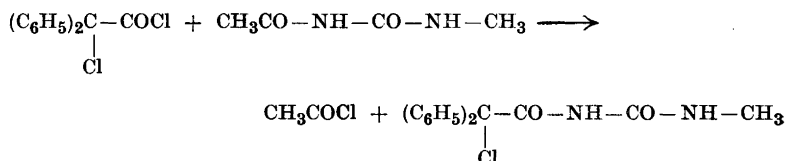


The Reaction between Diphenylchloroacetyl Chloride and Methylurea

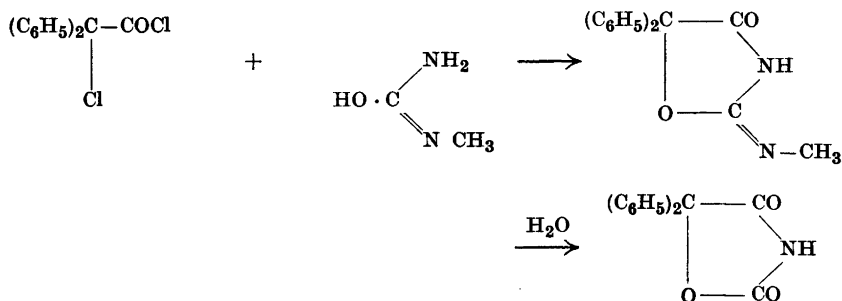
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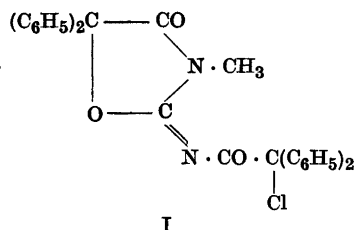
Some years ago Aspelund and Holmberg¹ investigated the reactions between diphenylchloroacetyl chloride and substituted ureas. Only one aliphatic urea, acetylmethylurea, was studied at that time and it was established that following reaction took place.



As it was of some interest to extend the investigations to methylurea, experiments were performed with this substance and diphenylchloroacetyl chloride both in the absence of and in the presence of pyridine. In the first case 5,5-diphenyloxazolidione was formed, apparently by the following mechanism.

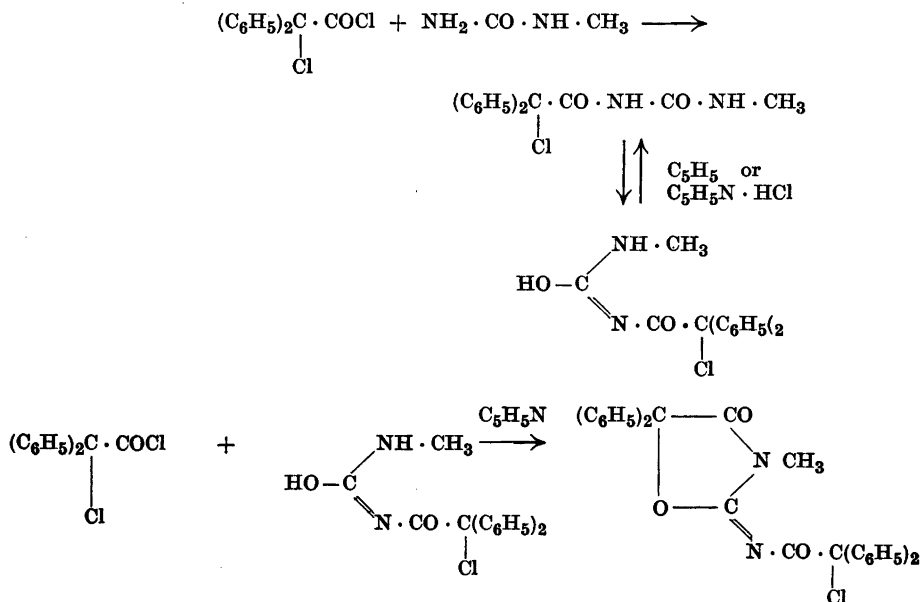


When the reaction was carried out in the presence of pyridine, a crystalline substance, $C_{30}H_{23}O_3N_2Cl$, was obtained, which was hydrolyzed to 3-methyl-5,5-diphenyloxazolidione by treatment with alcoholic hydrochloric acid. The initial product is therefore 2-(diphenylchloroacetylmino)-3-methyl-5,5-diphenyloxazolidone, I.



In addition to these substances, considerable quantities of resinous oils were obtained.

N-methyl-*N'*-phenylchloroacetylurea and *N*-methyl-*N'*-chloroacetylurea respectively are formed when phenylchloroacetyl chloride and chloroacetyl chloride are allowed to react with methylurea or acetylmethylurea², *i.e.* the reaction products are the same whether methylurea or its acetyl derivative is used. If diphenylchloroacetyl chloride reacts in the same manner the formation of 2-(diphenylchloroacetylmino)-3-methyl-5,5-diphenyloxazolidone could be explained as follows:



This, however, proved to be incorrect, because 5,5-diphenyloxazolidione and benzoic acid and not the acylated iminoöxazolidone were isolated when diphenylchloroacetyl chloride and *N*-methyl-*N'*-diphenylchloroacetylurea were heated together in the presence of pyridine.

Aspelund² showed that *N*-phenyl-*N'*-phenylchloroacetylurea is formed when phenylchloroacetyl chloride reacts with phenylurea, *i.e.* a derivative of type *A* is formed, but when Aspelund and Holmberg¹ treated diphenylchloroacetyl chloride with phenylurea they isolated 3,5,5-triphenylhydantoin and 3,5,5-triphenyloxazolidione, *i.e.* compounds of type *B*. A similar change in the point of attack of the acyl chlorine atom is observed in the reactions between



methylphenylurea on one hand and phenylchloroacetyl chloride, chloroacetyl chloride, and diphenylchloroacetyl chloride on the other. Chloroacetyl chloride and methylphenylurea give *N*-phenyl-*N'*-methyl-*N'*-chloroacetyl urea² while phenylchloroacetyl chloride and methylphenylurea give 2-phenylimino-3-methyl-5-phenyloxazolidione and 1,5-diphenyl-3-methylhydantoin². All these reaction products contain the same group, *viz.* *C*. However, diphenylchloroacetyl chloride and methylphenylurea give 3,5,5-triphenyloxazolidione¹, containing the group *D*.

As, in the absence of pyridine, diphenylchloroacetyl chloride and methylurea give only small amounts of 5,5-diphenyloxazolidione (type *A*) it could be possible that methylurea represents a borderline case, and that the main product would be 2-imino-3-methyl-5,5-diphenyloxazolidione (type *B*). But if this is the case, 2-methylimino-5,5-diphenyloxazolidione must have polymerized or decomposed in the presence of pyridine. However, when *N*-methyl-*N'*-diphenylchloroacetylurea and a small quantity of pyridine are heated, a very good yield of 5,5-diphenyloxazolidione is obtained. This shows that the 2-methylimino derivative does not undergo any change under the conditions of the experiment.

In order to prove that the 2-methylimino and 2-imino derivatives are not formed simultaneously, diphenylchloroacetyl chloride and methylurea were allowed to react in the absence of pyridine. Unreacted methylurea was then removed and the heating was continued after the addition of diphenylchloroacetyl chloride and pyridine. If the 2-imino derivative had formed in the absence of pyridine it should have been possible to isolate the acylated imino compound from the reaction mixture, but only a very small amount of 5,5-diphenyloxazolidione was, however, obtained.

These two experiments show that pyridine or its hydrochloride has a directing influence on the reaction between diphenylchloroacetyl chloride and methylurea. It is difficult to decide its role in the reaction mechanism, but it seems possible that it forms a complex with either diphenylchloroacetyl chloride or methylurea, the complex then reacting with the other component. It is, however, evident that diphenylchloroacetyl chloride reacts with methylurea in the absence of pyridine in the same way as phenylchloroacetyl chloride and chloroacetylchloride, *i.e.* the acyl group becomes attached to the primary amino group of the urea.

EXPERIMENTAL

The reaction in the absence of pyridine

A mixture of methylurea (0.74 g) and diphenylchloroacetyl chloride (3.18 g, 1.20 equiv.) in dry benzene (25 ml) was heated for 8 hours on the boiling water bath. The following day the solvent was evaporated, and the residue was treated with a mixture of ether and water. The ether solution was separated and shaken with aqueous sodium bicarbonate for 45 minutes and then with 1 *N* sodium hydroxide solution (12 ml + 3 × 4 ml). After this treatment the ether solution yielded a tarry resinous oil (1.58 g) that did not crystallize.

The sodium bicarbonate solution was acidified, whereupon benzoic acid (0.16 g, m.p. 150°) separated.

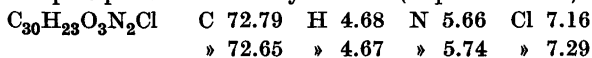
The first sodium hydroxide extract was slowly acidified with 1 *N* hydrochloric acid and the material which separated when the solution was still slightly alkaline to litmus was extracted with ether and the material recovered from the ether solution was treated with benzene, yielding impure 5,5-diphenyloxazolidione (0.06 g, m.p. 129–130°). On further addition of hydrochloric acid to the aqueous solution an oil separated and this after working up as before gave more 5,5-diphenyloxazolidione (0.06 g, m.p. 129–131°).

The second alkaline extract gave 0.20 g of the same substance (m.p. 130–132°) after the solution had been made slightly acid to litmus. When the acidification was continued until the solution was acid to congo red, only 0.16 g of a resinous substance was isolated.

The two last extracts gave only small amounts of resinous substances after acidification.

The reaction in the presence of pyridine

A mixture of methylurea (0.74 g), diphenylchloroacetyl chloride (3.18 g, 1.20 equiv.), and dry pyridine (1.90 g) in dry benzene (20 ml) was heated on the boiling water bath for 8 hours. The benzene was distilled off and the residue was treated with water and ether. After some time crystals began to separate from the ether solution and at the interface. After three hours the crystals (1.01 g) were collected and purified by solution in benzene and precipitation with ethyl alcohol (m.p. 172–173°).



This substance, 2-(diphenylchloroacetyl-imino)-3-methyl-5,5-diphenyloxazolidone, is readily soluble in benzene but sparingly soluble in alcohol and ether.

The separated ether layer was shaken for two hours with 1 *N* sodium hydroxide (60 ml). The alkaline aqueous solution was acidified with hydrochloric acid and the oil that separated was dissolved in ether. The substance dissolved in this ether solution was completely extracted with solutions of sodium bicarbonate and sodium carbonate. When these solutions were acidified 0.18 g of acids with a melting range between 80 and 140° were isolated.

Evaporation of the ether solution that had been separated from the 60 ml quantity of 1 *N* sodium hydroxide yielded a tarry resinous oil (0.97 g). In order to hydrolyze any imino or acylated compounds the oil was boiled with a mixture of alcohol (50 ml) and conc. hydrochloric acid (20 ml) for one hour. The alcohol was distilled off and the remaining acid solution was extracted with ether, and the ether solution was shaken with dilute sodium hydroxide. Evaporation of the ether yielded a tarry resinous oil (0.90 g, probably unchanged material). When the alkaline aqueous solution was acidified, only a very small amount of a resinous oil separated.

Hydrolysis of the acylated iminoöxazolidone

2-(Diphenylchloroacetylmino)-3-methyl-5,5-diphenyloxazolidone (0.5 g) was boiled with a mixture of ethyl alcohol (50 ml) and conc. hydrochloric acid (20 ml) for 1.5 hours, *i.e.* half an hour after the substance had dissolved. The alcohol was evaporated *in vacuo* and the oil remaining was treated with ether and water. The ether phase was shaken with 1 *N* sodium hydroxide (10 ml) and evaporated giving an oil (0.48 g) from which 3-methyl-5,5-diphenyloxazolidone (0.20 g, m.p. 97–98°) was isolated by treatment with ethyl alcohol.

The acid aqueous solution was neutralized and the alkaline solution was acidified, but no material separated from either solution.

Attempts to prepare the acylated iminoöxazolidone in other ways

Experiment 1. A mixture of *N*-methyl-*N'*-diphenylchloroacetylurea (1.25 g), diphenylchloroacetyl chloride (1.10 g), and pyridine (0.9 g) dissolved in dry benzene (20 ml) was heated for three hours on the boiling water bath. The benzene was evaporated *in vacuo* and the residue was dissolved in ether and water to which a small quantity of conc. hydrochloric acid had been added. The mixture was set aside over night, but no crystals were deposited. The ether solution was shaken with dilute sodium hydroxide, and dilute hydrochloric acid was added to the latter until a small amount of an oil had separated. The oil (0.22 g) recovered by ether extraction did not crystallize. The addition of hydrochloric acid to the aqueous solution was continued until the latter was neutral to congo red. The oil which separated (1.40 g) was recovered with ether and then treated with benzene. The solid so obtained (0.96 g, m.p. 109–130°) was dissolved in dilute sodium hydroxide, and dilute hydrochloric acid was added to the mixture. When it was slightly alkaline to litmus 5,5-diphenyloxazolidone (0.04 g, m.p. 129–130°) separated. After further addition of hydrochloric acid another sample of the same substance (0.35 g, m.p. 133–133.5°) was obtained when the solution was acid to litmus but not to congo red. A mixture of substances (0.41 g, melting range 109–134°) separated finally when more hydrochloric acid was added. This last mixture was boiled with water and the clear hot

solution was decanted. From this solution slightly impure benzoic acid (0.29 g, m.p. 146–148°) crystallized.

Experiment 2. A mixture of methylurea (0.74 g) and diphenylchloroacetyl chloride (3.18 g) in dry benzene (20 ml) was heated on the boiling water bath for 8 hours. The next morning the clear solution was decanted from unreacted methylurea which is almost insoluble in benzene. Diphenylchloroacetyl chloride (2.00 g) and dry pyridine (4 ml) were added to the solution, and the mixture was heated for 8 hours on the boiling water bath. The solvent was evaporated, and the residue was treated with ether and water to which a small quantity of hydrochloric acid had been added. The solutions remained clear and the ether layer was extracted with dilute sodium hydroxide, then evaporated, yielding a tarry resinous oil (4.27 g) which did not crystallize. The aqueous solution was acidified and the oil that separated (0.72 g) was collected by ether extraction and dissolved in dilute sodium hydroxide. Dilute hydrochloric acid was gradually added to the solution. When an oil began to separate the solution was extracted with ether and in this way 0.05 g of resinous substance was removed. When the solution was neutral to litmus an oil (0.14 g) was obtained by ether extraction. This sample, however, crystallized after it had been treated with benzene, yielding 5,5-diphenyloxazolidione (m.p. 128–130°). The addition of hydrochloric acid was continued and when the solution was acid to litmus but not to congo red another sample of the same substance (0.20 g, m.p. 130–131°) was obtained by ether extraction and treatment with benzene. On further addition of hydrochloric acid only oil precipitated.

Ring closure of *N*-methyl-*N'*-diphenylchloroacetylurea

N-Methyl-*N'*-diphenylchloroacetyl urea (1.00 g) was dissolved in dry benzene (20 ml) and pyridine (0.9 g) was added. The mixture was heated on the boiling water bath for three hours. The benzene was evaporated, and the residue was dissolved in ether and water to which a small quantity of hydrochloric acid had been added. After some time the clear solutions were separated and the organic phase was shaken with dilute sodium hydroxide. After acidifying the alkaline solution, 5,5-diphenyloxazolidione (0.76 g, 91 per cent of the theoretical amount, m.p. 128–130°) separated.

Evaporation of the ether yielded oily material (0.03 g).

SUMMARY

The reaction between diphenylchloroacetyl chloride and methylurea has been studied both in the presence of and in the absence of pyridine. The reaction mechanisms have been discussed.

The author wishes to express his gratitude to Professor Helge Aspelund for kind advice and criticism in connection with this work.

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