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REACTION OF THE SODIUM SALT OF 2-HYDROXYIMINOCYCLOHEXANONE WITH HYDROXYLAMMONIUM CHLORIDE

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INTRODUCTION

There has been a number of methods used in the past for the preparation of the alicyclic *vic*-dioximes for use as analytical reagents. Two methods that give fair yields are the selenium dioxide method of Rauh (4) and the isonitrosocyclohexanone method of Banks (4). The first method consists of oxidizing the monoketone to the *vic*-diketone with selenium dioxide and then oximating with hydroxylammonium chloride to form the corresponding *vic*-dioxime. The over-all yield of *vic*-dioxime from this procedure is about 28% with cyclohexanone, but the method suffers from the expense and the difficulty in procuring selenium dioxide and the toxicity of the selenium dioxide.

The method used by Banks (4) consists of condensing cyclohexanone with 2-ethylhexyl nitrite in the presence of sodium ethoxide and then oximating the sodium salt of 2-hydroxyiminocyclohexanone obtained from this reaction with hydroxylammonium chloride in methanol. This method also has an over-all yield of about 28%, but this could be increased considerably merely by increasing the oximation yield. This paper will deal with the possibility of increasing the yield in this last step.

The yield in the condensation step was increased 5% by using a special rubber diaphragm over a Büchner funnel to aid in keeping the sodium salt from absorbing atmospheric moisture while being filtered. Banks (4) has tried a number of different oximation conditions but found that only the methanol solution of the sodium salt with no buffering agent present would yield any 1,2-cyclohexanedionedioxime when reacted with hydroxylammonium chloride. A series of oximations were carried out, varying the moles of hydroxylammonium chloride, the time of refluxing the reaction mixture, the solvent, and the buffering agents. Only one of these conditions gave a crystalline solid. All the others gave uncrystallizable brown viscous oils which gave an orange-red colored precipitate with nickel (II) chloride. The oximation that was carried out in an aqueous solution with a 3:1 mole ratio of hydroxylammonium chloride to sodium salt and that contained an excess of calcium carbonate and was then refluxed for 48 hours, yielded fine crystalline needles after standing a few days. These crystals after recrystallizing from water with Norit several times melted at 173–174° and gave no precipitate with nickel (II) chloride. This compound is quite obviously not the desired end product, 1,2-cyclohexanedionedioxime, but the nature of this oximation product might throw some light on the side reactions that are taking place that would

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tend to decrease the yield of the *vic*-dioxime. For these reasons the nature of the oximation product was investigated.

DISCUSSION

A qualitative elemental analysis showed the presence of carbon and nitrogen. It was assumed that both hydrogen and oxygen were also present. The quantitative elemental analysis indicated that the empirical formula was $C_4H_7N_2O$. The conditions of the reactions should not have been vigorous enough to break the alicyclic ring so that the true formula would be some multiple of the empirical formula such as three-halves or three, yielding $C_6H_{10.5}N_3O_{1.5}$ and $C_{12}H_{21}N_6O_3$, respectively.

A solubilities analysis put the oximation product in the acidic compound group which includes oximes, phenols, and imides. Functional group analyses were made on the oximation product to determine the presence or absence of groups which might be expected from a consideration of the reaction mixture from a mechanistic standpoint and the solubility class of the compound. A nonaqueous titration indicated the absence of amino or imino groups. Another nonaqueous titration using potassium methoxide in benzene as the titrant indicated the presence of weakly acidic hydrogens such as those in 1,2-cyclohexanedionedioxime. The equivalent weight found from this titration was 146. A consideration of the ultraviolet absorption spectra (Table I and Figure 1) precludes the presence of more than one replaceable hydrogen since the absorption peak at 297 mμ did not shift with increasing *p*H as was observed by Banks and Carlson (1) to be the case with several dibasic *vic*-dioximes. The *p*K′ for the oximation product was found to be 8.78 as compared to 10.3 for the pK_1' of 1,2-cyclohexanedionedioxime.

TABLE I

EFFECT OF *p*H ON THE ABSORPTION SPECTRA OF THE OXIMATION PRODUCT

SOLUTION No.	*p*H	A_s^{257}	A_s^{297}
1	7.25	0.45	0.035
2	8.72	.325	.30
3	12.40	.15	.64
4	12.62	.145	.645
5	12.88	.140	.655
6	13.06	.140	.655

An infrared spectrum was run on the oximation product and it showed many similarities to the spectrum of other alicyclic *vic*-dioximes (Figures 2 and 3). The main differences were exhibited in the 3.0 μ, 6.6 μ, and 11.0 μ band regions. This might indicate a different type of nitrogen-nitrogen bond that does not occur in other *vic*-dioximes. From these similarities it would seem that the alicyclic ring structure and possibly the $>C=N-$ chromophore were still present. The $>C=N-$ chromophore is also indicated by the ultraviolet absorption spectra.

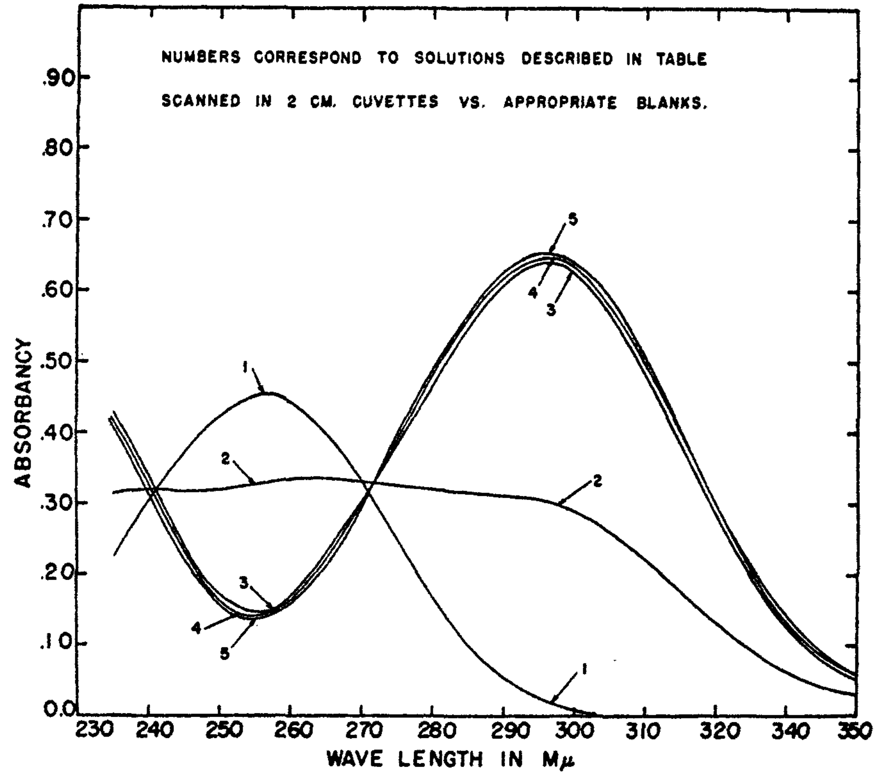


FIG. I. ABSORPTION CURVES ILLUSTRATING EFFECT OF VARYING pH OF 1.962 x 10^{-4} gm/ml SOLUTION OF OXIMATION PRODUCT AT IONIC STRENGTH OF 0.5.

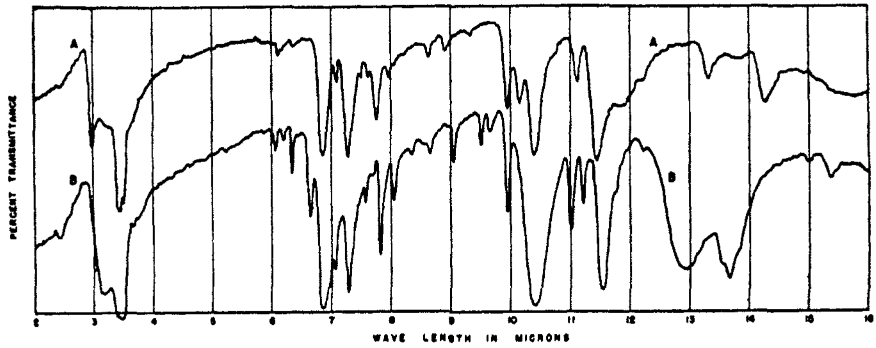


FIG. 2. A - NIOXIME IN NUJOL MULL. B - OXIMATION PRODUCT IN NUJOL MULL.

The absence of a peak around 5.8–5.9 μ eliminates the possibility of a keto group being present, while the peak at 6.1 μ indicates the presence of water in the molecule. It is interesting to note that the formula $C_6H_{10.5}N_3O_{1.5}$ corresponds very closely to $C_6H_9N_3O \cdot \frac{1}{2}H_2O$. Although the amount of water indicated in the

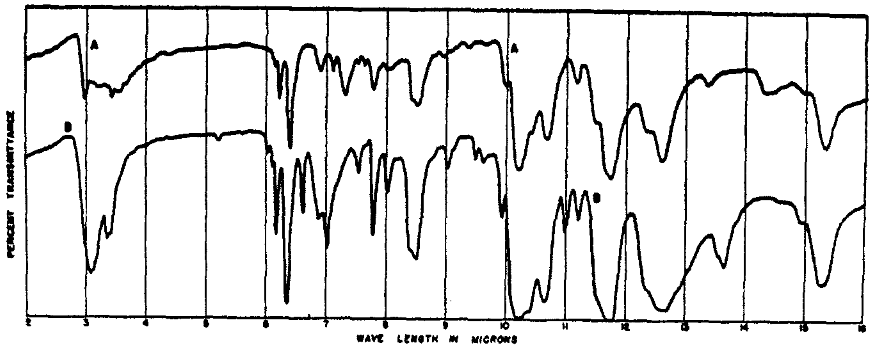


FIG. 3. A-NIOXIME IN HEXACHLOROBUTADIENE MULL B-OXIMATION PRODUCT IN HEXACHLOROBUTADIENE MULL.

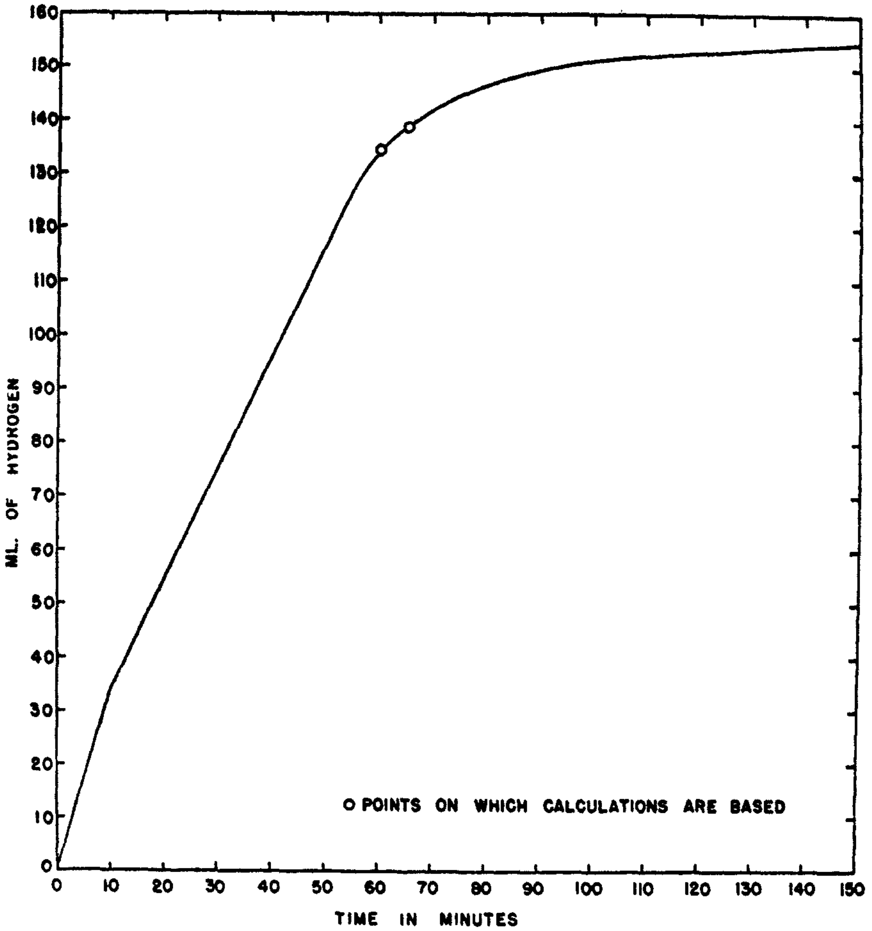
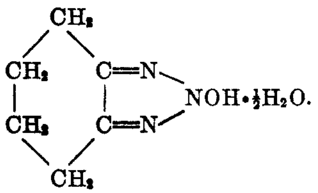


FIG. 4. HYDROGENATION CURVE OF OXIMATION PRODUCT

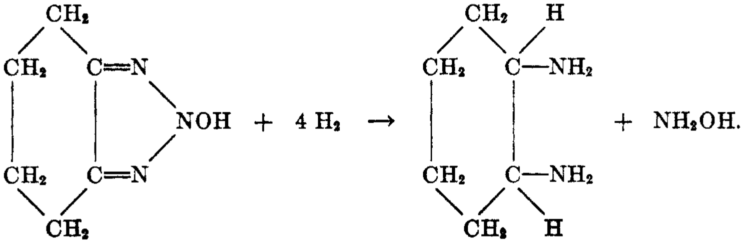
formula, $C_6H_9N_3O \cdot \frac{1}{2}H_2O$, would be about 6.6%, the actual amount found (0.7% to 2%) would seem to indicate that at least some water was present in the oximation product.

The molecular weight found, using absolute ethanol as the solvent, was 152 for the oximation product that had been recrystallized from water. This is in good agreement with the equivalent weight as determined by non-aqueous titration. On recrystallizing the compound from benzene the melting point was raised to 179–180°, and the molecular weight was found to be 136. These crystals upon being exposed to the air for a short time again melted at 173–174°.

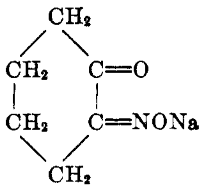
From the X-ray analysis the unit cell size was found to be eight, which would allow the presence of a water of hydration. The molecular weight of 151, calculated from X-ray data, is in excellent agreement with the ebullioscopic value. A structural formula that seems to be consistent with all of these data is as follows:



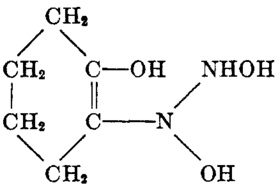
The name proposed for this compound was devised in the fashion of the Baeyer system used by Chemical Abstracts. It may be named 2,3,4-triazabicyclo[3.4.0]-3-hydroxy-1,4-nonadiene hemihydrate. The destructive hydrogenation (Figure 4) would appear to be good confirmatory proof of this structure since four moles of hydrogen were absorbed per mole of the oximation product, and the proposed structure would also require four moles of hydrogen if destructively hydrogenated as follows:



The following base-catalyzed mechanism is proposed to add credence to the structural formula suggested above. If a hydroxylamine molecule, a nucleophilic reagent because of the unshared pair of electrons, attacked the sodium salt of 2-hydroxyiminocyclohexanone (I), the compound II would be formed.

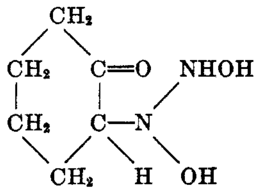


I

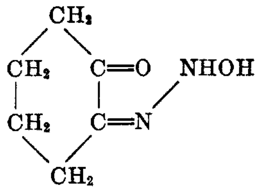


II

The compound II rearranges to yield the keto form (III), and then a molecule of water is lost forming IV.

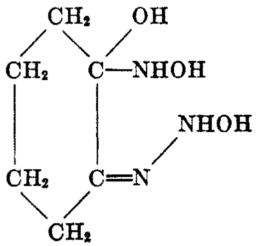


III

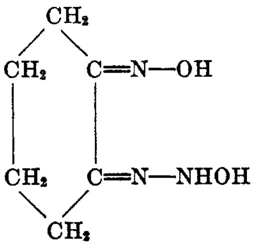


IV

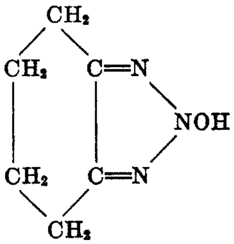
At this point IV undergoes a keto-enol tautomerization and becomes the point of attack for the nucleophilic agent, hydroxylamine, to form V. The compound V, formed in this manner rearranges to form VI, and then simply dehydrates to form VII, the proposed oximation product.



V



VI



VII

Some support is lent to this mechanism being driven by the keto group in the manner shown by the fact that this compound could not be prepared, under the same conditions, using two moles of hydroxylammonium chloride to one mole of 1,2-cyclohexanedionedioxime. This would seem to indicate that the keto group may be responsible for the formation of the compound herein proposed.

EXPERIMENTAL WORK

Synthesis of 2-ethylhexyl nitrite. 2-Ethylhexanol was converted to the nitrite by the method of Forman, Carr, and Krantz (2); yield 93%; b.p. 63–64°/19 mm.

Condensation of cyclohexanone with 2-ethylhexyl nitrite. The procedure of Rauh, Smith, Banks, and Diehl (4) was used; yield 87% based on cyclohexanone used.

Oximation of the sodium salt of 2-hydroxyiminocyclohexanone. Dissolve 200 g. (1.34 moles) of the sodium salt of 2-hydroxyiminocyclohexanone in 2500 ml. of water. Dissolve 280 g. (4.03 moles) of hydroxylammonium chloride in 1000 ml. of water and mix with the first solution in a five-liter beaker. Add 60 g. (0.6 mole) of calcium carbonate, mix thoroughly, pour into a five-liter Erlenmeyer flask and reflux for 48 hours at a gentle rate. A black oil forms as the refluxing progresses. After three days crystals form under the oil. These crystals are filtered off and recrystallized from water and Norit. The melting point of the pure oximation product is 173–174°. The yield is 50.2 g.

Quantitative elemental analysis. The following elemental analyses were performed using micro-technique. Found: C, 48.1; H, 7.0; N, 28.1; O (by difference), 16.8.

Solubility classification. A series of solubilities tests were run on the oximation product and 1,2-cyclohexanedionedioxime. The oximation product was insoluble in water and hydrochloric acid and soluble in diethyl ether, sodium hydroxide, and sulfuric acid. 1,2-Cyclohexanedionedioxime was found to have the same solubility classification but was somewhat more soluble in water and hydrochloric acid and less soluble in diethyl ether than the oximation product. These solubilities place the oximation product in the acidic compound group which contains oximes, imides, phenols, etc.

Functional group analyses. Functional group analyses were run to determine which of the groups were present. The amino group was ruled out by a non-aqueous titration using the method of Fritz (3). This consists of dissolving the compound in glacial acetic acid and titrating with 0.1 *N* perchloric acid using Methyl Violet in chlorobenzene as the indicator. The oximation product was not even basic to the indicator so no amino or imino groups were present.

A method was devised to titrate active hydrogens of weak acids such as oximes in a non-aqueous solvent. The solvent was ethylenediamine (95–100%), the titrant potassium methoxide in benzene, and the indicator was *o*-nitroaniline in benzene. The titrant was prepared by dissolving 3.9 g. of potassium metal in 50 ml. of methanol mixed with benzene to slow down the reaction, and then diluting to a liter with a 1 to 10 solution of methanol in benzene. This solution was standardized against U. S. National Bureau of Standards benzoic acid. The titrations were run in 50-ml. standard taper Erlenmeyer flasks so that the flasks could be stoppered during dissolution of the samples and carbon dioxide could be excluded from the ethylenediamine. The tip of a 10-ml. burette was inserted in a hole in a rubber diaphragm which fit tightly over the top of the flask and the solution was stirred by means of a Teflon-covered magnet and a magnetic stirrer.

The acid to be titrated was dissolved in ethylenediamine and a qualitative run was made using three drops of the *o*-nitroaniline as the indicator by adding potassium methoxide swiftly until a yellow to orange endpoint was noticed. Then several samples were run adding the indicator within a ml. or so of the previously observed endpoint. Both hydrogens of 1,2-cyclohexanedionedioxime were titrated by this method to less than 1% error. The oximation product when titrated in the above manner gave 146 as the average equivalent weight.

$$\text{Equivalent weight} = \frac{(1000)(\text{wt. of sample in g.})}{(N \text{ of KOMe})(\text{ml. of KOMe})}$$

A series of aqueous solutions of the oximation product at various *p*H values and constant ionic strength was scanned in the ultraviolet with a Cary, model 12, recording spectrophotometer. The ionic strength was adjusted carefully to exactly 0.5 by the addition of the proper amount of 5 *N* sodium chloride solution. The *p*H was adjusted with 10 *N* sodium hydroxide and was read on a Beckman, model G, *p*H meter. As the *p*H was increased the absorption maximum at 257 mμ gradually decreased and a new absorption maximum at 297 mμ appeared. Two isosbestic points were evident. The *p*K′ was determined from these data by the method of Stenström and Goldsmith (5).

$$K' = \frac{A_s - A_s^0}{A_s' - A_s}[H^+]$$

$$pK' = -\log K'$$

where

K' = Ionization constant for compound being studied.

$[H^+]$ = Molar concentration of the hydrogen ion of a solution the *p*H of which is near the *p*K′ being determined.

A_s = Absorbancy of a mixture of unionized and ionized molecules at a *p*H which is near the *p*K′ being determined.

A_s^0 = Absorbancy of unionized molecules.

A_s' = Absorbancy of ionized molecules.

The absorbancy has been substituted for the molar absorbancy index because the concentration and cell length remained constant throughout the determination. The term, μ, denotes ionic strength, here $\mu = 0.5$.

The infrared spectra were determined on a Baird recording infrared spectrophotometer by the mull technique. Both hexachlorobutadiene and Nujol were used as mulling agents (see Figures 2 and 3). Sodium chloride prisms and cells were used.

Water of hydration. A water of hydration determination was made using an Abderhalden drying pistol with cyclohexanone, acetic anhydride, and glacial acetic acid as solvents. Only the glacial acetic appeared not to cause any sublimation to occur. A platinum boat was dried, weighed, the sample added and then weighed again. The filled boat was placed in the pistol and dried under a vacuum at the refluxing temperature of the solvent for an hour. The weight loss was 2%.

A direct titration was made with the Karl Fischer reagent. The ordinary titration yielded 0.7% water. Another titration was tried, refluxing the oximation product in pyridine that had been refluxed over sodium hydroxide and then distilled to remove the water. This method also gave 0.7% water.

Ebullioscopic molecular weight. The molecular weight was determined by the Menzies-Wright ebullioscopic method. Benzene was used as a solvent but the compound apparently associated in this solvent since the molecular weight increased as the concentration of the oximation product increased. For this reason absolute ethanol was used as the solvent. Approximately 28 ml. of ethanol was used with samples varying in size from 0.05 to 0.15 g. The average molecular weight found for the oximation product that had been recrystallized from water was 152. On recrystallizing the compound from dry benzene the melting point was raised to 179–180° and the molecular weight was found to be 136.

X-Ray crystallography. An X-ray analysis was run to determine the unit cell size and the molecular weight. Powder photographs were made with a precession camera. The measurements of the cell yielded: $a = 13.75$ Å; $b = 6.06$ Å; $c = 17.1$ Å; $\beta = 87° \pm 1°$. The density, φ, of this compound was found to be 1.41. The unit cell size was calculated to be eight. The molecular weight was calculated from the following formula:

$$\text{Molecular Weight} = \frac{(N_0)(\varphi)(\text{Volume of the unit cell})}{\text{No. of molecules/unit cell}}$$

where

N_0 = Avogadro's number

φ = Density of solid crystalline compound

Volume of unit cell = abc in cubic centimeters.

The molecular weight was found to be 151.

Destructive hydrogenation. A destructive hydrogenation was performed in glacial acetic acid. The oximation product (0.21686 g.) was added to 50 ml. of glacial acetic acid and 0.01322 g. of platinum oxide. The hydrogenation apparatus was flushed out several times with hydrogen and then the flask containing the mixture was placed on it. Readings were taken every five minutes for three hours (Figure 4). The calculations are based on the first large change of rate designated on the curve. Based on a molecular of 148, it was found that 4.02, and 4.15 moles of hydrogen were absorbed per mole of oximation product at the two points shown on the curve.

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SUMMARY

A new compound has been prepared by the oximation of the sodium salt of 2-hydroxyiminocyclohexanone in an aqueous solution containing calcium car-

bonate. A structural formula is proposed. The name given to the oximation product is 2,3,4-triazabicyclo[3.4.0]-3-hydroxy-1,4-nonadiene hemihydrate.

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