

In the experimental examination of these results it was found that iodoform alone retarded lipolysis in direct proportion to the concentration of the iodoform present. This varied from a 15% retardation with 0.03% concentration of iodoform to a 55% retardation with 0.5% concentration of the antiseptic.

It was found, also, that old solutions of iodoform in acetone contain free iodine which has a marked effect on lipase activity. Iodine, in concentrations of 0.045% or more, inhibited lipolysis entirely.

Results similar to those with iodine were obtained using bromine water. Higher concentrations of bromine were found necessary to inhibit the lipase, however, concentrations of 0.25% retarding the enzyme activity only 93 to 94%.

The results with the formaldehyde and the halogens are discussed with reference to their bearing on the possible constitution of lipase.

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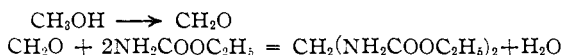
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY COLLEGE OF CALCUTTA]

HALOGENATION. XXI. SOME DERIVATIVES OF CARBAMIC ESTERS. CHLORINE AS A SIMULTANEOUS OXIDIZING AND CONDENSING AGENT

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It has been shown¹ that when chlorine is passed through an aqueous solution of various alkyl carbamic esters, mono- and dichloro substitution products are formed, the chlorine replacing the hydrogen of the amido group to form substituted nitrogen chlorides. It has been found that when chlorine is passed into carbamic esters in alcoholic solutions, the alcohol is oxidized to the corresponding aldehyde which immediately condenses with the carbamic esters to form dicarbamic esters. Thus, when chlorine is passed into a methyl alcoholic solution of urethane, the methyl alcohol is first oxidized to formaldehyde which then condenses with two molecules of urethane to form methylene diurethane.



In a similar manner, chlorination of methyl carbamic ester in methyl alcoholic solution, gives rise to methylene dicarbamic methyl ester, $\text{CH}_2(\text{NHCOOCH}_3)_2$.

These compounds were prepared previously by Conrad and Hock² by the condensation of formaldehyde with ethyl carbamic and with methyl carbamic esters, respectively.

¹ Datta and Gupta, *THIS JOURNAL*, **36**, 386 (1914); Ref. 6.

² Conrad and Hock, *Ber.*, **36**, 2206 (1903).

The following compounds have been prepared for the first time.

Methylene dicarbamic propyl ester has been prepared by passing a current of chlorine into methyl alcoholic solution of propylcarbamic ester. *Isobutyl*carbamic ester condenses with methyl alcohol in the presence of chlorine to form methylene dicarbamic *isobutyl* ester. *Iso*-amyl carbamic ester gives similarly with methyl alcohol, methylene dicarbamic *iso*-amyl ester.

With benzyl alcohol, the same type of reaction takes place and benzylidene diurethane, $C_6H_5.CH(NHCOOC_2H_5)_2$, results when chlorine is passed into a benzyl alcoholic solution of urethane, the benzyl alcohol being oxidized to benzaldehyde in the first instance. This compound has been prepared by Bischoff³ by condensing benzaldehyde with urethane in the presence of hydrochloric acid.

When chlorine acts on urethane dissolved in ethyl alcoholic solution, the reaction is not as simple as in the preceding cases. Here, the ethyl alcohol is chlorinated and, at the same time, oxidized to aldehyde which finally condenses with 2 molecules of urethane forming dichloro-ethylidene diurethane, $CHCl_2(NHCOOC_2H_5)_2$.

This compound was prepared by Schmidt⁴ by the action of chlorine upon urethane at temperatures ranging between 90° and 100°. In the case of substituted urethanes such as phenyl urethane, $C_6H_5NH.COOC_2H_5$, and α -naphthyl urethane, $C_{10}H_7.NH.COOC_2H_5$, the same type of reaction is observed but, on account of the reactivity of these aromatic groups, they are chlorinated at the same time. With phenyl urethane in methyl alcohol, methylene di-*p*-chlorodiphenyldiurethane, $CH_2(C_6H_4Cl.N.COOC_2H_5)_2$ is formed; the chlorine assumes the *para* position, which is generally the case according to the law of substitution. With α -naphthyl urethane and methyl alcohol, methylene ditetrachloro- α -naphthyl diurethane, $CH(C_{10}H_5Cl_2.N.COOC_2H_5)_2$, is produced; the position of the chlorine in the naphthalene ring is not definitely known.

Condensations of this type failed in the case of secondary alcohols. Thus, when urethane dissolved in *isopropyl* alcohol is chlorinated, no condensation product is formed, but a complete decomposition of the urethane molecule takes place with the formation of ammonium chloride.

Incidentally, it has been found that ethyl-monochlorocarbamic ester undergoes hydrolysis when kept in contact with water; a cyclic compound, diethyl-4-chloromethyl-cyclomethylene-hydrazine-imide-1,3-dicar-

boxylate, is formed, $CH_2Cl.CH \begin{array}{c} \diagup \\ \diagdown \end{array} \begin{array}{c} N. COOC_2H_5 \\ NH \\ N. COOC_2H_5 \end{array}$. Its formation may be explained

³ Bischoff, *Ber.*, **7**, 634 (1874).

⁴ Schmidt, *J. prakt. Chem.*, [2] **24**, 120 (1881).

by the condensation of two urethane molecules with ammonia and chloro-acetaldehyde, produced by the hydrolytic oxidation of the urethane molecule. Its constitution has been proved by the formation of a

substituted nitrogen chloride, $\text{CH}_2\text{Cl}.\text{CH} \begin{array}{c} \text{N. COOC}_2\text{H}_5 \\ \diagup \quad \diagdown \\ \text{N.Cl} \\ \diagdown \quad \diagup \\ \text{N. COOC}_2\text{H}_5 \end{array}$, in which the imide

hydrogen is substituted. It also forms an acetyl derivative.

$\text{CH}_2\text{Cl}.\text{CH} \begin{array}{c} \text{N. COOC}_2\text{H}_5 \\ \diagup \quad \diagdown \\ \text{N.CO.CH}_3 \\ \diagdown \quad \diagup \\ \text{N. COOC}_2\text{H}_5 \end{array}$ in which the imide hydrogen is acetylated.

It may be mentioned that Datta and Das Gupta⁵ obtained this chloro compound by adding monochloro-urethane to ethyl alcohol, though they were not successful in determining its constitution fully or in preparing its acetyl derivative. The substances obtained by both methods have been found to be identical, as ascertained by a mixed melting point. Acetyl derivatives of the substances obtained by both methods were also found to have the same melting point.

It has been mentioned by Datta and Gupta⁵ that they could not prepare the substituted nitrogen chloride derivative of methyl urethane. It has now been found that the substance they chlorinated was the methyl derivative of urethane, $\text{NHCH}_3.\text{COOC}_2\text{H}_5$, and it is quite natural that it would not form any chloro derivative. The dichloro derivative, $\text{NCl}_2.\text{COOCH}_3$, has been found to be formed quite easily by passing a current of chlorine through an aqueous solution of the methyl ester of carbamic acid.

Experimental

Action of Chlorine on a Methyl Alcoholic Solution of Ethyl Urethane. Methylene Diurethane, $\text{CH}_2(\text{NHCOOC}_2\text{H}_5)_2$.—Twenty g. of urethane was dissolved in 25 cc. of methyl alcohol and a stream of chlorine was passed through it. During the course of the reaction, white fumes were evolved, and the solution became quite hot. The reaction was generally complete in about 3 to 4 hours and was marked by the appearance of a white solid consisting of ammonium chloride which increased as the passing of chlorine was continued. As soon as the white solid began to make its appearance, the reaction was stopped and the solution evaporated nearly to dryness, when the product crystallized. The solid was separated from the mother liquor by suction and crystallized from dilute alcohol. Two crystallizations generally gave a pure product in the form of white, silky needles melting at 131° .

Analysis. Subs., 0.2161: 28.7 cc. N_2 (25° and 760.8 mm.). Calc. for $\text{C}_7\text{H}_{14}\text{O}_4\text{N}_2$: N, 14.74. Found: 14.93.

Action of Chlorine on a Methyl Alcoholic Solution of Methyl Urethane. Methylene Dicarbamic Methyl Ester, $\text{CH}_2(\text{NHCOOCH}_3)_2$.—Six g. of methyl urethane was dissolved

⁵ Unpublished work.

⁶ Datta and Gupta, *THIS JOURNAL*, **37**, 569 (1915).

in 10 cc. of methyl alcohol and a current of chlorine was passed through it for several hours until a white solid began to appear. During the process, white fumes were evolved and the solution became hot. The resulting product was evaporated nearly to dryness and the crystals that separated as the product cooled were collected and drained by suction. These were then crystallized from ether, when the substance was obtained in beautiful fine white needles melting at 124° . On account of its very great solubility in alcohol, it could not be recrystallized from this solvent. It is also soluble in water.

Analysis. Subs., 0.0849: 13.5 cc. N_2 (28° and 762 mm.). Calc. for $C_3H_{10}O_4N_2$: N, 17.28. Found: 17.83.

Action of Chlorine on a Methyl Alcoholic Solution of Propyl Urethane. Methylene Dicarbamic Propyl Ester, $CH_2(NHCOOC_3H_7)_2$.—Seven g. of propyl urethane, dissolved in 15 cc. of methyl alcohol, was chlorinated for several hours until the solution acquired a green color. Much heat was evolved during the reaction. The product on evaporation on a water-bath deposited a white solid which was freed from mother liquor by suction. Recrystallized from dil. alcohol, it was obtained as white silky needles melting at 113° .

Analysis. Subs., 0.1643: CO_2 , 0.2887; H_2O , 0.1179. Subs., 0.0684: 7.8 cc. N, (27° and 760 mm.). Calc. for $C_3H_{10}O_4N_2$: C, 49.54; H, 8.26; N, 12.84. Found: C, 47.93; H, 7.98; N, 12.81.

Action of Chlorine on a Methyl Alcoholic Solution of Isobutyl Urethane. Methylene Dicarbamic Isobutyl Ester, $CH_2(NHCOOC_4H_9)_2$.—Six g. of *isobutyl* urethane was dissolved in 12 cc. of methyl alcohol and the solution chlorinated as usual. The solid after evaporation of the alcohol was recrystallized from dil. alcohol. It formed fine needles melting at 115° .

Analysis. Subs., 0.1245: CO_2 , 0.2465; H_2O , 0.1064. Subs., 0.1266: 13.4 cc. N_2 (31° and 760.3 mm.). Calc. for $C_{11}H_{22}O_4N_2$: C, 53.66; H, 8.94; N, 11.38. Found: C, 54.00; H, 9.50; N, 11.69.

Action of Chlorine on a Methyl Alcoholic Solution of Iso-amyl Urethane. Methylene Dicarbamic Iso-amyl Ester, $CH_2(NHCOOC_5H_{11})_2$.—Two and a half g. of *iso-amyl* urethane dissolved in 10 cc. of methyl alcohol was treated with chlorine as usual. Recrystallized from dil. alcohol, the product was a white powder consisting of very small crystals melting at 80° .

Analysis. Subs., 0.0733: 6.5 cc. N_2 (31° and 671 mm.). Calc. for $C_{13}H_{26}O_4N_2$: N, 10.22. Found: 9.80.

Action of Chlorine on a Benzyl Alcoholic Solution of Ethyl Urethane. Benzylidene Diurethane, $C_6H_5CH(NHCOOC_2H_5)_2$.—Eleven g. of urethane was dissolved in 25 cc. of benzyl alcohol so as to make a solution nearly saturated. Chlorine passed through the solution caused fumes to be liberated. The chlorination was discontinued when feathery crystals began to appear. The solution, which became heated, solidified almost completely as it cooled. This product was drained by suction to remove adhering liquor and then recrystallized from dil. alcohol. Silky needles melting at 175° were obtained.

Analysis. Subs., 0.1561: 14.2 cc. N_2 (26° and 762 mm.). Calc. for $C_{13}H_{18}O_4N_2$: N, 10.53. Found: 10.30.

Action of Chlorine on an Ethyl Alcoholic Solution of Ethyl Urethane. Dichloroethylidene Diurethane, $CHCl_2CH(NHCOOC_2H_5)_2$.—Twenty g. of urethane was dissolved in 30 cc. of ethyl alcohol and a current of chlorine passed through the solution until a white solid began to appear. During the process, copious white fumes were evolved and the solution became hot. The solution was evaporated nearly

to dryness and the crystals freed from the mother liquor by suction. When recrystallized from dil. alcohol, the compound was obtained as fine needles melting at 122°; this melting point is the same as that of Schmidt's compound. Its identity was established also by a nitrogen determination.

Analysis. Subs., 0.1548: 14.6 cc. N₂ (26° and 761 mm.). Calc. for C₈H₁₄O₄N₂Cl₂: N, 10.26. Found: 10.65.

Action of Chlorine on Phenyl Urethane in Methyl Alcoholic Solution. Methylene-*p*-chlorodiphenyl Diurethane, CH₂(C₆H₄ClNCOOC₂H₅)₂.—Five g. of phenyl urethane was dissolved in 12 cc. of methyl alcohol and the solution chlorinated as usual. Evolution of white fumes and rise of temperature occurred. After about half an hour, the solution began to thicken and then solidified *en masse*. The solid was removed, pressed on a porous plate and recrystallized from absolute alcohol. It consisted of white needles melting at 87°.

Analyses. Subs., 0.0742: CO₂, 0.1529; H₂O, 0.0349. Subs., 0.1428: 8.8 cc. N₂ (32° and 761 mm.). Subs., 0.1541: AgCl, 0.1071. Calc. for C₁₉H₂₀O₄N₂Cl₂: C, 55.47; H, 4.87; N, 6.81; Cl, 17.27. Found: C, 56.18; H, 5.23; N, 6.79; Cl, 17.20.

Action of Chlorine on α -Naphthyl Urethane in Methyl Alcoholic Solution. Methylene-ditetrachloro- α -naphthyl Diurethane, CH₂(C₁₀H₅Cl₂NCOOC₂H₅)₂.—Five g. of α -naphthyl urethane were dissolved in 25 cc. of methyl alcohol and a current of chlorine passed through the solution. Much heat was evolved and a white asbestos-like substance began to form, clogging the delivery tube, and finally the whole mixture solidified to a dense mass of fibrous crystals. This material was recrystallized from absolute alcohol. The crystals were found generally contaminated with a red substance which had to be removed by repeated crystallization. Finally, the compound was obtained as white needles melting at 160–161°.

Analyses. Subs., 0.0971: CO₂, 0.1965; H₂O, 0.0427. Subs., 0.0818: 3.9 cc. N₂ (30° and 761 mm.). Subs., 0.0820: AgCl, 0.080. Calc. for C₂₇H₂₂O₄N₂Cl₄: C, 55.86; H, 3.79; N, 4.83; Cl, 24.48. Found: C, 55.22; H, 4.89; N, 5.30; Cl, 24.16.

Hydrolysis of Monochloro-urethane. Diethyl-4-chloromethyl-cyclomethylene-hydrazine-imide-1,3-dicarboxylate, CH₂ClCH(NCOOC₂H₅)₂NH.—Twenty g. of urethane was dissolved in 100 cc. of water and a stream of chlorine passed into the solution for about 3 hours. Monochloro-urethane separated as a heavy yellow oil and the supernatant liquid was completely saturated with chlorine. The product was kept in the open air. At the end of about 3 days white crystals began to form which gradually developed till the whole vessel was filled, the oil disappearing at the same time. This generally occupied 8 to 10 days. The crystals were filtered at the pump and dried on a porous plate. Yield, 3.5 g. When the substance was recrystallized from hot water it formed milk-white needle-shaped crystals melting at 143–144°. It is soluble in alcohol, ether, chloroform and benzene.

Analyses. Subs., 0.1643: CO₂, 0.2325; H₂O, 0.0843. Subs., 0.2021: 30.8 cc. N₂ (32° and 754.6 mm.). Subs., 0.1037: AgCl, 0.0586. Subs., 0.3083: AgI, 0.5078. Calc. for C₈H₁₄O₄N₂Cl: C, 38.17; H, 5.56; N, 16.69; Cl, 14.11; OEt, 35.78. Found: C, 38.60; H, 5.70; N, 16.65; Cl, 13.98; OEt, 31.45.

ACETYL DERIVATIVE, CH₂Cl.CH(NCOOC₂H₅)₂NCOCH₃.—The acetyl derivative was prepared by heating the substance under a reflux condenser with acetic anhydride with the addition of a few drops of pyridine. At the end of 4 to 5 hours, the brownish solution obtained was distilled under reduced pressure to remove unchanged acetic anhydride. The residue at the bottom of the flask containing some tarry substance was next extracted with hot water. The aqueous solution was evaporated to dryness on the water-bath and the residue extracted with benzene. The benzene solution deposited

brownish-white crystals. These were drained and recrystallized from benzene several times, when the compound was obtained in white granular crystals melting at 117–118°. The yield was very small.

Analyses. Subs., 0.0942: CO₂, 0.1435; H₂O, 0.0511. Subs., 0.0753: 9.7 cc. N₂ (30° and 761 mm.). Calc. for C₁₀H₁₆O₅N₃Cl: C, 40.89; H, 5.45; N, 14.31. Found: C, 41.54; H, 6.03; N, 14.32.

IMIDE CHLORIDE, CH₂ClCH(NCOOC₂H₅)₂NCl.—The substance was dissolved in boiling water and filtered through a hot filter into a beaker placed on a bath of warm water, and a current of chlorine was passed through the solution at the same time. As the addition of the chlorine was continued the crystals deposited at the bottom of the vessel began to turn soft and pasty and the solution became turbid. At this stage the current of chlorine was shut off and the solid filtered by suction and dried on a porous plate. On recrystallization in the cold, it is obtained in the shape of granular crystals melting at 75–76°. The substance is unstable and decomposes gradually with the evolution of chlorine.

Analyses. Subs., 0.1056: 35.8 cc. 0.1 *N* thiosulfate solution. Calc. for C₅H₁₃O₄N₃-Cl₂: Cl as =N.Cl, 12.41. Found: 12.06.

Dichlorocarbamic Methyl Ester, NCl₂.COOCH₃.—Two g. of methyl carbamate was dissolved in 20 cc. of water and a current of chlorine was passed through it when a yellow oil separated at the bottom. The separation of the oil was very slow at first but after a time it was very rapid. The current of chlorine was stopped when no more oil formed. The oil was separated, washed with water and dried over calcium chloride. The yield was nearly quantitative.

Analysis. Subs., 0.1863: 26.3 cc. of 0.1 *N* thiosulfate solution. Calc. for C₂H₅O₂-NCl₂: Cl, as =NCl, 49.31. Found: 50.12.

Investigations on similar lines are being continued.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

THE OXIDATION OF POTASSIUM ACETATE TO POTASSIUM OXALATE¹

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The following experiments on the oxidation of potassium acetate to potassium oxalate were carried out because the literature contains conflicting data in reference to the possibility of such a reaction. Under chosen experimental conditions oxalic acid is obtained as an oxidation product when certain methyl-containing compounds such as ethyl alcohol and acetaldehyde are oxidized with alkaline potassium permanganate. It became of much interest, therefore, to know whether acetates were oxidized to oxalates with neutral or with alkaline solutions of permanga-

¹ Presented at the New York meeting of the American Chemical Society, September, 1921.