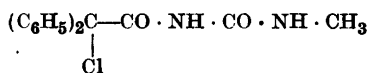


The Reaction between Diphenylchloroacetylmethylurea and Alcohols in the Presence of Alkali

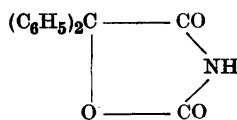
GUST.-AD. HOLMBERG

Institute of Organic Chemistry, Åbo Akademi, Åbo, Finland

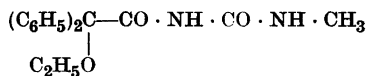
In 1943 Aspelund and Holmberg¹ published results of work concerning the reactions between diphenylchloroacetyl chloride and substituted ureas. They found that when N-diphenylchloroacetyl-N'-methylurea (I) reacted with alkali in approximately 22 per cent aqueous ethyl alcohol, there were formed a small amount of 5,5-diphenyloxazolidinedione-2,4 (II) and a relatively large amount of a chlorine-free substance melting at 106° after purification. This substance was not then examined, but when the experiment was repeated this year it was established that the chlorine-free substance was N-diphenylethoxyacetyl-N'-methylurea (III). This was done by allowing N-diphenylchloroacetyl-N'-methyl-



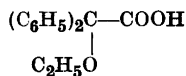
I



II



III



IV

urea and ethyl alcohol to react in a solution containing alkali and only a small amount of water and by treating the product with aqueous alkali. The first operation gave the chlorine-free substance and no 5,5-diphenyloxazolidinedione-2,4 and from the alkaline solution diphenylethoxyacetic acid (IV) was isolated.

In order to prove clearly that the chloro substituted urea had reacted with the solvent, the reaction was performed in *n*-propyl and isopropyl alcohol and the corresponding alkoxy derivatives were isolated. Alkaline degradation of these substances gave diphenyl-*n*-propoxyacetic acid and diphenylisopropoxyacetic acid, respectively.

One of the unusual features of this etherification reaction is that it occurs in 22 per cent ethyl alcohol, and comes to the end within five minutes. Diphenylchloroacetylmethylurea accordingly reacts much faster with alcohol than with water.

EXPERIMENTAL

Action of alkali on *N*-diphenylchloroacetyl-*N'*-methylurea in 22 per cent ethanol

The experiment of Aspelund and Holmberg was repeated and could be verified in detail. The chlorine-free neutral substance (m. p. 106°) proved to be *N*-diphenylethoxyacetyl-*N'*-methylurea.

$C_{18}H_{20}O_3N_2$	Calc.	N	8.97	Found	N	9.10
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One fourth of a gram of this substance was mixed with 20 ml of 1 *N* sodium hydroxide solution, and the mixture was first heated on the water bath for 23 hours and then boiled for four hours. When the clear solution had cooled a slight turbidity appeared, but it was removed by ether extraction. Hydrochloric acid was added to the aqueous solution whereupon 0.15 g of diphenylethoxyacetic acid precipitated. Its identity was established by a combustion analysis and from a mixed melting point determination with a sample of pure diphenylethoxyacetic acid.

$C_{16}H_{16}O_3$	Calc.	C	74.98	H	6.29
		»	75.03	»	6.28

Synthesis of *N*-diphenylethoxyacetyl-*N'*-methylurea in 94.5 per cent ethyl alcohol

Five grams of diphenylchloroacetylmethylurea were dissolved in 50 ml of 96 per cent ethyl alcohol and to this solution 1.85 ml of 50 per cent potassium hydroxide solution were added. Potassium chloride separated almost at once. The mixture was boiled for five minutes and the solvent was then evaporated under reduced pressure. Water, ether, and 0.6 ml of 50 per cent potassium hydroxide solution were added and the mixture was thoroughly shaken. After separation the ether layer was dried with sodium sulfate. When the ether had been evaporated, there remained 4.99 g of an oil which crystallized after some time. The solid substance was treated with water and filtered. After recrystal-

lization it melted at 105–106°. The yield was 3.22 g. The identity of this substance with the chlorine-free substance obtained in the experiment of Aspelund and Holmberg was established by the mixed melting point method.

When the alkaline aqueous layer was acidified with hydrochloric acid no substance separated.

Synthesis of N-diphenyl-n-propoxyacetyl-N'-methylurea

The synthesis was performed in the way described above from 2 g of diphenylchloroacetylmethylurea, 25 ml of n-propyl alcohol, and 0.74 ml of 50 per cent potassium hydroxide solution. Even in this case nothing could be isolated from the alkaline aqueous solution. The ether solution contained 2.13 g of an oil, which was treated with water after it had crystallized. The substance obtained was dissolved in 4 ml of ethyl alcohol and precipitated by adding 3 ml of water. The yield was 1.60 g and the substance, diphenyl-n-propoxymethylurea, melted at 109–110°.

$C_{19}H_{22}O_3N_2$ Calc. N 8.58 Found N 8.46

Eight-tenths of a gram of this substance was mixed with 5 g of potassium hydroxide dissolved in 100 ml of water. After the mixture had been heated for 23 hours on the water bath it was boiled for 6 hours. After cooling a slight precipitate was filtered and hydrochloric acid was added to the filtrate. Diphenyl-n-propoxyacetic acid separated and was filtered when the crystallization was complete. It melted at 114–115° and the yield was 0.45 g.

$C_{17}H_{18}O_3$ Calc. C 75.53 H 6.71
 » 75.64 » 6.97

Synthesis of N-diphenylisopropoxyacetyl-N'-methylurea

This synthesis was performed as described in the preceding synthesis, isopropyl alcohol being used instead of n-propyl alcohol. The crude product did not crystallize when it was treated with water. The oil was therefore dissolved in a small amount of ethyl alcohol. When water was added 1.00 g of diphenylisopropoxyacetylmethylurea, m. p. 100–101°, precipitated.

$C_{19}H_{22}O_3N_2$ Calc. N 8.58 Found N 8.66

Half a gram of this substance was degraded with a solution of 4 g of potassium hydroxide in 80 ml of water for 23 hours. To complete the reaction the mixture was boiled for 6 hours. After acidifying, 0.30 g of diphenylisopropoxyacetic acid, m. p. 143–144°, could be isolated.

$C_{17}H_{18}O_3$ Calc. C 75.53 H 6.71
 Found » 75.30 » 6.85

SUMMARY

The neutral chlorine-free substance that Aspelund and Holmberg obtained when they treated N-diphenylchloroacetyl-N'-methylurea with alkali in 22 per cent aqueous ethanol is N-diphenylethoxyacetyl-N'-methylurea. The corresponding n-propoxy and isopropoxy derivatives have been prepared.

REFERENCES

1. Aspelund, H., and Holmberg, G. A. *Finska Kemistsamfundets Medd.* **52** (1943) 250.

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