[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

ISOXAZOLINE OXIDES. IX. THE REACTION BETWEEN TRIPHENYL ISOXAZOLINE OXIDE AND ORGANIC MAGNESIUM COMPOUNDS

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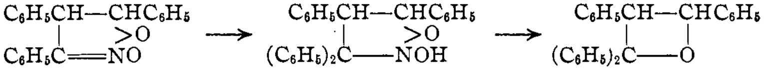
RECEIVED JANUARY 16, 1930 PUBLISHED MAY 8, 1930

Inasmuch as the mode of addition of organic magnesium compounds to cyclic nitrones has been definitely established,[1] it is possible, now, to interpret with more confidence the results of an investigation of the reaction between organic magnesium compounds and isoxazoline oxides that was completed several years ago. The investigation is one of a series that deals with the mode of addition to substances containing the unsaturated system $>C=\overset{|}{N}O$. Triphenyl isoxazoline oxide was one of the compounds selected for study because it contains a highly phenylated ring and therefore might be expected to offer but one point of attack to the reagent. The reaction was tried with methyl, ethyl, benzyl and phenyl magnesium halides, but the outcome was not so favorable as had been anticipated because it was rarely possible to arrest the action at the first stage.

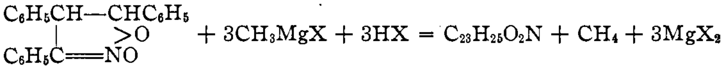
Of all the reagents tried, phenyl magnesium bromide alone gave a product that was formed by the addition of but one molecule of reagent to one of the oxide. The mode of addition appears to be the same as that to the cyclic nitrone, but the product is extremely unstable, decomposing spontaneously both in solution and in solid form. In glacial acetic acid it loses both nitrogen and oxygen and passes into one of the few known derivatives of propylene oxide



$$\begin{array}{l} C_6H_5CH{-}CHC_6H_5 \\ \quad | \qquad\quad >O \\ C_6H_5C{=\!=}NO \end{array} \longrightarrow \begin{array}{l} C_6H_5CH{-}CHC_6H_5 \\ \qquad\ \ | \qquad >O \\ (C_6H_5)_2C{-\!-}NOH \end{array} \longrightarrow \begin{array}{l} C_6H_5CH{-}CHC_6H_5 \\ \qquad\ \ | \qquad\ \ | \\ (C_6H_5)_2C{-\!-}O \end{array}$$

I II III

In the reaction with methyl magnesium iodide gas was evolved in the cold. A quantitative determination showed that one molecule of the oxide reacts with three molecules of the reagent and liberates one molecule of methane. The composition of the product confirms this relation, the reaction being represented by the equation



$$\begin{array}{l} C_6H_5CH{-}CHC_6H_5 \\ \quad | \qquad\quad >O \\ C_6H_5C{=\!=}NO \end{array} + 3CH_3MgX + 3HX = C_{23}H_{25}O_2N + CH_4 + 3MgX_2$$

The product of the reaction is a base. It reacts with methyl magnesium iodide, liberating two molecules of methane and forming a magnesium derivative from which it is regenerated by acids; and when it is acetylated it forms, in succession, a mono- and a diacetyl derivative. It, there-

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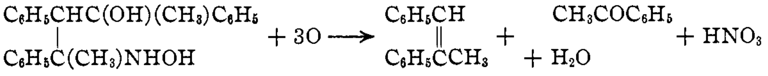
[1] Kohler and Addinall, THIS JOURNAL, **52**, 1590 (1930).

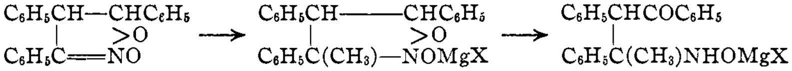
fore, contains two active hydrogen atoms and its two oxygen atoms are presumably present as hydroxyl. In acetone the Grignard product reduces permanganate in the cold, being oxidized to water, nitric acid, acetophenone, and methyl stilbene—all primary oxidation products because permanganate does not oxidize methyl stilbene under these conditions. By combining these facts with the formula of the oxide, we arrive at formula IV for the product, the oxidation proceeding in accordance with the scheme



$$\begin{array}{l} C_6H_5CHC(OH)(CH_3)C_6H_5 \\ \quad | \\ C_6H_5C(CH_3)NHOH \end{array} + 3O \longrightarrow \begin{array}{l} C_6H_5CH \\ \quad \| \\ C_6H_5CCH_3 \end{array} + H_2O + CH_3COC_6H_5 + HNO_3$$

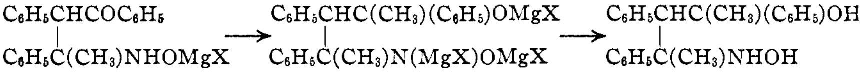
IV

The formation of the hydroxylamine derivative is most easily accounted for by assuming that, in this case also, the reaction begins with addition to the unsaturated system, and that the primary product—an isoxazolidine derivative—immediately undergoes a well-known rearrangement



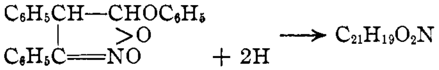
$$\begin{array}{l} C_6H_5CH{-}CHC_6H_5 \\ \quad | \qquad >O \\ C_6H_5C{=\!=}NO \end{array} \longrightarrow \begin{array}{l} C_6H_5CH{-\!-\!-}CHC_6H_5 \\ \quad | \qquad\qquad >O \\ C_6H_5C(CH_3){-}NOMgX \end{array} \longrightarrow \begin{array}{l} C_6H_5CHCOC_6H_5 \\ \quad | \\ C_6H_5C(CH_3)NHOMgX \end{array}$$

The resulting open-chained compound then reacts with two more molecules of the reagent



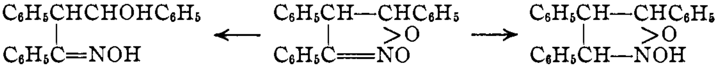
$$\begin{array}{l} C_6H_5CHCOC_6H_5 \\ \quad | \\ C_6H_5C(CH_3)NHOMgX \end{array} \longrightarrow \begin{array}{l} C_6H_5CHC(CH_3)(C_6H_5)OMgX \\ \quad | \\ C_6H_5C(CH_3)N(MgX)OMgX \end{array} \longrightarrow \begin{array}{l} C_6H_5CHC(CH_3)(C_6H_5)OH \\ \quad | \\ C_6H_5C(CH_3)NHOH \end{array}$$

In the case of ethyl magnesium bromide the quantitative picture[2] is far less definite. At the ordinary temperature the reaction consumes 2.8 moles of reagent and liberates 0.6 mole of gas. The gas is not homogeneous, being composed of ethane and ethylene in the proportion of four to one. The formation of ethane implies a reaction similar to that with methyl magnesium iodide, and the formation of ethylene indicates reduction. No substance corresponding to that obtained with methyl magnesium iodide was isolated. A very small quantity of a substance that appears to be an addition product was obtained, but most of the solid material was a reduction product that is formed in accordance with the equation



$$\begin{array}{l} C_6H_5CH{-}CHOC_6H_5 \\ \quad | \qquad >O \\ C_6H_5C{=\!=}NO \end{array} + 2H \longrightarrow C_{21}H_{19}O_2N$$

This same reduction product had been obtained previously[3] by reducing the oxide with zinc and acetic acid, and two formulas for it were considered at the time



$$\begin{array}{l} C_6H_5CHCHOHC_6H_5 \\ \quad | \\ C_6H_5C{=}NOH \end{array} \longleftarrow \begin{array}{l} C_6H_5CH{-}CHC_6H_5 \\ \quad | \qquad >O \\ C_6H_5C{=\!=}NO \end{array} \longrightarrow \begin{array}{l} C_6H_5CH{-}CHC_6H_5 \\ \quad | \qquad >O \\ C_6H_5CH{-}NOH \end{array}$$

V I B

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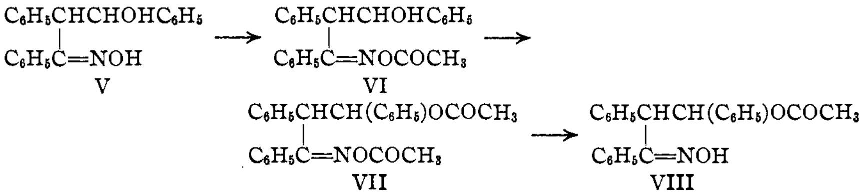
[2] Kohler and Barrett, This Journal, **46,** 2112 (1924).

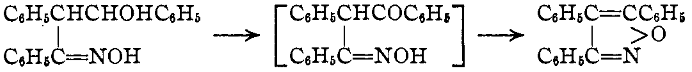
[3] Ref. 2, p. 2110.

The cyclic formula B was preferred to the open-chained formula V largely because the substance is capable of forming a copper derivative. We have now succeeded in getting this copper derivative in a crystalline form, and we have found that it contains one atom of copper to the molecule. It therefore cannot be a derivative of the cyclic form. Moreover, we have found that when the substance is acetylated exhaustively, it forms not only the mono-acetate previously described, but also a di-acetate which on partial hydrolysis passes into a mono-acetate that is isomeric with that obtained by partial acetylation. These facts cannot be reconciled with the cyclic formula. They show that the Grignard product must be the open-chained oxime and that β- as well as α-hydroxy oximes[4] can form copper derivatives when their ethereal solutions are shaken with copper acetate



$$\begin{array}{l} C_6H_5CHCHOHC_6H_5 \\ \quad | \\ C_6H_5C{=}NOH \\ \qquad V \end{array} \longrightarrow \begin{array}{l} C_6H_5CHCHOHC_6H_5 \\ \quad | \\ C_6H_5C{=}NOCOCH_3 \\ \qquad VI \end{array} \longrightarrow \begin{array}{l} C_6H_5CHCH(C_6H_5)OCOCH_3 \\ \quad | \\ C_6H_5C{=}NOCOCH_3 \\ \qquad VII \end{array} \longrightarrow \begin{array}{l} C_6H_5CHCH(C_6H_5)OCOCH_3 \\ \quad | \\ C_6H_5C{=}NOH \\ \qquad VIII \end{array}$$

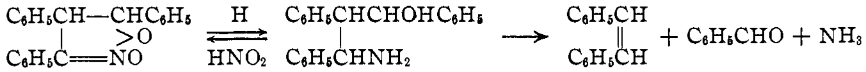
The behavior of the reduction product on oxidation and on further reduction likewise shows that it must be the open-chained oxime. It does not reduce permanganate but it is easily oxidized by chromic acid. The product is triphenyl isoxazole, which, as is known, is readily formed from the monoxime of phenyl dibenzoyl methane[5]



$$\begin{array}{l} C_6H_5CHCHOHC_6H_5 \\ \quad | \\ C_6H_5C{=}NOH \end{array} \longrightarrow \left[\begin{array}{l} C_6H_5CHCOC_6H_5 \\ \quad | \\ C_6H_5C{=}NOH \end{array}\right] \longrightarrow \begin{array}{l} C_6H_5C{=}CC_6H_5 \\ \quad |\quad\ \ >O \\ C_6H_5C{=}N \end{array}$$

IX

On further reduction, which can be accomplished by prolonged heating with zinc and acetic acid, both the Grignard product and the parent isoxazoline oxide are converted into the corresponding amine—a strong base which forms a hydrochloride that is not hydrolyzed by water. Like the oxime, the amine liberates two molecules of methane from methyl magnesium iodide and forms a magnesium derivative from which it is regenerated by acids. When it is heated it decomposes into ammonia, benzaldehyde and stilbene. Its behavior toward nitrous acid is surprising; instead of forming the corresponding di-hydroxyl compound it reverts to the isoxazoline oxide



$$\begin{array}{l} C_6H_5CH{-}CHC_6H_5 \\ \quad |\quad\ \ >O \\ C_6H_5C{=}NO \end{array} \underset{HNO_2}{\overset{H}{\rightleftarrows}} \begin{array}{l} C_6H_5CHCHOHC_6H_5 \\ \quad | \\ C_6H_5CHNH_2 \end{array} \longrightarrow \begin{array}{l} C_6H_5CH \\ \quad \| \\ C_6H_5CH \end{array} + C_6H_5CHO + NH_3$$

X

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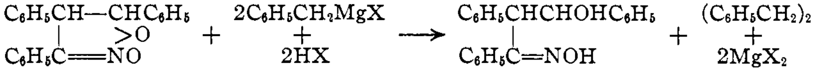
[4] Feigl, Sicher and Singer, *Ber.*, **58**, 2294 (1925).

[5] Marshall, *J. Chem. Soc.*, **107**, 521 (1915).

The reaction between the oxide and benzyl magnesium chloride is relatively free from complications. Reduction predominates and the principal products are dibenzyl and the same open-chained oxime that is formed, in small quantities, in the reaction with ethyl magnesium bromide



$$\begin{array}{l} C_6H_5CH{-}CHC_6H_5 \\ \quad | \qquad >O \\ C_6H_5C{=\!=}NO \end{array} + \begin{array}{c} 2C_6H_5CH_2MgX \\ + \\ 2HX \end{array} \longrightarrow \begin{array}{l} C_6H_5CHCHOHC_6H_5 \\ \quad | \\ C_6H_5C{=}NOH \end{array} + \begin{array}{c} (C_6H_5CH_2)_2 \\ + \\ 2MgX_2 \end{array}$$

Experimental Part

Preparation of Triphenyl Isoxazoline Oxide, I.—Since the oxide prepared according to previous directions[6] often contained triphenyl isoxazole, from which it could not be completely freed by crystallization, it was found necessary to modify the procedure so that no isoxazole would be formed. The operations are as follows: to 9 g. of nitro stilbene and 6 g. of phenyl nitromethane in 100 cc. of gently boiling dry methyl alcohol is added a solution of 0.9 g. of sodium in 50 cc. of dry methyl alcohol in the course of three minutes; the solution is allowed to boil for one minute more, then cooled for two minutes by shaking it in a freezing mixture; the mixture of oxide and nitrite is filtered by suction, washed three times with water, then three times with 15-cc. portions of methyl alcohol. The yield is 8.5 g. of oxide melting at 156–159°. Once recrystallized from acetone it melts at 160–162°.

Reaction with Phenylmagnesium Bromide

A Grignard reagent made from 7.5 g. of magnesium and 52 g. of bromobenzene in ether is chilled in ice; to it is added 15.7 g. of solid oxide in the course of two minutes. The mixture is stirred for fifteen minutes, then removed from the ice-bath and stirred for fifteen minutes more. Prolonged stirring is disadvantageous and may result in failure to isolate any solid product.

Decomposition of the reaction mixture is effected by pouring it on ice; crystals appear in the ether layer when the sides are rubbed with a glass rod. A 1:1 mixture of ice and concentrated hydrochloric acid is added to dissolve the basic magnesium salts and then petroleum ether to decrease the solubility of the crystalline product. The mixture is kept cold and stirred for fifteen minutes before filtering. The solid is washed on the filter with water, a little ether, and then thoroughly with petroleum ether.

The Grignard product crystallizes in small colorless needles melting at about 105°, with decomposition. The low melting point implies solvent of crystallization and the analytical results indicate that the crystal solvent is benzene, but since the substance cannot be recrystallized, the significance of the result is doubtful. The substance cannot be benzoylated by the Schotten–Baumann method and an attempt to benzoylate it in pyridine gave but a very small quantity of solid.

2,2,3,4-Tetraphenyl Trimethylene Oxide, III.—When the Grignard product is shaken for an hour with enough glacial acid to cover it, it disappears and the solution gradually deposits the oxide. After washing with ether, the oxide was recrystallized from acetone and methyl alcohol. It separated in diamond-shaped plates melting at 162°.

Anal. Calcd. for $C_{27}H_{22}O$: C, 89.5; H, 6.1; mol. wt., 362. Found: C, 89.1; H, 6.0; mol. wt., 340.

Structure and Cleavage.—The structural formula assigned to the oxide is based upon its behavior toward methyl magnesium iodide and upon its cleavage. When it was treated with methyl magnesium iodide in an apparatus with which it is possible to determine both the amount of reagent consumed and the volume of the gas evolved,

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[6] Ref. 2, p. 2109.

it was found that it consumed one mole of reagent and evolved only a negligible volume of gas. The oxide underwent no change when heated to 220° in a vacuum but it was readily cleaved in the following manner.

A solution of one g. of the oxide in 40 cc. of absolute methyl alcohol containing 5 drops of acetyl chloride was heated on a steam-bath for twenty-five minutes. The alcohol was evaporated nearly to dryness, cooled and inoculated; it deposited 0.56 g. of very pure triphenyl ethylene. The filtrate from the unsaturated hydrocarbon was diluted with water and then shaken with ether. From the ethereal solution sodium bisulfite extracted benzaldehyde, which was liberated with sodium carbonate and turned into its phenyl hydrazone for comparison with a known sample.

Dibenzophenone Peroxide, $(C_6H_5)_2CO_2O_2C(C_6H_5)_2$.—Before triphenyl ethylene was available for comparison, a sample of the cleavage product was ozonized in the following manner. A current of ozonized oxygen containing about 5% of ozone was passed through a solution of 4 g. of the hydrocarbon in 30 cc. of dry chloroform. At first, feathery needles appeared on the surface of the vessel; this was, doubtless, the ozonide because it became pasty when rubbed on a drying plate. Later, sharply defined crystals appeared in the liquid. These were separated by evaporating the solvent under diminished pressure, diluting the viscous residue with a little ether and filtering. The crude peroxide was recrystallized from ether.

Anal. Calcd. for $C_{26}H_{20}O_4$: C, 78.8; H, 5.0; mol. wt., 396. Found: C, 78.6; H, 5.1; mol. wt. (in freezing naphthalene), 350.

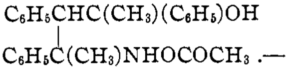
The peroxide dissolves slowly in most organic solvents. It crystallizes from ether in flattened prisms and melts between 200–220°, depending upon the rate at which the temperature is raised. When it is heated with phosphorus pentachloride it liberates chlorine and when it is heated by itself it passes quantitatively into benzophenone and free oxygen.[7]

Reaction between the Oxide and Methyl Magnesium Iodide

The reaction between the oxide and methyl magnesium iodide, when carried out in the "machine"[8] was found to consume 2.92 moles of reagent and liberate 1.11 moles of gas. The evolved gas was collected and analyzed; it was pure methane. For the purpose of isolating the product the oxide was added to a large excess (6 moles) of methyl magnesium iodide at the ordinary temperature. The mixture was left to itself overnight, then decomposed with ice and cautiously treated with acid. At times this treatment left a sparingly soluble iodide, which separated in colorless needles melting at about 100°, and from which the product was liberated with sodium carbonate. Generally the product remained in solution, from which it was isolated by evaporation.

α,γ-Dimethyl-α,β,γ-triphenyl-γ-hydroxy Propylhydroxylamine, IV.—The hydroxyamine was purified by recrystallization from ether–petroleum ether or from dilute alcohol from which it separated in stout needles melting at 180–195°, depending upon the rate of heating.

Anal. Calcd. for $C_{23}H_{25}O_2N$: C, 79.5; H, 7.2. Found: C, 79.1; H, 7.3.



$$\begin{array}{l} C_6H_5\underset{|}{C}HC(CH_3)(C_6H_5)OH \\ C_6H_5C(CH_3)NHOCOCH_3 \end{array}$$

The Monoacetate, $C_6H_5C(CH_3)NHOCOCH_3$.—The oxime dissolves in cold acetic

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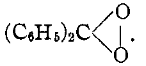
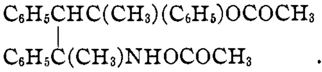
[7] By the action of ozone on a tetraphenyl butene, Lebedev, Andreevski, and Matiushkina [*Ber.*, **56**, 2349 (1923)] obtained a benzophenone peroxide which began to melt at 170° and which they represent as the monomolecular peroxide .

[8] Kohler, Stone and Fuson, THIS JOURNAL, **49**, 3181 (1927).

anhydride to form the monoacetate, which was isolated by decomposing the excess of reagent with water and extracting with ether. The substance crystallizes from a mixture of ether and petroleum ether in small prisms; it melts to a colorless liquid which turns yellow and then red between 135–155°.

Anal. Calcd. for $C_{25}H_{27}O_3N$: C, 77.1; H, 6.9. Found: C, 77.7; H, 7.1.



The Diacetate, $\begin{array}{l} C_6H_5CHC(CH_3)(C_6H_5)OCOCH_3 \\ \qquad | \\ C_6H_5C(CH_3)NHOCOCH_3 \end{array}$.—The diacetate was obtained by warming a solution of the oxime in acetic anhydride for an hour on the steam-bath and then allowing it to evaporate slowly over solid potassium hydroxide in a vacuum desiccator. It was purified by recrystallization from a mixture of ether and petroleum ether; it separated in small needles that melt with decomposition at about 172°. In the machine it liberated only a negligible volume of gas.

Anal. Calcd. for $C_{27}H_{29}O_4N$: C, 75.2; H, 6.7. Found: C, 75.0; H, 6.8.

Oxidation.—The hydroxylamine derivative instantly decolorizes a cold solution of permanganate in acetone. A solution of 3.6 g. of the compound (1 mole) reduced 3.2 g. of permanganate instead of 3.4 g. (2 moles) calculated. The manganese was removed by filtration and the filtrate evaporated to small volume; it deposited potassium nitrate. The acetone solution was then diluted with water and extracted with ether. The ethereal solution on evaporation left an oil. This oily residue was distilled with steam. The first 500 cc. of distillate contained acetophenone, which was recognized by its odor and completely identified by condensing it with meta nitro benzaldehyde.

The remainder of the steam distillate yielded a light-colored oil that solidified when rubbed. This was identified as methyl stilbene by comparison with a sample made by Ley's modification[9] of the method devised by Klages.[10] Methyl stilbene did not reduce permanganate in acetone at the ordinary temperature.

Reaction with Benzyl Magnesium Chloride

To a chilled Grignard reagent made from 7.2 g. of magnesium and 42 g. of benzyl chloride was added 18.9 g. of the oxide. The mixture was left to itself overnight, then decomposed with ice and hydrochloric acid. The ethereal solution yielded 12.3 g. of solid product (V) and the residue that was left after the solid had been removed, on distillation gave 9.7 g. of dibenzyl. The solid crystallized from ether in needles melting between 180–200°, depending on the rate of heating. A comparison of the substance itself and of its monobenzoate with *two* substances described by Kohler and Barrett[3] proved their identity. In the machine one mole of the substance liberated 2.06 moles of methane and formed a magnesium derivative from which it was regenerated by acids. It therefore cannot have the formula previously ascribed to it.

The Copper Derivative.—An ethereal solution of the hydroxy oxime when shaken with aqueous copper acetate precipitates a very finely divided copper derivative that coagulates as the ether evaporates during persistent filtration under suction. Thus obtained, the copper compound is a dull greenish-brown powder that can be purified by extraction with alcohol and with boiling ether. Upon treatment with 1:1 hydrochloric acid it regenerates the hydroxy oxime.

Anal. Calcd. for $C_{21}H_{17}O_2NCu$: C, 66.6; H, 4.5; Cu, 16.8. Found: C, 65.9; H, 4.8; Cu, 16.5.

The Mono-acetate, VI.—The monoacetate was made by Kohler and Barrett and described as the acetate of the hydroxy isoxazolidine B. It crystallizes with water and melts with decomposition at 100–110°.

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[9] Ley, *Ber.*, **50**, 249 (1917).

[10] Klages, *ibid.*, **35**, 2648 (1902).

The Di-acetate, VII.—The di-acetate was obtained by heating the hydroxy oxime with acetic anhydride on a steam-bath for thirty minutes and then allowing the excess of anhydride to evaporate slowly over solid potassium hydroxide in a vacuum desiccator. The thick oil that remained crystallized readily when moistened with methyl alcohol. The solid crystallized from a mixture of ether and petroleum ether in clusters of large needles melting at 131–132°.

Anal. Calcd. for $C_{25}H_{23}O_4N$: C, 74.8; H, 5.7. Found: C, 74.8; H, 5.8.

The Isomeric Mono-acetate, VIII.—A second mono-acetate was obtained by shaking an ethereal solution of the di-acetate for twenty hours with a concentrated solution of ammonia. The ethereal layer deposited small prisms which after recrystallization from a mixture of ether and petroleum ether melted, with decomposition, at 170–176°.

Anal. Calcd. for $C_{23}H_{21}O_3N$: C, 76.9; H, 5.8. Found: C, 76.9; H, 5.9.

Oxidation with Chromic Acid.—A solution of the hydroxy oxime in glacial acetic acid was warmed for five minutes on a steam-bath with an excess of chromic acid. The solution was poured into a large volume of water, and the suspension extracted with ether. The ethereal solution was freed from acetic acid, dried and evaporated. It deposited fine needles of the triphenyl isoxazole (IX)—identified by comparison with a sample on hand.

A small quantity of the oxime of phenyl dibenzoyl methane,[5] which is, doubtless, the intermediate in this reaction, was dissolved in hot glacial acetic acid. The solution began to deposit the isoxazole derivative within thirty seconds.

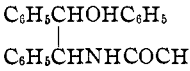
Reduction of Hydroxy Oxime. α-Hydroxy- γ-amino-α,β,γ-triphenyl Propane, X.—Two g. of zinc dust was added to a solution of the hydroxy oxime in glacial acetic acid diluted with 10% of water. The suspension was warmed on a steam-bath for an hour, then greatly diluted with water and extracted with ether, which removed a small quantity of unchanged oxime. The acid solution, upon neutralization with ammonia, precipitated a white solid which was extracted with ether. The ethereal solution, dried and concentrated, deposited the amine in a yield of 70%.

The same amine was obtained directly from triphenyl isoxazoline oxide by boiling the oxide for six hours with zinc and acetic acid. The yield was 30%.

The amine crystallizes from a mixture of ether and petroleum ether in two forms: long glistening needles melting at 123°, and shorter, stouter prisms melting at 128–129°. The melting point of a mixture of the two forms shows no depression, and if the lower melting amine is kept at 120° for ten minutes its melting point becomes 128–129°. Either the needles or the prisms can be obtained at will from an ether–petroleum ether solution by inoculation with the desired form.

Anal. Calcd. for $C_{21}H_{21}ON$: C, 83.2; H, 6.9. Found: (123°) C, 83.2; H, 7.1; (128°) C, 82.6; H, 7.0.

The Hydrochloride.—A benzene solution of the amine was saturated with dry hydrogen chloride and set aside overnight. Since no solid separated from the solution, it was evaporated. The residue was an oil which solidified when ether was added. The solid melted at 232°, dissolved in water without undergoing hydrolysis and regenerated the amine when it was treated with ammonia.

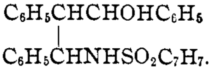


$$\begin{array}{l} \quad\;\; C_6H_5CHOHC_6H_5 \\ \qquad\quad | \\ C_6H_5CHNHCOCH_3 \end{array}$$

The Acetyl Derivative, $C_6H_5CHNHCOCH_3$.—Both forms of the amines are readily acetylated by cold acetic anhydride and they give the same mono-acetyl derivative. This mono-acetyl derivative was also obtained when a solution of the amine in acetic anhydride was warmed for half an hour on a steam-bath, and then allowed to evaporate slowly over potassium hydroxide in a vacuum desiccator. From a mixture of ether and petroleum ether the acetyl derivative crystallized in flattened needles which apparently contain ether of crystallization, because when they are heated rapidly in a capillary tube (plunge method) immediately after crystallization they melt with decomposition at about 135°, while they melt at 142° when heated slowly. After drying overnight at 105°, the melting point is 142° regardless of the rate of heating.

Anal. Calcd. for $C_{23}H_{23}O_2N$: C, 80.0; H, 6.7. Found: C, 79.6; H, 6.8.

In the machine the acetyl derivative consumed 1.9 moles of reagent and liberated 1.9 moles of gas, and it was regenerated when the resulting magnesium compound was treated with acid. It was slowly hydrolyzed to the amine and acetic acid when it was boiled with hydrochloric acid; but it was recovered unchanged after treatment with sodium nitrite in glacial acetic acid. It is, therefore, not the isomeric amino acetate which would be obtained by replacing the hydrogen of the hydroxyl group with an acetyl group.



The *p*-Toluene Sulfonamide, $\begin{array}{l}C_6H_5CHCHOHC_6H_5\\ \quad\;\;|\\ C_6H_5CHNHSO_2C_7H_7\end{array}$.—A solution of 0.5 g. of the amine and 4 g. of *p*-toluene sulfone chloride in 10 g. of pyridine was heated for ten minutes, then poured on ice. The resulting suspension was extracted with ether, freed from pyridine, dried and evaporated. It left 0.55 g. of the sulfonamide which, by recrystallization from ether–petroleum ether, was obtained in small prisms melting at 146–148°. It is insoluble in aqueous alkalies and it is precipitated from its solution in methyl alcoholic potash by addition of water.

Anal. Calcd. for $C_{28}H_{27}O_3NS$: C, 73.5; H, 5.9. Found: C, 73.4; H, 6.2.

Action of Nitrous Acid on the Amine.—To a solution of 1 g. of the amine in glacial acetic acid was added 0.7 g. of solid sodium nitrite. When the formation of gas bubbles had ceased, the solution was poured into water and extracted with ether. The ethereal solution was freed from acetic acid, dried over calcium chloride and evaporated. Addition of petroleum ether to the concentrated solution resulted in the separation of 0.4 g. of triphenyl isoxazoline oxide melting at 155–157°. After one recrystallization from dilute acetone, it melted at 159–161°, and the addition of pure oxide produced no depression in the melting point. A small portion was converted into triphenyl isoxazole to complete the identification.

Thermal Decomposition.—The amine was heated in a small distilling flask until the temperature of the metal-bath reached 330°. Ammonia and benzaldehyde were recognized by their odors and the residue in the flask—which solidified on cooling—was identified as stilbene by comparison with a sample on hand.

Reaction between the Oxide and Ethyl Magnesium Bromide

The reaction with ethyl magnesium bromide has been briefly described by Kohler and Barrett,[2] who obtained a moderate yield of the same reduction product that is formed in the reaction with benzyl magnesium chloride. Since the mechanism by which the oxide is reduced must be very different in the two cases, we have repeated the experiments mainly for the purpose of determining the quantitative relationships. To this end we prepared a solution of ethyl magnesium bromide in iso-amyl ether and with this solution determined the amount of reagent consumed, the volume of the gas evolved and the composition of the gas. We found that 2.8 moles of reagent disappears and that 0.6 mole of gas was liberated. By a suitable contrivance a quantity of the gas was collected over mercury and analyzed. It contained only ethane and ethylene and these were present in the ratio of four to one.

We also repeated the experiment with a reagent made in ethyl ether, but added the oxide to the chilled reagent and decomposed the product an hour later. Under these conditions the amount of reduction produced was much less than that reported by

Kohler and Barrett and in addition to the reduction produced we isolated a small quantity of another solid product. By recrystallization from 50% methyl alcohol this new product was obtained in colorless plates melting at 126°.

Anal. Calcd. for $C_{23}H_{23}O_2N$: C, 80.0; H, 6.7. Found: C, 80.0; H, 6.6.

The composition indicates the addition of C_2H_6 to the oxide, but the substance was obtained in an amount too small for further investigation.

Summary

There are two types of reaction between isoxazoline oxides and organic magnesium compounds.

In one type of reaction the organic magnesium combines at the ends of the unsaturated system C=NO. The extremely unstable products of this system usually undergo rearrangement to open-chained compounds which react with two more molecules of the reagent.

In another type of reaction the magnesium compounds act as reducing agents. The product of this reaction is an open-chained hydroxy oxime formed by adding two atoms of hydrogen to the oxide.

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STUDIES IN THE DIPHENYL SERIES. II. SOME ANTIMONY DERIVATIVES OF DIPHENYL

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Received January 16, 1930 Published May 8, 1930

The physiological activity of certain organo-metallic compounds has revived interest and attention to this great class of compounds in the past two or three decades. This has been particularly true of arsenic and in a previous communication[1] some arsenic derivatives of diphenyl were described. While the antimonials have not been as thoroughly studied, it has been found that in certain diseases of protozoan origin they are even more efficacious than arsenicals, a fact that naturally has stimulated work in this field. No work, however, has been done previously in the diphenyl series; therefore some of the more accessible antimonials containing diphenyl have been prepared in this Laboratory and their properties studied.

Tri-biphenylstibine was obtained, using the method of Michaelis and Reese,[2] by the action of an excess of sodium on 4-chlorodiphenyl and antimony chloride dissolved in benzene. The yield was excellent. As in similar condensations with arsenic chloride, diphenyl was formed as a by-prod-

$$3C_6H_5C_6H_4Cl + SbCl_3 + 6Na = (C_6H_5C_6H_4)_3Sb + 6NaCl$$

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[1] Worrall, This Journal, 52, 664 (1930).

[2] Michaelis and Reese, *Ber.*, 15, 2877 (1882).