

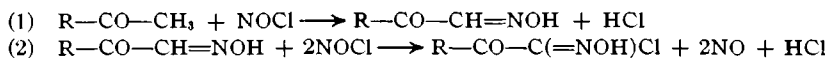
3. Variations in the melting point of acetylsalicylic acid after crystallization from different solvents are caused by differences in the physical structure of the crystals, since grinding to a fine powder gives a uniform melting point.

LABORATORIES,
MONSANTO CHEMICAL WORKS,
ST. LOUIS, MISSOURI.

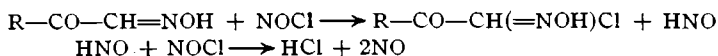
NITROSYL CHLORIDE AND KETONES.

BY E. V. LYNN AND FRANK ANDREW LEE.

Since the review (1) published more than a year ago, covering the chemical action of nitrosyl chloride, our attention was called to a report (2) of Rheinboldt and Schmitz-Dumont which had appeared but a short time before. They found that certain ketones were converted by this gas into chlorinated isonitroso compounds, $R-CO-C(=NOH)Cl$. The exact mechanism of this change is not clear, but it is difficult to interpret it in any other way than simple chlorination. Because the intermediate isonitroso compounds could be isolated in some cases and because they could then be converted by further action under the same conditions, producing two molecules of nitric oxide, the authors express the opinion that the reaction proceeds in two steps:



The second stage could be expressed by production of a hypothetical HNO:



Acetone, methyl propyl ketone, methyl isopropyl ketone, pinacolone, levulinic acid, methyl *p*-tolyl ketone, benzal acetone and anisal acetone gave, in this way, chlorisonitroso derivatives, *p*-chloracetophenone and phenylacetone gave merely the isonitroso compound, while anisalacetone yielded both forms. Acetophenone, under the conditions gave no reaction, but vapors of the reagents reacted to give chlorisonitrosoacetophenone. The nitrosyl chloride compound of stannic chloride carried the reaction only as far as the isonitrosoacetophenone.

Our experiments, started some time ago, have led to results which are somewhat at variance with these and which open up a fertile field of investigation. With acetone undiluted, there is an immediate and quiet reaction in the cold to give isonitrosoacetone and phorone, the latter being subsequently converted into mono, and probably a dinitrosochloride. No trace of a chlorinated product could be separated, nor was there any indication of nitric oxide evolution. If, however, the acetone is previously diluted with carbon tetrachloride, the results of Rheinboldt and Schmitz-Dumont are confirmed. It seems rather remarkable that undiluted acetone should react to give less complete action than does the diluted substance, and we are now engaged in studying this phase. The natural supposition would be to attribute this to the fact that the process requires a longer time when the acetone is first dissolved, but our experience indicates that this is by no means a satisfactory explanation.

Another notable result obtained by the German investigators was evidence of oxidation by nitrosyl chloride. Acetophenone boiled with a solution of the gas gave benzoic acid, although there was no indication of action in the cold. We have been unable to bring about oxidation at any temperature below that of the room, even with such good reducing agents as acetaldehyde, benzyl alcohol and benzaldehyde, and the tendency at higher temperatures seems small. These results we will report shortly in connection with work on aldehydes and alcohols.

EXPERIMENTAL.

The nitrosyl chloride used in these experiments was prepared by adding nitrosyl sulfate to sodium chloride and warming to 60° C. The former was made by the method of Girard and Pabst (3), modified by Dr. Waldo Semon, of this school, as follows:

In a beaker arranged for external cooling and fitted with an efficient mechanical stirrer is mixed 140 cc. of fuming nitric acid (sp. gr. 1.50) and 210 cc. of sulphuric acid (sp. gr. 1.84). There is now added slowly and in small portions, 38 Gm. of freshly dried and sifted flowers of sulphur, the temperature being kept around 40° C. With care neither sulphur dioxide nor nitric oxide will be evolved. The resulting mixture, which usually contains an excess of sulphur may be used directly for the preparation of nitrosyl chloride. If desired it may be stored in glass-stoppered bottles, where it will shortly set to a mass of crystals of nitrosyl sulphuric acid.

Acetone.—The material which was labeled “chemically pure,” was dehydrated by refluxing over anhydrous lime and then carefully fractionated, the fraction boiling at 59° C. being selected for treatment. This was cooled to about -10° C. by means of a freezing mixture and a slow stream of nitrosyl chloride passed into it in such a manner that there was no marked rise in temperature. The gas was all absorbed without changing the color of the acetone until a yellow color marked the completion of reaction and indicated an excess of the chloride. During one or two of the experiments, especially at low temperatures, a green color was observed, and blue spots appeared on upper parts of the vessel, indicating the formation of a true nitroso compound. The yellow color became gradually darker on standing until it was almost black at the end of twenty-four hours. The product had a distinctive odor, resembling hydrocyanic acid, but the source of this has not been traced. After standing for a few days crystals separated in the form of thick, colorless prisms, which were found to have a melting point of 175–176° C.

Isonitrosoacetone.—The reaction of nitrosyl chloride and acetone was allowed to proceed to the formation of a yellow color. The solution was evaporated immediately at a low temperature resulting in needle-like crystals of melting point 61° C. In all other properties this substance behaved as isonitrosoacetone (4), melting point 69° C.

Phorone Nitroschlorides.—The crystals which separated in large quantities from the reacting mixture were found to contain both nitrogen and chlorine. They distilled unchanged and were unaffected by cold sodium hydroxide or by boiling with sulphuric acid, which precluded any oxime character. The oily residue from the reaction of nitrosyl chloride on acetone was fractionally distilled under reduced pressure. That which came over at 52–80° C. (21–100 mm.) deposited crystals on standing, a melting point which showed them to be of the same substance as before.

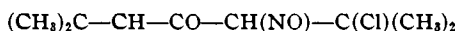
The easiest method of preparation of the crystalline material is as follows:

Add one Gm. molecule of nitrosyl chloride (calculated from the sulphate) to one of acetone, keeping the latter cool. When the reaction is complete, remove the excess of acetone and hydrochloric acid by direct distillation. Subject the residue to vacuum distillation and set the distillate aside in a freezing mixture. Collect the separated crystals and recrystallize from water.

Analysis for chloride showed that these are probably phorone mononitrosochloride; found 17.30, calculated 17.41 per cent.

In order to confirm this, the substance was converted to phorone. A solution of the chloride was subjected to steam distillation with sodium hydroxide. The oily layer of the distillate was extracted with ether and the latter allowed to evaporate spontaneously. The residue was cooled with a freezing mixture and finally solidified. A melting point of 28–29° and complete absence of nitrogen or chloride, together with the method of preparation left no doubt that this is phorone.

To make this entirely certain, however, an ether solution of phorone was treated with nitrosyl chloride at low temperatures. After a few seconds the mixture became milky and the ether was allowed to evaporate. In a short time crystals were deposited, melting point 168°. After recrystallization from water these melted at 174°. Phorone, therefore, forms a mononitrosochloride.



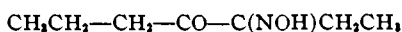
If phorone is treated with an excess of nitrosyl chloride, the primary milky solution clears up and becomes yellow. The same result is obtained if crystals of the mononitrosochloride are treated with the gas. Evaporation of the yellow solution leaves an uncrystallizable yellow oil, which gradually resinifies. The probabilities are that this is the dinitrosochloride.



Methyl Ethyl Ketone.—The material was prepared by fractionation from a stock bottle of pure substance. That boiling at 81° was selected for treatment. Nitrosyl chloride was run in at –5° to –10° C. until a yellow color was apparent, when the excess of ketone was removed by distillation under reduced pressure. On cooling the brown residue, it partially solidified. After recrystallization several times from chloroform, the product was nearly white and exhibited a melting point of 70–74° C., which indicates the compound as isonitroso methyl ethyl ketone:



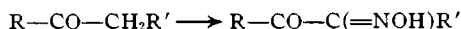
Di-n-Propyl Ketone.—This compound was prepared by distilling dry calcium *n*-butyrate and fractionating the product at 145° C. In carbon tetrachloride solution, nitrosyl chloride had apparently no action on the ketone, since all of the latter was recovered unchanged. When one molecule of the liquid chloride was added to the undiluted ketone, there was a gradual disappearance of the dark red color, an evidence of reaction. The product was distilled in a vacuum up to 150° C. at 80 mm. The oily residue was converted to an oxime by hydroxylamine in the usual way, yielding white crystals with a melting point of 165° C. The product is, therefore, isonitroso di-*n*-propylketone, whose oxime melts at 167° C:



No trace of a chlorine compound could be isolated.

CONCLUSIONS.

It is evident that dialkyl ketones or alkyl aryl ketones generally react readily with chloride to form isonitroso compounds, with substitution in alpha position to the carbonyl group.



Since reaction on paraffin hydrocarbons (5, 6) proceeds but very slowly and only by catalysis from certain wave-lengths of light, we can definitely conclude that presence of a carbonyl group greatly stimulates the reactivity of hydrogen in neighboring position. When R' is hydrogen, it then becomes labile enough, under certain conditions, to become chlorinated by the nitrosyl chloride.



Evidences for oxidizing properties of nitrosyl chloride were found by Rheinboldt and Schmitz-Dumont, but such a reaction seems improbable under anything but unusual conditions.

SUMMARY.

1. Acetone reacts under varying circumstances to give isonitroso acetone, chlorisonitrosoacetone, phorone mononitrosochloride, and probably phorone dinitrosochloride.
2. Methyl ethyl ketone gives the corresponding isonitroso compound.
3. Di-*n*-propylketone gives an isonitroso compound.

BIBLIOGRAPHY.

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- (2) Rheinboldt and Schmitz-Dumont, *Annalen*, 444, 113 (1925).
- (3) Girard and Pabst, *Bull. soc. chim.*, 30, 531 (1879).
- (4) Meyer, *Berichte*, 11, 696 (1878).
- (5) Lynn, *J. Am. Chem. Soc.*, 41, 368 (1919).
- (6) Lynn and Hilton, *Ibid.*, 44, 645 (1922).

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UNIVERSITY OF WASHINGTON,
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March 14, 1927.

SHORTAGE OF PHYSICIANS IN RURAL DISTRICTS DISCUSSED.

One of the outstanding problems considered at the conference of the Council on Medical Education and Hospitals of the American Medical Association, held at Chicago, February 14th to 16th, inclusive, was the shortage of general medical practitioners in rural towns and districts throughout the country which, it is said, has resulted from the mounting cost and higher standards of medical education in the United States.

LEPROSARIUM URGED ON ISLAND OF CULION.

Consideration is being given by the Government to bills in the Senate which provide for a leprosarium on the Island of Culion. The measure authorizes the expenditure of \$4,000,000 for the site and construction of buildings and maintenance. There are said to be nearly 6000 lepers on the Island, representing about one-half the number in the Philippine Islands.