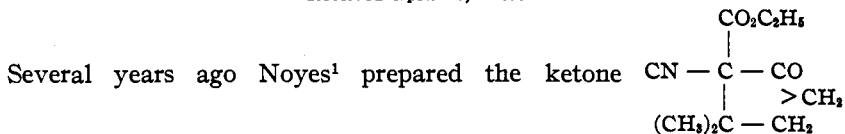


[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS.]

## CYANCARBOXETHYL 3,3-DIMETHYL CYCLOPENTANONE.

By W. A. NOYES AND C. S. MARVEL.

Received April 20, 1917.



and showed by the method of synthesis that it was a derivative of 3,3-dimethyl cyclopentanone. The ketone was prepared by a long series of reactions starting with isoamyl alcohol. The ketone itself was obtained by the condensation of the ethyl ester of  $\gamma$ -chloro-isocaproic acid with ethyl cyanoacetate. The compound formed might have either of two structures depending upon the manner in which alcohol splits out to close the ring. Since the methyl ester of  $\gamma$ -chloro-isocaproic acid condensed with the ethyl cyanoacetate<sup>2</sup> gives the same compound the structure given above was demonstrated. By some mistake it was stated in the paper referred to, that the ethyl ester of  $\gamma$ -chloro-isocaproic acid and methyl cyanoacetate had been used.<sup>3</sup>

This ketone is hydrolyzed<sup>4</sup> by hydrochloric acid to isocaprolactone

$$\begin{array}{c} \text{CH}_3 \\ \diagdown \\ \text{C} - \text{CH}_2\text{CH}_2\text{CO} \\ \diagup \\ \text{CH}_3 \end{array} \quad \text{and malonic acid, the latter decomposing further}$$

to acetic acid and carbon dioxide. While this is closely analogous to the usual acid decomposition of esters of  $\beta$ -ketonic acids it differs from it in that the malonic group separates from the two carbon atoms in the ring instead of one. So far as we know no other strictly similar decomposition has been observed. It has seemed desirable, therefore, to obtain additional evidence in support of the formula assigned to the compound.

We have found that if we convert the ketone into its oxime, the latter may be hydrolyzed without removing a carbon atom from the ring. The carboxethyl group is easily hydrolyzed to a carboxyl group by dilute alkali but the cyanogen group is not attacked even on long heating with that agent. By this hydrolysis the acid  $\text{C}_7\text{H}_{10}(\text{NOH})$  was obtained.

$$\begin{array}{c} \text{CN} \\ \diagdown \\ \text{C}_7\text{H}_{10}(\text{NOH}) \\ \diagup \\ \text{CO}_2\text{H} \end{array}$$

This acid readily loses carbon dioxide when heated to its melting point or when warmed with dilute hydrochloric acid. If the acid is heated

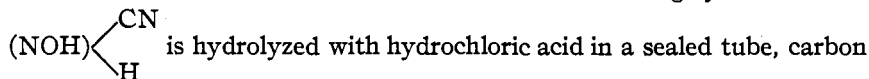
<sup>1</sup> Noyes, *THIS JOURNAL*, 23, 392 (1901).

<sup>2</sup> Noyes, *Ibid.*, 23, 135 (1901).

<sup>3</sup> An examination of the original notes of the experiment has shown that the methyl ester of  $\gamma$ -chloro-isocaproic acid was used.—W. A. N.

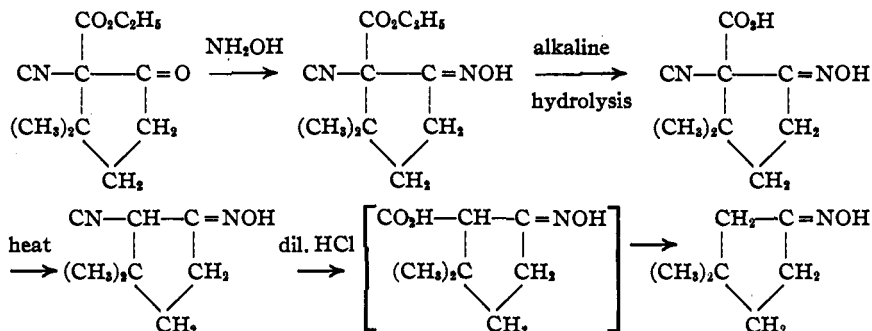
<sup>4</sup> Noyes, *THIS JOURNAL*, 23, 396 (1901).

until all of the carbon dioxide is liberated and the resulting cyanide  $C_7H_{10}$ -



is hydrolyzed with hydrochloric acid in a sealed tube, carbon dioxide and ammonia are formed. This can be explained only by assuming that the cyanogen group is hydrolyzed and the resulting acid loses carbon dioxide.

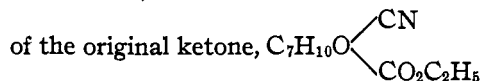
The following compounds are formed in this series of changes:



The end product then should be the oxime of 3,3-dimethyl cyclopentanone. This oxime is described by Blanc<sup>1</sup> as an oil. The ketone is a liquid boiling at  $154^\circ$  and easily yields a crystalline dibenzylidene compound when treated with benzaldehyde in alkaline solution.

The material obtained by hydrolysis with dilute (8-9%) hydrochloric acid was a viscous liquid with a strong penetrating odor. This liquid was further hydrolyzed with 20% hydrochloric acid in a sealed tube at  $100^\circ$  for several hours. The tube was opened and a few cc. were distilled over. The distillate had a strong peppermint-like odor. It seemed to react with benzaldehyde but owing to the very small amount of material no crystalline substance was obtained. The solution remaining in the distilling bulb reduced Fehling's solution, indicating the formation of hydroxylamine by the hydrolysis of the oxime.

The difficulty of obtaining the original ketone is so great that it was decided to discontinue the work. While pure 3,3-dimethylcyclopentanone was not obtained, fairly good evidence has been secured that this compound was formed, and there seems to be no reasonable doubt as to the structure



The isocapro lactone which was used in this synthesis was obtained by a slight modification of the method of Jones and Tattersall,<sup>2</sup> by the action of the Grignard reagent  $(CH_3MgI)$  on ethyl levulinate. This method of

<sup>1</sup> *Bull. soc. chim.*, [4] 3, 783 (1908).

<sup>2</sup> *J. Chem. Soc.*, 85, 1691-99 (1904).

preparing isocapro lactone is more satisfactory than the method previously described.

### Experimental.

**Preparation of Ethyl Levulinate.**<sup>1</sup>—200 g. of levulinic acid were dissolved in 600 g. of alcohol and 14 g. of dry hydrochloric acid gas were passed into the solution. After refluxing on the water bath for 5–6 hours the alcohol was rapidly distilled off. After washing with water the ester was distilled under diminished pressure and the portion boiling at 98–104° at 20–25 mm. pressure was collected. Yield 227 g., 90% of the theory.

**Preparation of isocapro lactone.**<sup>2</sup>—142.1 g. of methyl iodide were dissolved in an equal volume of anhydrous ether, and the solution was carefully dropped into a flask containing 24.32 g. of magnesium ribbon covered with dry ether.

The methyl magnesium iodide prepared as above described was slowly siphoned into a flask containing 144.1 g. of ethyl levulinate and 1250 cc. of dry ether. The reaction is quite vigorous. The addition product formed is insoluble in ether.

After the reaction was complete the material was cooled and decomposed with 100 cc. of 1 : 1 sulfuric acid. The dilute acid was prepared and poured into crushed ice. Then the ethereal solution was poured into this mixture of acid and ice and stirred thoroughly. The acid and ice were then poured into the flask containing the insoluble addition product. The mixture was kept cool until the addition product was entirely decomposed. The isocapro lactone was extracted from the solution with ether. The combined ethereal extracts were washed with a solution of acid sodium sulfite to remove free iodine, and dried with anhydrous sodium sulfate. The ether was distilled off and the residue fractionated. The fraction boiling at 205–210° under atmospheric pressure was saved. Yield 30–35% of the theory.

An attempt was made to prepare the ethyl ester of  $\gamma$ -chloro-isocaproic acid directly from the addition product of methyl magnesium iodide and ethyl levulinate by decomposition with dry hydrochloric acid gas. 28.8 g. of ethyl levulinate yielded about 2 g. of the  $\gamma$ -chloroester. The yield was too poor for practical use.

The methods used to prepare the ethyl ester of  $\gamma$ -chloro-isocaproic acid and to condense it with ethyl cyanoacetate were those previously described by Noyes.<sup>3</sup>

<sup>1</sup> Fischer and Speier, *Ber.*, **28**, 3252 (1895).

<sup>2</sup> Jones and Tattersall, *J. Chem. Soc.*, **85**, 1691 (1904).

<sup>3</sup> Noyes, *Am. Chem. J.*, **23**, 128 (1900).

**Preparation of the Oxime**  $C_7H_{10}(NOH)\begin{matrix} \diagup CN \\ \diagdown CO_2C_2H_5 \end{matrix}$  .—2.09 g. of the ketone  $C_7H_{10}O\begin{matrix} \diagup CN \\ \diagdown CO_2C_2H_5 \end{matrix}$  were dissolved in 60 cc. of absolute alcohol and 1.39 g. of hydroxylamine hydrochloride and 2.4 cc. of sodium hydroxide solution (3 cc. = 1 g.) were added. The solution was refluxed on the water bath for 8 hours and filtered hot from the sodium chloride. If the reaction was complete no ketone separated when the solution cooled. The alcohol was evaporated and the residue recrystallized from water. Yield 1.8 g. melting at 108–110°.

This compound has previously been prepared in this laboratory by C. K. Hewes. He gives the following analysis:<sup>1</sup>

Subst.: 0.1056 g., N 12.05 cc. at 22.7° and 741.5 mm.

Calc. for  $C_{11}H_{16}O_2N_2$ : N = 12.52.

Found: N = 12.65.

**Preparation of the Acid**  $C_7H_{10}(NOH)\begin{matrix} \diagup CN \\ \diagdown CO_2H \end{matrix}$  .—One g. of the oxime was dissolved in 35 cc. of 1% sodium hydroxide solution and the solution was heated 3–4 hours on the water bath. It was then cooled to about 0° and acidified with hydrochloric acid. The new acid separates in fine white needles. Yield about 0.5 g. After recrystallizing from dilute alcohol the acid melts at 142–143° with loss of carbon dioxide. The material was analyzed for nitrogen and the loss of carbon dioxide was determined quantitatively.

Subst.: 0.1054 g., N, 13.4 cc. at 22° and 748 mm.

Subst: 0.1420 g.  $CO_2$  loss 0.0314 g.

Calc. for  $C_7H_{10}(NOH)\begin{matrix} \diagup CN \\ \diagdown CO_2H \end{matrix}$  : N, 14.28;  $CO_2$  loss 22.44.

Found: N, 14.18;  $CO_2$  loss 22.1.

The decomposition by heating the acid in an oil bath is satisfactory if only a small amount (0.15 g.) is used. If larger amounts are heated the material decomposes and no definite products can be isolated. The loss of carbon dioxide seems to be exothermic and if once started the temperature rises to a point where the cyanide which is formed will decompose or polymerize.

**Preparation and Hydrolysis of the Cyanide**  $C_7H_{10}(NOH)\begin{matrix} \diagup CN \\ \diagdown H \end{matrix}$  .—0.1013 g. of the above acid was carefully heated in a small tube until the loss in weight showed the loss of carbon dioxide to be complete. The re-

<sup>1</sup> C. K. Hewes, *Thesis*, University of Illinois, 1914, p. 21.

sulting product was heated on the water bath in a sealed tube with 0.159 *N* sodium hydroxide for 2 hours but no hydrolysis occurred. The tube was opened and it was found that no ammonia had been formed. The solution was acidified with hydrochloric acid and the tube again sealed. After heating on the water bath for 3 hours the tube was cooled and opened. There was considerable pressure in the tube and the escaping gases were passed through lime water. A heavy precipitate of  $\text{CaCO}_3$  showed that carbon dioxide had been formed in the hydrolysis.

During the hydrolysis a dark-colored, oily layer was formed on the surface of the solution. This layer was taken up in ether. The substance contained nitrogen.

The aqueous solution separated from the ether was then rendered alkaline and ammonia determined by aeration. The results showed that ammonia had been formed during the hydrolysis.

Some of the cyanide  $\text{C}_7\text{H}_{10}(\text{NOH})\begin{matrix} \diagup \text{CN} \\ \diagdown \text{H} \end{matrix}$  was obtained fairly pure by heating the acid and recrystallizing the product from water. It melted at  $127\text{--}128^\circ$ . No analysis was made as the material was used for further hydrolysis.

**Acid Hydrolysis of the Acid**  $\text{C}_7\text{H}_{10}(\text{NOH})\begin{matrix} \diagup \text{CN} \\ \diagdown \text{CO}_2\text{H} \end{matrix}$ .— This acid when heated with dilute hydrochloric acid rapidly loses carbon dioxide, then the hydrolysis proceeds as did that of the cyanide. The hydrolysis of the acid was carried out quantitatively and the amount of ammonia formed was determined by aeration.

The  $\text{NH}_3$  from 0.2877 g. of subst. neutralized 15.23 cc. *N*/10 HCl.

The  $\text{NH}_3$  from 0.2968 g. of subst. neutralized 15.31 cc. *N*/10 HCl.

Calc. for hydrolysis of  $\text{C}_7\text{H}_{10}(\text{NOH})\begin{matrix} \diagup \text{CN} \\ \diagdown \text{CO}_2\text{H} \end{matrix}$  : N, 7.14.

Found: N, 7.4, 7.2.

The oily material from the hydrolysis was hydrolyzed in a sealed tube at  $100^\circ$  with 20% HCl for several hours. The contents of this tube were transferred to a small distilling flask and about 2 cc. distilled over. The distillate had a very penetrating peppermint-like odor. Treatment of the distillate with benzaldehyde and sodium hydroxide did not give a crystalline product owing to the small amount of material available. The solution in the distilling flask reduced Fehling's solution indicating the formation of hydroxylamine by hydrolysis of the oxime group.