\circ$.

Calculated for $C_{13}H_{13}N_3$: N, 19.90. Found, 19.81.

*1,3-Di-*o*-tolyl-2-benzoylguanidine*, $C_6H_5CON : C(NHC_6H_4CH_3)_2$.—From orthotoluidine and benzoylisocyanchloride. It crystallized from 95% alcohol in flat prisms, which melted at 126° .

Calculated for $C_{22}H_{21}ON_3$: N, 12.24. Found, 11.84.

*1,3-Di-*m*-tolyl-2-benzoylguanidine*, $C_6H_5CON : C(NHC_6H_4CH_3)_2$.—From *m*-toluidine and benzoylisocyanchloride. It is soluble in boiling benzene and separates from a hot 95% alcohol solution in needles, which melt at $177-178^\circ$.

Calculated for $C_{22}H_{21}ON_3$: N, 12.24. Found, 12.30.

*Di-*m*-tolylguanidine*, $HN : C(NHC_6H_4CH_3)_2$.—A quantitative yield of this base was obtained by hydrolysis of the preceding benzoyl derivative

with potassium hydroxide. It was purified by crystallization from 95% alcohol and melted at 108–109° to a clear oil.

Calculated for $C_{15}H_{14}N_3$: N, 17.56. Found, 17.71.

1,3-Di-p-tolyl-2-benzoylguanidine, $C_6H_5CON : C(NHC_6H_4CH_3)_2$.—From *p*-toluidine and benzoylisocyanchloride. It crystallized from benzene in rhombic prisms, which melted at 190°.

Calculated for $C_{22}H_{21}ON_3$: N, 12.24. Found, 12.40.

Hydrochloride, $C_{22}H_{21}ON_3 \cdot 2HCl$.—This salt is very soluble in alcohol and crystallizes from benzene in prisms, which melt at 190–191° with decomposition.

Calculated for $C_{22}H_{21}ON_3 \cdot 2HCl$: N, 10.09. Found, 10.01.

Benzoyltetraphenylguanidine, $C_6H_5CON : C[N(C_6H_5)_2]_2$.—From diphenylamine and benzoylisocyanchloride. This was obtained as a colorless solid which crystallized from 95% alcohol in prismatic crystals. It melted at 142–144°.

Calculated for $C_{32}H_{22}ON_3$: N, 8.99. Found, 8.66.

1,3-Dimethyl-1,3-diphenyl-2-benzoylguanidine, $C_6H_5CON : C[N(CH_3)C_6H_5]_2$.—From monomethylaniline and benzoylisocyanchloride. It crystallized from 95% alcohol in well-developed rhombic prisms, which melted at 135°.

Calculated for $C_{22}H_{21}ON_3$: N, 12.24. Found, 12.00.

1,3-Di-p-anisyl-2-benzoylguanidine, $C_6H_5CON : C(NHC_6H_4OCH_3)_2$.—From paraanisidine and benzoylisocyanchloride. It crystallized from alcohol in needles, which melted at 128° to an oil.

Calculated for $C_{22}H_{21}O_3N_3$: N, 11.20. Found, 11.09.

Di-p-anisylguanidine, $HN : C(NHC_6H_4OCH_3)_2$.—Separated from hot alcohol in flakes, which melted at 153°.

Calculated for $C_{18}H_{17}O_2N_3$: N, 14.91. Found, 14.87.

1,3-Di-β-naphthyl-2-benzoylguanidine, $C_6H_5CON : C(NHC_{10}H_7)_2$.—From β-naphthylamine and benzoylisocyanchloride. This base crystallized from alcohol in prisms, which melted at 162°.

Calculated for $C_{28}H_{21}ON_3$: N, 10.07. Found, 10.04.

Di-β-naphthylguanidine, $HN : C(NHC_{10}H_7)_2$.—A quantitative yield of this guanidine is obtained by hydrolysis of the above benzoyl compound. It melted at 197°, with slight effervescence.

Calculated for $C_{21}H_{17}N_3$: N, 13.50. Found, 13.61.

NEW HAVEN, CONN., Nov. 28, 1911.

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY.]

2,2,3-TRIMETHYLPENTANE.

BY LATHAM CLARKE AND WEBSTER NEWTON JONES.

Received December 2, 1911.

The hydrocarbons of the formula C_8H_{18} have been a subject of study