



THE SYNTHESIS OF SOME 1,
4-DISUBSTITUTED-5-IMINOTETRAZOLINES

Thesis for the Degree of M. S.
MICHIGAN STATE UNIVERSITY
Willard Jason Haak
1957

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EAST LANSING, MICHIGAN

THE SYNTHESIS OF SOME 1,4-DISUBSTITUTED-5-IMINO-TETRAZOLINES

By

Willard Jason Hask

A THESIS

**Submitted to the College of Science and Arts of Michigan
State University of Agriculture and Applied Science
in partial fulfillment of the requirements
for the degree of**

MASTER OF SCIENCE

Department of Chemistry

1957

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ACKNOWLEDGMENT

The writer wishes to express his appreciation to Doctor Robert M. Herbst for his most helpful counsel and assistance during the performance of this work.

1. *Chlorophyll a* and *Chlorophyll b* contents were determined using a spectrophotometer (Shimadzu UV-160U) at 663 nm and 646 nm, respectively. The concentrations were calculated using the following equations:

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一、**總論**
 二、**本國之經濟發展**
 三、**國際經濟之趨勢**
 四、**我國經濟之現狀**
 五、**我國經濟之展望**
 六、**結論**

THE SYNTHESIS OF SOME 1,4-DISUBSTITUTED-
5-IMINO-2,4-DIAZOLINES

By

Willard Jason Haak

AN ABSTRACT

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Department of Chemistry

Year 1957

Approved

Robert M. Heist

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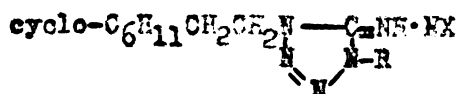
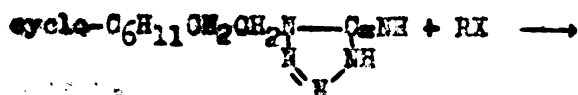
Robert M. Coates

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Recent work (1) has shown that 1-p-chlorobenzyl-4-n-octyl-5-aminotetrazoline has cidal action against Trichomonas festus in vitro. It was also highly active against certain fungi, Candida albicans and Trichophyton mentagrophytes v. interdigitalis.

A series of new 1,4-disubstituted-5-aminotetrazolines were prepared for testing using the cyclohexylethyl group in place of the n-octyl group. The series has the following groups in the 4-position: benzyl, o-chlorobenzyl, p-chlorobenzyl, 2,4-dichlorobenzyl, 3,4-dichlorobenzyl, m-nitrobenzyl, p-nitrobenzyl, 3-phenylpropyl and 2-phenylethyl.

The 5-aminotetrazolines were prepared by alkylation of 1-(2-cyclohexylethyl)-5-aminotetrazole with the aralkyl halide using the method of Herbst, Roberts and Harvill (2) with some modifications.



R = aralkyl

1-(2-Cyclohexylethyl)-5-aminotetrazole is a new compound prepared by the following series of reactions: 2-Cyclohexylethylamine, an intermediate, was prepared from 3-cyclohexylpropionic acid by the Schmidt reaction using hydrazoic acid (3).



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• *Environ Biol Fish* 2012;95:103–112. doi:10.1007/s10641-011-9914-7

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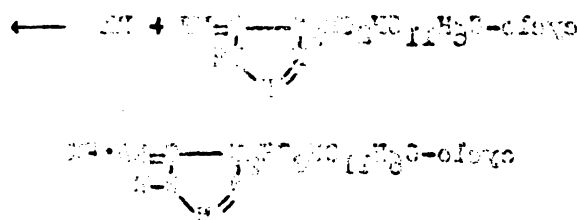
$\frac{d}{dt} \left(\frac{\partial L}{\partial \dot{x}} \right) = \frac{\partial L}{\partial x}$, where $L = T - V$. In our case, $T = \frac{1}{2} m \dot{x}^2$ and $V = \frac{1}{2} kx^2$.

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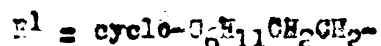
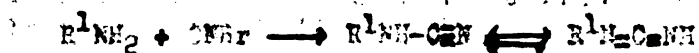
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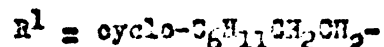
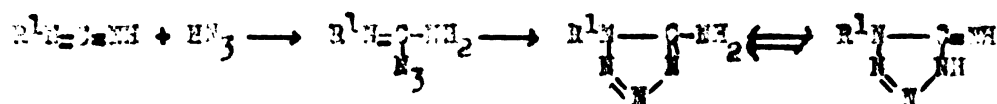


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The amine was then allowed to react with cyanogen bromide to form the monosubstituted cyanamide.



The 2-cyclohexylethylcyanamide was treated with hydrazoic acid and the resulting product cyclized to 1-(2-cyclohexylethyl)-5-aminotetrazole (4).

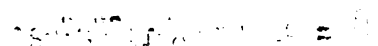


1-(2-Cyclohexylethyl)-5-aminotetrazole was characterized as the pure solid, acetyl derivative, and infrared spectra.

Characterization of the 1-(2-cyclohexylethyl)-4-alkyl-5-imino-tetrazolines was as the hydrochloride, phenylthiourea and the solid free base when it could be obtained.

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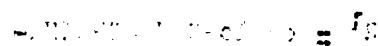
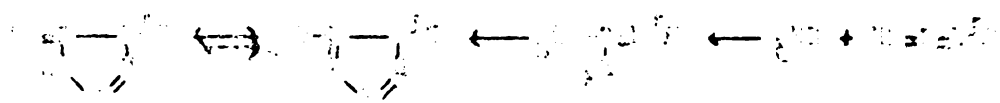
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LITERATURE CITED

1. E. F. Elslager, T. F. Reutner, and J. C. Peters, Abstracts of Papers Presented at the Meetings of the American Chemical Society, Dallas, Texas, 7th (April 1955).
2. R. M. Herbst, C. Roberts, E. Harvill, J. Org. Chem., 16, 139 (1951) with modifications.
3. K. Wilson, unpublished work.
4. W. Garbrecht and R. M. Herbst, J. Org. Chem., 18, 1003 (1953) with modifications.

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INTRODUCTION

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Recently a series of 1-4,disubstituted-5-aminotetrazoline hydrochlorides have been tested in the Parke, Davis Laboratories (1) for their cidal effects against Trichomonas foetus in vitro. The testing showed that, of the compounds tested, 1-(p-chlorobenzyl)-4-octyl-5-aminotetrazoline proved to be the most effective and is presently being prepared for clinical testing. These compounds were also tested and were active against Trichomonas vaginalis and as fungicides against Candida Albicans and Trichophyton mentagraphytes v. interdigitale.

It was decided to prepare a series of similarly substituted 5-aminotetrazolines as their hydrochlorides with the n-octyl group replaced by a 2-cyclohexylethyl group. These salts are presently being tested for antitrichomonal and other chemotherapeutic effects.

A new monosubstituted 5-aminotetrazole, 1-(2-cyclohexylethyl)-5-aminotetrazole was prepared as an intermediate for the synthesis of the tetrazolines.

The tetrazole was characterized by infrared spectra, melting point, and as the acetyl derivative. The tetrazolines were characterized as the free bases, hydrochlorides and phenylthioureas.

7. The results of the present study are summarized in Table I.

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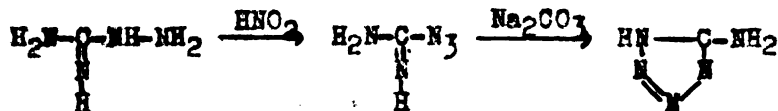
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23. The results of the present study are summarized in Table I.

HISTORICAL

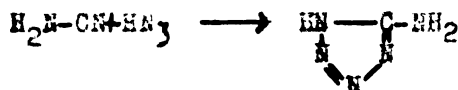
1. *Phragmites* (common)
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The synthesis of 5-aminotetrazole was first reported by Thiele (2) who prepared guanyl azide by interaction of aminoguanidine and nitrous acid. The guanyl azide was heated with aqueous sodium carbonate or sodium acetate to bring about ring closure to 5-aminotetrazole.

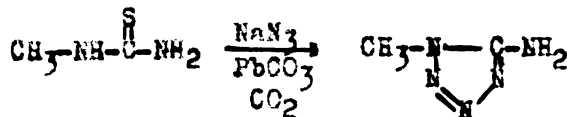


Thiele and Ingle (3) reported a number of products obtained from the direct alkylation of 5-aminotetrazole. Methylation, ethylation, and benzoylation led to mixtures of products, both mono and disubstituted aminotetrazoles. The preparation of some of these compounds was repeated by Herbst and Percival (4) and it was found that the dimethyl, diethyl and "alpha" dibenzyl 5-aminotetrazoles obtained by Thiele and Ingle were 1,4-disubstituted-5-aminotetrazoles.

Sodium azide and hydrazoic acid have frequently been used in the synthesis of substituted 5-aminotetrazoles. Cyanamide (5) or diacyandiamide (6), which dissociates to cyanamide, react with hydrazoic acid to give 5-aminotetrazole.



Stolle (7) prepared 1-methyl-5-aminotetrazole by interaction of N-methylthiourea with sodium azide in an atmosphere of carbon dioxide in the presence of lead carbonate.



By this reaction he also prepared a number of 1-aryl-5-aminotetrazoles from the corresponding N-arylthioureas (8,9).

The synthesis of β -substituted α -keto acids is described by the following reaction scheme (1). The reaction of a substituted α -keto acid with a substituted β -keto acid in the presence of a catalyst yields a substituted β -keto acid.

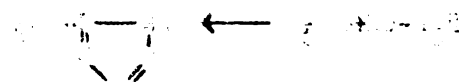


where R_1 and R_2 are substituents on the α -keto acid, and R_3 and R_4 are substituents on the β -keto acid.

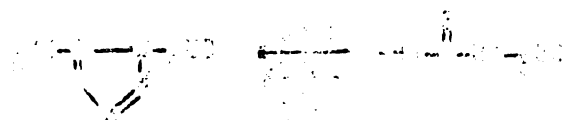
The reaction of a substituted α -keto acid with a substituted β -keto acid in the presence of a catalyst yields a substituted β -keto acid. The reaction of a substituted α -keto acid with a substituted β -keto acid in the presence of a catalyst yields a substituted β -keto acid. The reaction of a substituted α -keto acid with a substituted β -keto acid in the presence of a catalyst yields a substituted β -keto acid. The reaction of a substituted α -keto acid with a substituted β -keto acid in the presence of a catalyst yields a substituted β -keto acid.

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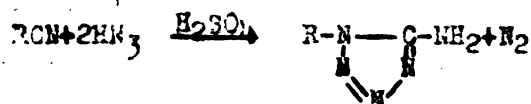


The reaction of a substituted α -keto acid with a substituted β -keto acid in the presence of a catalyst yields a substituted β -keto acid. The reaction of a substituted α -keto acid with a substituted β -keto acid in the presence of a catalyst yields a substituted β -keto acid. The reaction of a substituted α -keto acid with a substituted β -keto acid in the presence of a catalyst yields a substituted β -keto acid.

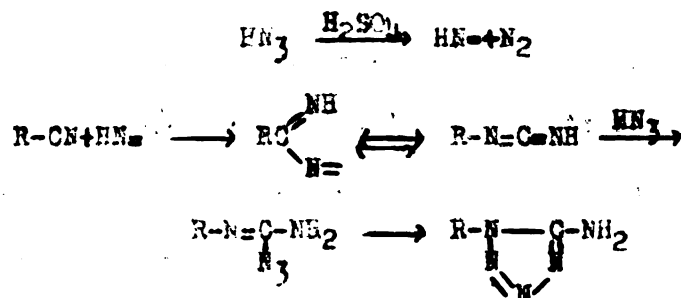


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A procedure that eliminates the use of lead carbonate in the presence of sodium azide or hydrazoic acid was developed by von Braun and Keller (10). The procedure involves the interaction of nitriles and hydrazoic acid in the presence of concentrated sulfuric acid according to the following equation.



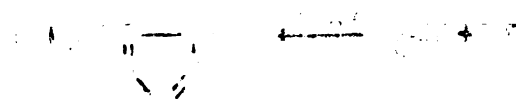
The intermediate was assumed to be a substituted carbodiimide to which the second mole of hydrazoic acid added, followed by cyclization.



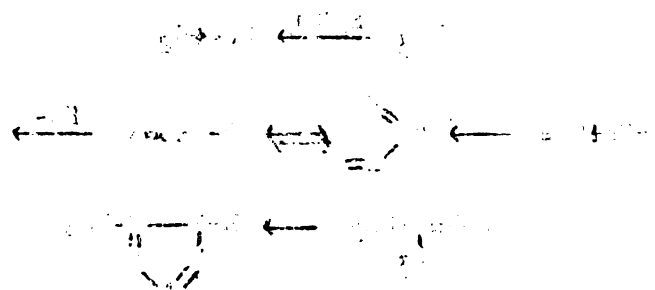
A more logical explanation of this sequence of reactions was offered by Herbst, Roberts and Harvill (11) which did not use the free imine radical (HN_2), first postulated by Schmidt (12) and used by von Braun and Keller. Herbst, et al. (11) suggested the addition of hydrazoic acid directly to the cyanide linkage, followed by an acid catalyzed rearrangement accompanied by the elimination of nitrogen, similar to the Curtius rearrangement for acid azides. The same intermediate is assumed to result. After the addition of another molecule of hydrazoic acid to the rearrangement product, the resulting guanyl azide cyclizes to the 1-alkyl-5-aminotetrazole.

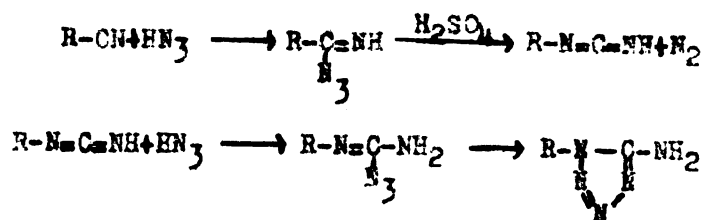
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Oct 11: 2006, Oct 18: 2006, Oct 25: 2006, Nov 1: 2006, Nov 8: 2006, Nov 15: 2006, Nov 22: 2006, Nov 29: 2006, Dec 6: 2006, Dec 13: 2006, Dec 20: 2006, Dec 27: 2006, Jan 3, 2007: 2006, Jan 10:

1. The first step in the process of the investigation is to identify the problem. This is done by the investigator who is responsible for the investigation. The investigator will then determine the scope of the investigation and the methods to be used. The investigator will then collect the data and analyze it. The final step is to report the results of the investigation.



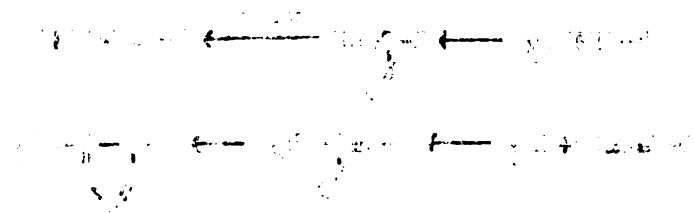
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Garbrecht and Herbst (13) have extended the work of Hantzsch and Vagt (5) and found that the action of hydrazoic acid on monosubstituted cyanamides led to the production of only 1-substituted-5-aminotetrazoles. In this method the alkylcyanamide is allowed to react with hydrazoic acid in ether or aqueous alcohol solution.

Recently several methods for the alkylation of monosubstituted 5-aminotetrazoles have been developed by Herbst, Roberts and Harvill (11). The products are 1,4-disubstituted-5-iminotetrazolines (as mentioned before on p. 3). These methods use alkyl sulfonates, alkyl sulfates, aralkyl and alkyl halides as alkylating agents. With some modifications of technique (14) these methods were employed for the syntheses of the iminotetrazolines in this thesis.



It is noted that the above scheme (1) is not the only one

which can be used to explain the results obtained in the above experiments. It is possible that the reaction is more complicated than the above scheme.

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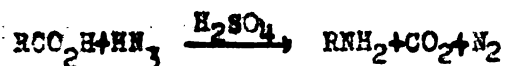
which can be used to explain the results obtained in the above experiments.

It is noted that the above scheme (1) is not the only one

DISCUSSION

Abstract

The Schmidt reaction (15) in which primary amines are prepared from the carboxylic acid containing one more carbon by the action of hydrazoic acid was used in the preparation of

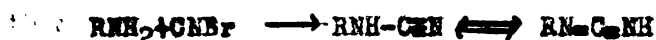


2-cyclohexylethylamine (18). One requirement of the Schmidt reaction is that the organic acid used be stable to sulfuric acid. 3-Cyclohexylpropionic acid, which was used here, satisfied this requirement.

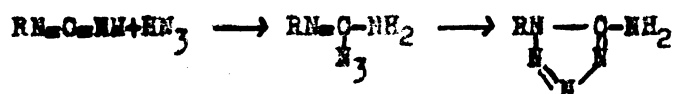
When compared with other methods for the preparation of primary amines from carboxylic acids such as the Hofmann and Curtius reactions several advantages of the Schmidt reaction are apparent: (1) the yields from longer chain acids are usually better and (2) only a single step is involved. Initiation and control of the reaction, which is exothermic, often are difficult since best results are obtained if the temperature is kept between 40-60°C. These problems were solved in the present case by raising the temperature of the reaction mixture to 30-35°C. before beginning addition of the hydrazoic acid solution. Subsequently, the temperature rose to 55-60°C. where it could be maintained easily by adjusting the rate of addition of hydrazoic acid and the degree of immersion in the cooling bath.

In the preparation of the benzene solution of hydrazoic acid by addition of concentrated sulfuric acid to a water slurry of sodium azide (19) covered with benzene, it was found that by using half again as much water as suggested by Garbrecht and Herbst (16) a benzene solution of hydrazoic acid of comparable concentration was obtained. The additional water permitted better stirring and the temperature could be more easily controlled.

Benson (17) in his survey of the chemistry of tetrazoles has included several methods for the preparation of 1-substituted 5-amino-tetrazoles. Some of these have been described in the historical part. It was decided that the method of Garbrecht and Herbst (13) in which a monosubstituted cyanamide is treated with hydrazoic acid would be used. The cyanamide is prepared by interaction of cyanogen bromide and a primary amine.



The cyanamide is then allowed to react with hydrazoic acid to form a substituted guanyl azide which then cyclizes to the 5-aminotetrazole.



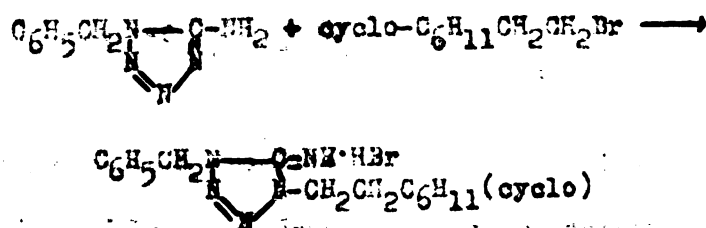
With recent improvements of technique from this laboratory there is no need for separating the cyanamide, and the hydrazoic acid is generated in the reaction vessel.

These improvements in the method of preparation of the tetrazole and the preparation of the amine by the Schmidt reaction have reduced the overall time required for the preparation of the tetrazole starting with the carboxylic acid when compared with the method of von Braun and Keller (10), where preparation of the nitrile may be necessary. The methods give reasonable yields of a product which is quite easily purified.

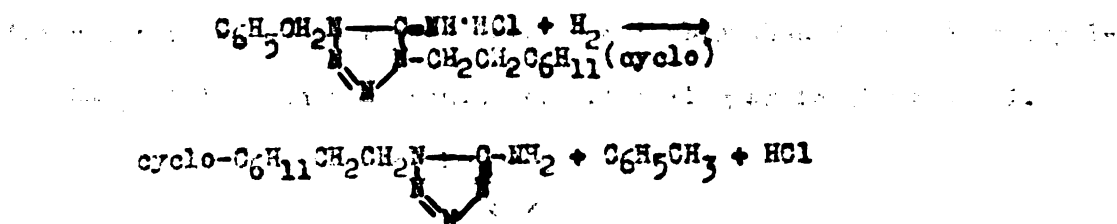
Since 1-(2-cyclohexylethyl)-5-aminotetrazole had not been prepared before it was also prepared by another method. Alkylation of 1-benzyl-5-aminotetrazole^(a) with 2-cyclohexylethyl bromide (20) gave 1-benzyl-

^(a) The 1-benzyl-5-aminotetrazole was prepared in this laboratory by the method of Garbrecht and Herbst (13).

4-(2-cyclohexylethyl)-5-aminotetrazoline hydrobromide. The hydrobromide was converted to the hydrochloride



by liberating the base with potassium hydroxide and treating the free base with concentrated hydrochloric acid. The hydrochloride was then debenzylated by hydrogenolysis using the general techniques of Birchner (21).

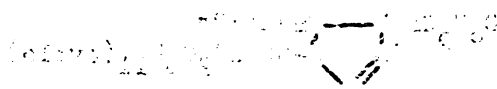
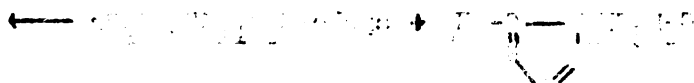


In the first method the tetrazole ring was formed from 2-cyclohexylethylamine in such a way that the amino-N became the 1-nitrogen of the tetrazole ring; in the second method the 2-cyclohexylethyl group was added as a ring substituent on a preformed tetrazole structure. The formation of the same compound by both procedures supports the assignment of the structure of the product as 2-cyclohexylethyl-5-amino-tetrazole.

Infrared spectra, figures I and II, and mixture melting points which gave no depression were used to show that the products of the two methods were identical. Benzoylation of the 1-(2-cyclohexylethyl)-5-amino-tetrazole

4-(2-oxo-1,2-dihydro-3H-imidazol-3-yl)-2-oxo-1,2-dihydro-3H-imidazole

Structure of 4-(2-oxo-1,2-dihydro-3H-imidazol-3-yl)-2-oxo-1,2-dihydro-3H-imidazole

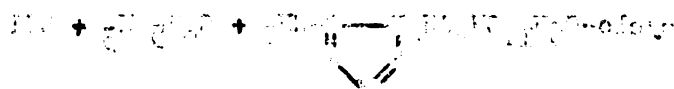
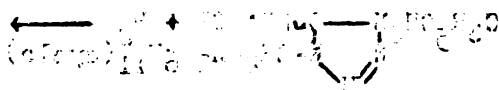


4-(2-oxo-1,2-dihydro-3H-imidazol-3-yl)-2-oxo-1,2-dihydro-3H-imidazole

Structure of 4-(2-oxo-1,2-dihydro-3H-imidazol-3-yl)-2-oxo-1,2-dihydro-3H-imidazole

4-(2-oxo-1,2-dihydro-3H-imidazol-3-yl)-2-oxo-1,2-dihydro-3H-imidazole

Structure of 4-(2-oxo-1,2-dihydro-3H-imidazol-3-yl)-2-oxo-1,2-dihydro-3H-imidazole



In the first step, a tetraolide ring was formed from 2-oxo-1,2-dihydro-3H-imidazole

4-(2-oxo-1,2-dihydro-3H-imidazol-3-yl)-2-oxo-1,2-dihydro-3H-imidazole

of the tetraolide ring; in the second step, the 2-oxo-1,2-dihydro-3H-imidazole

group was added as a ring substituent on a tetraolide ring.

The formation of the acid was followed by both infrared spectra and the

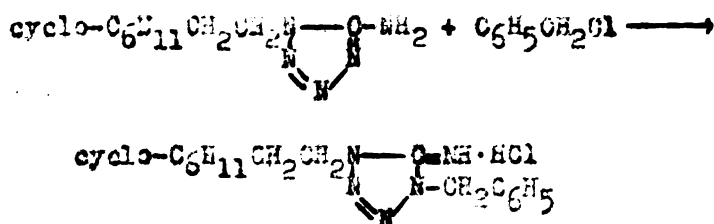
assignment of the structure of the product as 4-(2-oxo-1,2-dihydro-3H-imidazol-3-yl)-2-oxo-1,2-dihydro-3H-imidazole.

Structure of 4-(2-oxo-1,2-dihydro-3H-imidazol-3-yl)-2-oxo-1,2-dihydro-3H-imidazole

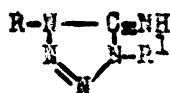
Infrared spectra, the two I and II, and visible melting points which

were no depression were used to show that the products of the two methods

were identical. Identification of the 4-(2-oxo-1,2-dihydro-3H-imidazol-3-yl)-2-oxo-1,2-dihydro-3H-imidazole



gave a product whose hydrochloride was identical with that obtained from the alkylation of 1-benzyl-5-aminotetrazole, described above, as shown by infrared spectra, figures III and IV, and mixture melting points, which showed no depression. Since the same compound is formed regardless of the order in which the two substituents are introduced, the 2-cyclohexylethyl and benzyl groups must occupy equivalent positions on the tetrazole ring. This requirement is met only when R and R¹ occupy 1- and 4- positions on the 5-aminotetrazole ring as in structure I.



I

R or R¹ = 2-cyclohexylethyl or benzyl.

Structure I was further substantiated by the debenzylation of the tetrazoline formed from the alkylation of 1-benzyl-5-aminotetrazole with 2-cyclohexylethyl bromide, to give 1-(2-cyclohexylethyl)-5-aminotetrazole in 71% yield, indicating that the 2-cyclohexylethyl group occupied the 1- (or 4-) position on the ring. Since only the 4- position is equivalent to the 1- position, substitution in any other position in the ring would lead to different products. Rearrangement during the debenzylation is rather unlikely since rather mild conditions were used.

The 1-(2-cyclohexylethyl)-4-alkyl-5-iminotetrazoline hydrochlorides were prepared by the method of Herbst, Roberts and Harvill (11) with more recent improvements in technique from this laboratory (14). The method

involved the heating of the aralkyl halide with the 1-alkyl-5-amino-tetrazole at temperatures of 120-150°C. for a period of time. Usually a homogeneous melt formed, followed by a mildly exothermic reaction. The salt of the 1-4-disubstituted-5-iminotetrazoline crystallized from the hot mixture and was purified by steam distilling the excess benzyl halide from the mixture. The free base was formed and then extracted either with ether or benzene. The hydrochloride was formed by evaporating the dried ether solution, dissolving the residual oil in aqueous alcohol and adding concentrated hydrochloric acid, or by treating the dried benzene solution with anhydrous hydrochloride.

It was found in the preparation of this series of tetrazoline hydrochlorides that the use of a larger excess (50%) of benzyl halide made it easier to handle and dissolve the crude tetrazoline salts.

No dialkylation was apparent even with the large excess of halide.

In the purification complete solution of the crude tetrazoline salt in alcohol before steam distillation was necessary to insure the complete removal of the alkylating agent.

All of the 1-(2-cyclohexylethyl)-4-aralkyl-5-iminotetrazoline hydrochlorides prepared are listed in Tables I and II.

The lower yield of the p-nitrobenzyl substituted tetrazoline hydrochloride was due to the dark colored impurities in the crude product which caused greater losses during purification.

Longer reaction times were used for the alkylations with 3-phenylpropyl and 2-phenylethyl halides because of the lower reactivity of these reagents compared with that of the benzyl halides.

During the preparation of the tetrazoline hydrochlorides it was found that the free tetrazoline base of the 2,4-dichlorobenzyl

substituted tetrazoline was a solid. Attempts to prepare the free bases of the other tetrazolines were made by treating the pure hydrochloride with potassium hydroxide and extracting with ether. After drying the ether solution, the ether was evaporated and the residual oil crystallized. The free bases were recrystallized from either cyclohexane or petroleum ether.

Solid bases were obtained for all but the 1-(3-phenylpropyl)-4-(2-cyclohexylethyl)-5-iminotetrazoline. Formulae, melting points and analyses are found in Table IV.

EXPERIMENTAL

Benzene Solution of Hydrazoic Acid

The method of Garbrecht and Herbst (16) was used with slight modifications of technique to permit easier handling.

The benzene solutions of hydrazoic acid were prepared as follows: 300 ml. of water are added to 208 g. of sodium azide in a 3 l. flask fitted with an alcohol thermometer, efficient stirrer and a 200 ml. dropping-funnel with outlet below the liquid level. The flask should be vented. Six hundred milliliters of benzene are added. While keeping the temperature below 30°C. with an ice-water bath, 100 ml. of concentrated sulfuric acid are added dropwise over a period of one and a half hours. The solution turns a deep red until the last 5-10 ml. of acid are added. Stirring is continued for two hours and the mixture is allowed to stand for one hour after which the benzene layer is decanted and dried over sodium sulfate.

The concentration of the hydrazoic acid was determined by titration of an aliquot with standard aqueous alkali using phenolphthalein indicator. The above procedure gives solutions containing initial concentrations of 15-17 g. of hydrazoic acid per 100 ml. of solution.

2-Cyclohexylethylamine

The technique developed by Wilson (22) for the preparation of a primary amine by the Schmidt reaction from the corresponding acid was employed with slight modification as follows: 203 g. (1.3 moles) of 3-cyclohexylpropionic acid are dissolved in 2.2 l. of benzene in a 5 l. flask fitted with an alcohol thermometer, efficient stirrer, 500 ml. dropping-funnel and a reflux condenser. Six hundred and twenty milliliters of concentrated sulfuric acid are added with stirring. Four hundred and eighty milliliters of a benzene solution of hydrazoic acid (14.6 g. of hydrazoic acid per 100 ml., 1.625

Experiment 11: The Reaction of Potassium with Water

The reaction of potassium with water is shown by the following equation:

$$2K + 2H_2O \rightarrow 2KOH + H_2$$

The potassium metal is placed in a beaker of water and the reaction is observed.

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Experiment 12: The Reaction of Potassium with Ethanol

The reaction of potassium with ethanol is shown by the following equation:

$$2K + 2C_2H_5OH \rightarrow 2C_2H_5OK + H_2$$

The potassium metal is placed in a beaker of ethanol and the reaction is observed.

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moles) are then added dropwise with stirring at such a rate as to maintain a reaction temperature of 60°C. The addition of the hydrazoic acid solution required about one hour. After complete addition of the hydrazoic acid stirring is continued for an hour while the reaction vessel is in a water bath at 65°C.

After separating the benzene layer the sulfuric acid layer is poured in a very thin stream into 3,000-4,000 g. of ice in a 4 l. beaker. A voluminous precipitate presumably of the amine acid sulfate results. The mixture is poured onto a large filter and suction applied until the surface of the precipitate begins to liquify. Retain the last 100 ml. of filtrate. The precipitate and the last 100 ml. of the filtrate are returned to the 5 l. flask, dissolved in 1 l. of water and the solution made basic to litmus with 50% potassium hydroxide solution. The amine is steam distilled until about 1 l. of distillate is obtained. One hundred milliliters of ether are added to the distillate and the ether layer separated. The water layer is extracted three times with 50 ml. portions of ether, the ether layers are combined and dried over potassium carbonate. The ether is removed by distillation using a Vigreux column. The amine may be further dried after the ether is removed by adding 20 ml. of benzene and distilling the azeotropic mixture through the column. The column is removed for the final distillation and the amine collected, BP 184-185°C. (uncorrected) n_D^{25} 1.4637 (18) yield 134 g. (82%) based on 3-cyclohexylethylpropionic acid.

1-(2-Cyclohexylethyl)-5-Aminotetrazole

The methods described by Garbrecht and Herbst (16) for the synthesis of 1-alkyl-5-aminotetrazoles were used in a modified form evolved in this laboratory.

moles) are then added to the mixture of about 10 ml of water. The addition of the hydrochloric acid solution results in the formation of the polymer.

Acid addition is continued for 10 min after the reaction vessel

is in a water bath at 50°C.

After neutralizing the mixture with sodium hydroxide, the

product is a very fine white solid, $\text{C}_{10}\text{H}_{12}\text{O}_2$, $\text{M}_n = 160$.

Product is obtained as a white solid. The mixture is poured into a 100 ml beaker and the white

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1-(2-ethyl-1-oxocyclohexyl)-2-methyl-2-butanol

The mixture described by Gershwin and Leiser (19) for the synthesis

of 1-(2-ethyl-1-oxocyclohexyl)-2-methyl-2-butanol was used in a modified form evolved in this

laboratory.

The tetrazole was prepared as follows: 127 g. (1 mole) of 2-cyclohexylethylamine are dissolved in 800 ml. of 95% ethanol in a 3 l. flask fitted with an alcohol thermometer, efficient stirrer, and a 500 ml. dropping-funnel. The flask must be vented. After cooling below 10°C. (a) in an ice-water bath 106 g. (1 mole) of cyanogen bromide, dissolved in 200 ml. of water and 200 ml. of 95% ethanol, are added dropwise. Forty grams (1 mole) of sodium hydroxide, dissolved in 100 ml. of water, are added and the solution stirred for an hour and a half. Seventy-eight grams (1.2 moles) of sodium azide, dissolved in 240 ml. of water, are added followed by 200 ml. (1.2 moles) of 1:1 hydrochloric acid added dropwise. After stirring for a half hour after the hydrochloric acid is added, the solution is boiled under reflux on a steam bath for six hours. The reaction mixture is allowed to cool slowly to room temperature and then is chilled in an ice-water bath. The precipitate is filtered (b) and dried over calcium chloride and potassium hydroxide in a vacuum dessicator. The dried product is refluxed with 500 ml. of 99% isopropyl alcohol, the suspension cooled, filtered and dried. The yield was 89.1 g., 47% (based on amine), MP 212.5°-213.5°C. (uncorrected).

Analysis. Calc'd. for $C_{12}H_{17}N_5$: C, 55.36; H, 8.78; N, 35.87. Found: C, 55.35; H, 8.53; N, 35.80.

Acetyl Derivative of 1-(2-Cyclohexylethyl)-5-Aminotetrazole

Two grams of the tetrazole are refluxed with 10 ml. of acetic anhydride for half an hour. Ten milliliters of isopropyl alcohol and 10 ml. of water

(a) The temperature should be kept below 10°C. until refluxing is begun. Vigorous stirring should be continuous throughout the process.

(b) This is done in the hood because of the excess hydrazoic acid present.

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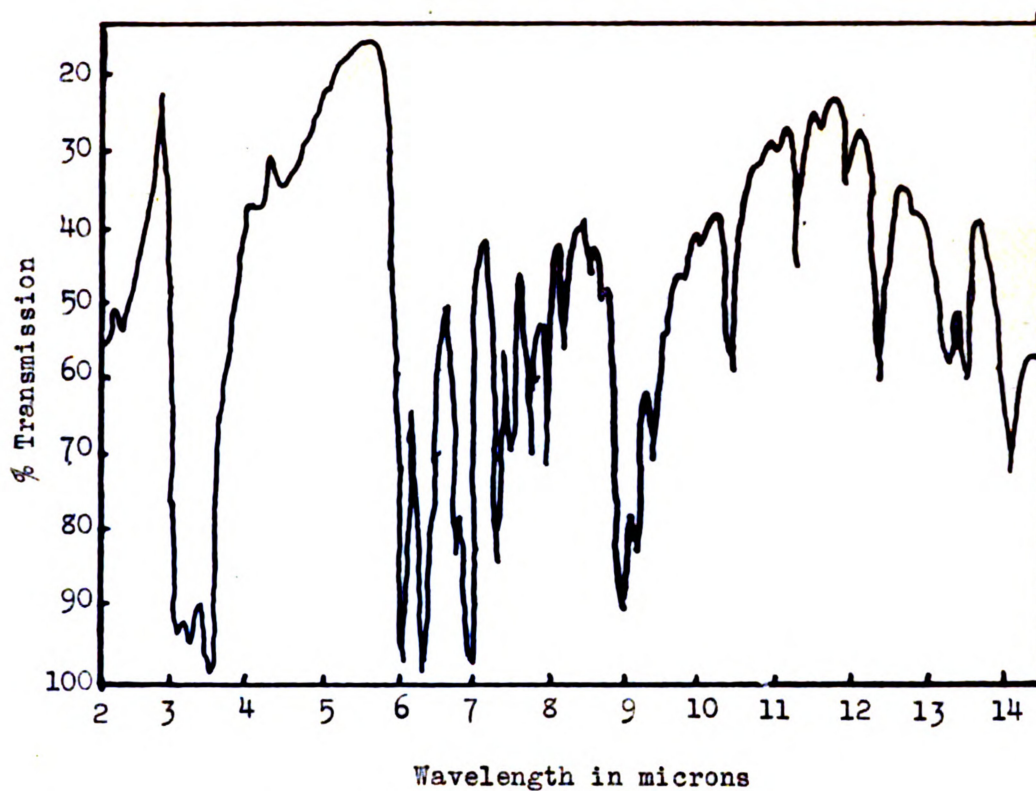


Figure I. Infrared spectrum of 1-(2-cyclohexylethyl)-5-amino-tetrazole from amine. (Nujol mull)

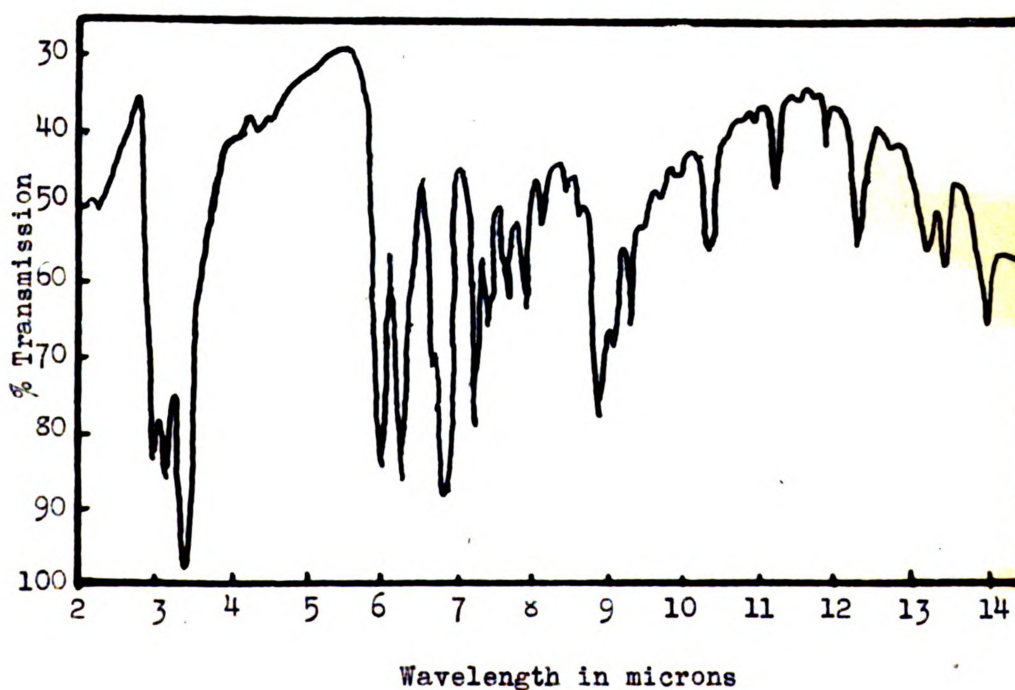


Figure II. Infrared spectrum of 1-(2-cyclohexylethyl)-5-amino-tetrazole from debenzylation. (Nujol mull)

are added and the solution is heated on a steam bath to remove the excess anhydride. The oily product is crystallized from cyclohexane, MP 95.5°-96.5°C. (uncorrected).

Analysis. Calc'd. for $C_{11}H_{19}N_5O$: C, 55.67; H, 8.07; N, 29.72. Found: C, 55.59; H, 7.98; N, 29.72.

1-(2-Cyclohexylethyl)-4-Aryl-5-Iminotetrazoline Hydrochlorides

The methods of Herbst, Roberts and Harvill (11) and Herbst (14) were used. Two procedures were used for the extraction of the amine and precipitation of the hydrochloride. Examples of both procedures are given below.

The formation of 1-(2-cyclohexylethyl)-4-m-nitrobenzyl-5-imino-tetrazoline hydrochloride will illustrate method A. The tetrazoline hydrochloride is prepared as follows: 11.8 g. (.06 moles) of 1-(2-cyclohexylethyl)-5-aminotetrazole are heated with 15.4 g. (.09 moles) of m-nitrobenzyl chloride at 140°C. in an oil bath. Formation of a homogeneous melt is followed by a rapid exothermic reaction after which the mixture solidifies. The bath is kept at 140°C. for an hour and a half after the exothermic reaction subsides. The crude product is dissolved in 300 ml. of boiling ethanol. Five hundred milliliters of water are added and the mixture steam distilled until the distillate is clear. More water is added slowly during the distillation to maintain a volume of about 300 ml. of water in the flask. Thirty grams of potassium hydroxide are slowly added to the warm residue and the solution stirred for two hours. One hundred and fifty milliliters of ether are added after cooling with ice. Stirring is continued for half an hour. The ether layer is separated and the water layer extracted three times with 50 ml. portions of ether. The combined ether solutions are dried over potassium

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These results of the hydrolysis of the polyacrylonitrile (PAN) and the polyacrylamide (PAA) are shown in Table I. The results of the hydrolysis of the polyacrylonitrile (PAN) and the polyacrylamide (PAA) are shown in Table I.

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carbonate. After evaporating the ether, the residual oil is dissolved in 300 ml. of 55% aqueous ethanol and 20 ml. of concentrated hydrochloric acid are added. The precipitate of the hydrochloride is redissolved by heating the suspension. The hot solution is filtered, cooled and the solid so obtained is filtered and dried.

Method B is as follows; the procedure is the same as method A through the addition of the potassium hydroxide and stirring. Benzene is used in similar quantities to extract the iminetetrasolines. The hydrochloride is formed by passing anhydrous hydrogen chloride through the dried benzene solution. The product is filtered and washed with 50 ml. of fresh benzene.

The addition of one gram of Norite was necessary to remove colored impurities in the purification of the p-nitrobenzyl- and 3-phenylpropyl-substituted tetrasolines.

Formulae, melting points, method, reaction times and analyses are given in Tables I and II.

Benzoylation of 1-(2-Cyclohexylethyl)-5-Aminotetrasole

1-(2-Cyclohexylethyl)-5-aminotetrasole (11.5 g., .06 moles) is heated at 150°C. in an oil bath with 11.4 g. (.09 moles) of benzyl chloride. Formation of a homogeneous melt is followed by a rapid exothermic reaction after which the mixture solidifies. The bath is kept at 150°-160°C. for two hours after the exothermic reaction subsides. The crude product is dissolved in 250 ml. of 95% ethanol and 600 ml. of water are added. The mixture is steam distilled until the distillate is clear. The warm residue is made basic with 15 g. of potassium hydroxide. After cooling, 150 ml. of ether are added and the mixture shaken vigorously for five

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TABLE I

1-(2-Cyclohexylethyl)-4-Aralkyl-5-Iminotetrazoline Hydrochlorides



R	Method of Preparation	Reaction (a) Time (hours)	Yield (b)		M.P. °C. (c)
			Based on Tetrazole		
Benzyl	A	3	81%	209	210
o-Chlorobenzyl	A	1.5	75%	223.5	224.5
p-Chlorobenzyl	B	3	81%	208	209
2,4-Dichlorobenzyl	A	1.5	74%	210.5	211.0
3,4-Dichlorobenzyl	B	1.5	71%	208.5	209.0
p-Nitrobenzyl	B	2.5	58%	209.5	210.5
m-Nitrobenzyl	A	1.5	73%	205.0	206.0
m-Nitro-3-Phenylpropyl	B	2.16	6.55%	214.0	215.0
3-Phenyl-2-Phenylethyl	A	10	52%	250.5	251.0

Analyses by Micro-Tech. Laboratories, Skokie, Illinois.

(a) Reaction times indicate the heating period after the exothermic reaction subsides.

(b) Pure products.

(c) Uncorrected. All of the hydrochlorides melt with decomposition.

1. INTRODUCTION

2. THEORETICAL BACKGROUND



Parameter	Value	Unit	Notes
Temperature	25	°C	Room temperature
Concentration	0.1	M	Stock solution
Time	10	min	Reaction time
Wavelength	254	nm	UV absorption

Sample 1	0.1	0.1	0.1
Sample 2	0.2	0.2	0.2
Sample 3	0.3	0.3	0.3
Sample 4	0.4	0.4	0.4
Sample 5	0.5	0.5	0.5

Sample 6	0.6	0.6	0.6
Sample 7	0.7	0.7	0.7
Sample 8	0.8	0.8	0.8
Sample 9	0.9	0.9	0.9
Sample 10	1.0	1.0	1.0

Sample 11	1.1	1.1	1.1
Sample 12	1.2	1.2	1.2
Sample 13	1.3	1.3	1.3
Sample 14	1.4	1.4	1.4
Sample 15	1.5	1.5	1.5

Sample 16	1.6	1.6	1.6
Sample 17	1.7	1.7	1.7
Sample 18	1.8	1.8	1.8
Sample 19	1.9	1.9	1.9
Sample 20	2.0	2.0	2.0

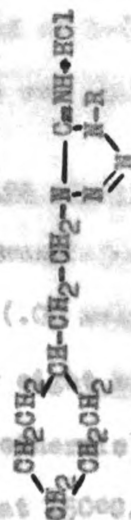
Sample 21	2.1	2.1	2.1
Sample 22	2.2	2.2	2.2
Sample 23	2.3	2.3	2.3
Sample 24	2.4	2.4	2.4
Sample 25	2.5	2.5	2.5

Sample 26	2.6	2.6	2.6
Sample 27	2.7	2.7	2.7
Sample 28	2.8	2.8	2.8
Sample 29	2.9	2.9	2.9
Sample 30	3.0	3.0	3.0

Sample 31	3.1	3.1	3.1
Sample 32	3.2	3.2	3.2
Sample 33	3.3	3.3	3.3
Sample 34	3.4	3.4	3.4
Sample 35	3.5	3.5	3.5

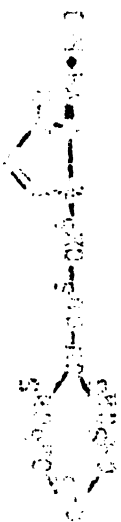
TABLE II

Analysis of 1-(2-Cyclohexylethyl)-4-Aralkyl-5-Iminotetrazoline Hydrochlorides



R	Formula	%C		%H		%N		%Cl	
		Calc.	Found	Calc.	Found	Calc.	Found	Calc.	Found
Benzyl	$C_{16}H_{24}ClN_5$	59.71	59.77	7.52	7.52	21.76	21.76	11.01	11.00
o-Chlorobenzyl	$C_{16}H_{23}Cl_2N_5$	53.93	54.00	6.51	6.35	19.66	19.74	19.90	19.70
p-Chlorobenzyl	$C_{16}H_{23}Cl_2N_5$	53.93	54.05	6.51	6.46	19.66	19.77	19.90	19.81
2,4-Dichlorobenzyl	$C_{16}H_{22}Cl_3N_5$	49.18	49.33	5.66	5.78	17.92	18.01	27.22	27.04
3,4-Dichlorobenzyl	$C_{16}H_{22}Cl_3N_5$	49.18	48.98	5.66	5.49	17.92	17.92	27.22	27.23
p-Nitrobenzyl	$C_{16}H_{23}ClN_6O_2$	52.38	52.70	6.32	6.47	22.91	23.06	9.67	9.37
m-Nitrobenzyl	$C_{16}H_{23}ClN_6O_2$	52.38	52.49	6.32	6.40	22.91	22.86	9.67	9.83
3-Phenylpropyl	$C_{18}H_{28}ClN_5$	61.78	62.03	8.07	8.07	20.02	20.28	10.13	10.21
2-Phenylethyl	$C_{17}H_{26}ClN_5$	60.78	60.84	7.80	7.77	20.85	20.87	10.56	10.67

Analyses by Micro-Tech. Laboratories, Skokie, Illinois.

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Year	Month	Day	Time	Location	Remarks
1941	Jan	1	10:00	San Francisco	Arrived
1941	Jan	2	10:00	San Francisco	Departed
1941	Jan	3	10:00	San Francisco	Arrived
1941	Jan	4	10:00	San Francisco	Departed
1941	Jan	5	10:00	San Francisco	Arrived
1941	Jan	6	10:00	San Francisco	Departed
1941	Jan	7	10:00	San Francisco	Arrived
1941	Jan	8	10:00	San Francisco	Departed
1941	Jan	9	10:00	San Francisco	Arrived
1941	Jan	10	10:00	San Francisco	Departed
1941	Jan	11	10:00	San Francisco	Arrived
1941	Jan	12	10:00	San Francisco	Departed
1941	Jan	13	10:00	San Francisco	Arrived
1941	Jan	14	10:00	San Francisco	Departed
1941	Jan	15	10:00	San Francisco	Arrived
1941	Jan	16	10:00	San Francisco	Departed
1941	Jan	17	10:00	San Francisco	Arrived
1941	Jan	18	10:00	San Francisco	Departed
1941	Jan	19	10:00	San Francisco	Arrived
1941	Jan	20	10:00	San Francisco	Departed
1941	Jan	21	10:00	San Francisco	Arrived
1941	Jan	22	10:00	San Francisco	Departed
1941	Jan	23	10:00	San Francisco	Arrived
1941	Jan	24	10:00	San Francisco	Departed
1941	Jan	25	10:00	San Francisco	Arrived
1941	Jan	26	10:00	San Francisco	Departed
1941	Jan	27	10:00	San Francisco	Arrived
1941	Jan	28	10:00	San Francisco	Departed
1941	Jan	29	10:00	San Francisco	Arrived
1941	Jan	30	10:00	San Francisco	Departed
1941	Jan	31	10:00	San Francisco	Arrived

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minutes. After separation of the ether layer 30 ml. of ethanol are added to the water layer to dissolve the remaining solids. The water solution is extracted with four 50 ml. portions of ether. The ether solutions are combined and dried over potassium carbonate. The ether is evaporated on a steam bath and 100 ml. of ethanol and 50 ml. of water are added to the oily residue. Concentrated hydrochloric acid is then added until Congo red indicator paper changed to blue (20 ml.). The hydrochloride is redissolved by heating the suspension. The hot solution is filtered, cooled and the solvent removed by suction on a filter. The solid is washed with 50 ml. of ethanol two times and dried. The yield of 1-(2-cyclohexylethyl)-4-benzyl-5-iminetetrazoline hydrochloride was 15.7 g. (81%), MP 209°-210°C. (uncorrected).

Alkylation of 1-Benzyl-5-Aminotetrazole with 2-cyclohexylethyl Bromide

1-Benzyl-5-aminotetrazole (10.5 g., .06 moles) (13) was heated with 17.5 g. (.09 moles) of 2-cyclohexylethyl bromide at 150°C. in an oil bath for eight hours. Formation of a homogeneous melt is followed by a rapid exothermic reaction after which the mixture solidifies. The bath is kept at 150°C. for eight hours after the exothermic reaction subsides. The mixture is dissolved in 200 ml. of boiling ethanol and 600 ml. of water is added. After steam distilling until about 500 ml. of distillate is obtained, the hot water layer of the residue is decanted from an oily brown liquid. Thirty grams of potassium hydroxide are added to the water solution and the solution stirred for half an hour. The water layer is cooled and 150 ml. of ether are added with shaking. The ether layer is separated and the water layer extracted with 100 ml. of ether and 50 ml. of benzene. The ether and benzene solutions are combined and the solvents

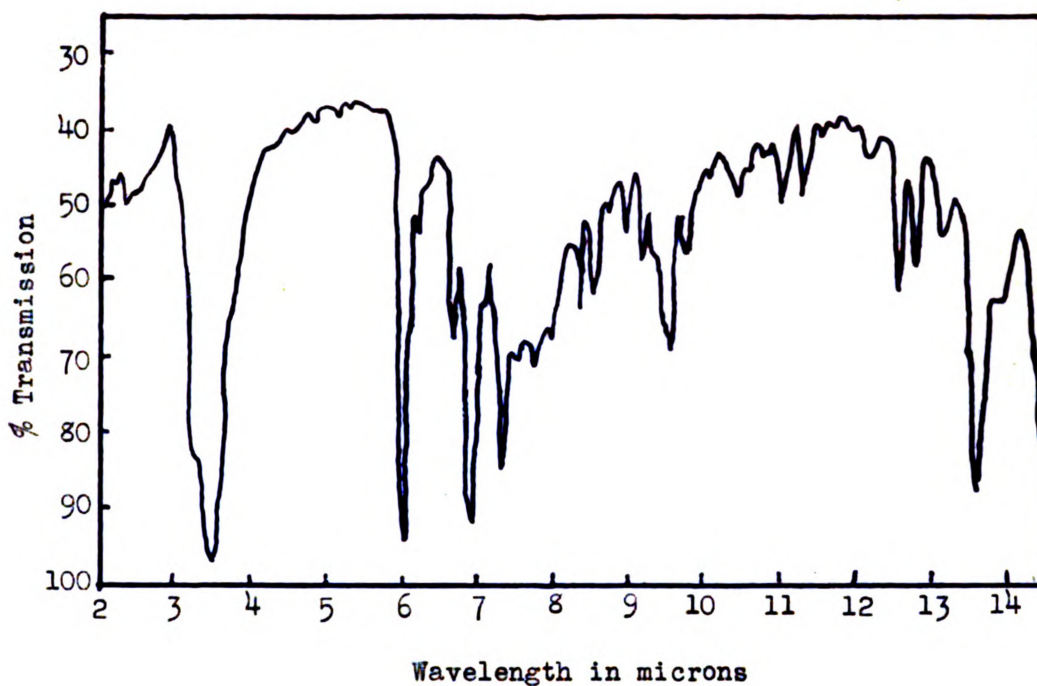


Figure III. Infrared spectrum of 1-(2-cyclohexylethyl)-4-benzyl-5-iminotetrazoline hydrochloride from 1-(2-cyclohexylethyl)-5-aminotetrazole. (Nujol mull)

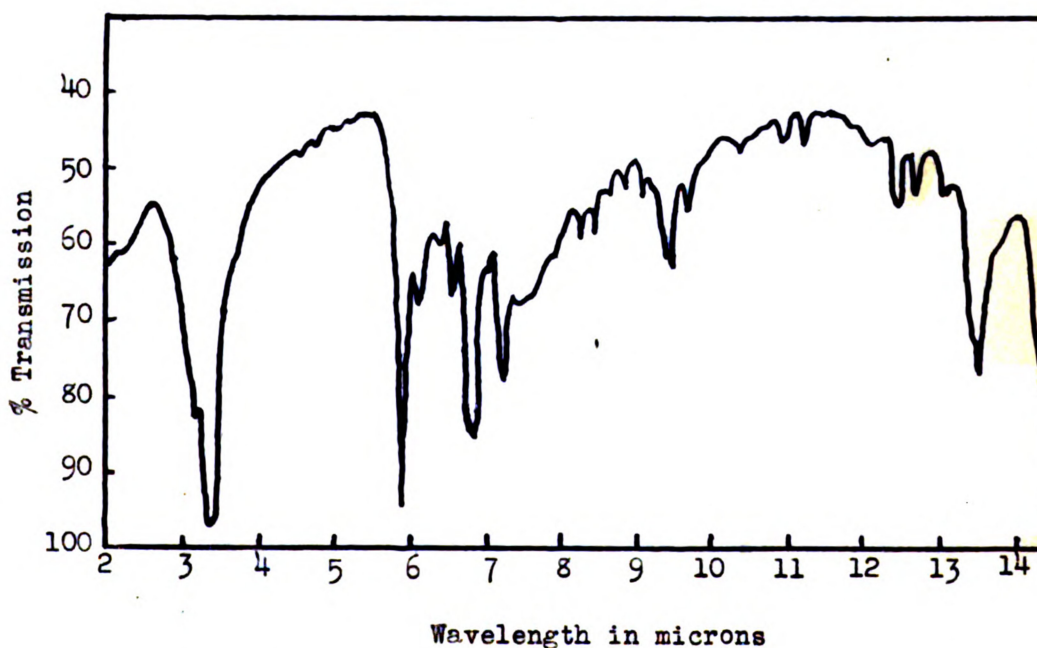


Figure IV. Infrared spectrum of 1-(2-cyclohexylethyl)-4-benzyl-5-iminotetrazoline hydrochloride from 1-benzyl-5-aminotetrazole. (Nujol mull)

evaporated. The residue is dissolved in 100 ml. of 95% ethanol and 50 ml. of water. A small amount of an insoluble product is formed when 30 ml. of concentrated hydrochloric acid have been added and is filtered off before the hydrochloride precipitates. The crude hydrochloride is redissolved by heating the suspension. The hot solution is filtered and chilled with an ice-water bath. The solid so obtained is filtered and dried. The yield of 1-(2-cyclohexylethyl)-4-benzyl-5-iminotetrazoline hydrochloride was 4.4 g. (23%). After two recrystallizations of this product from aqueous alcohol the product melted at 209°-210°C. Mixture melting points of this product and that made by the benzylation of 2-cyclohexylethyl-5-aminotetrazole showed no depression.

Debenzylation of 1-(2-Cyclohexylethyl)-4-Benzyl-5-Iminotetrazoline Hydrochloride

The method of Birkhofer (21) and Percival (4) was used. The hydrogenolysis or debenylation is done as follows: 1-(2-cyclohexylethyl)-4-benzyl-5-iminotetrazoline hydrochloride (3.22 g., .01 mole) is dissolved in 50 ml. of ethanol. One gram of 5% palladium on charcoal is added and 50 p.s.i. of hydrogen is applied to the system for two hours with shaking in a Burgess-Farr low pressure hydrogenation apparatus. The theoretical amount of hydrogen is absorbed in half an hour. The catalyst is filtered and washed with hot ethanol. Sodium carbonate (0.5 g.) is added and the solution is concentrated. Yield of 1-(2-cyclohexylethyl)-5-aminotetrazole was 1.4 g. (71%) MP 212.5°-213.5° (uncorrected).

A mixture melting point of this product and that produced by the reaction of 2-cyclohexylethylamine, cyanogen bromide and hydrazoic acid gave no depression.

1. The first of these is the fact that the Commission has not yet received any information from the Government of the United States regarding the activities of the American Friends Service Committee in the Philippines. It is therefore requested that the Commission be kept advised of any developments in this regard.

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1. The first of these is the fact that the Commission has not yet received any information from the Government of the United States regarding the results of its investigation of the activities of the United States in the area of the Commission's jurisdiction.

Phenylthioureas Derived from 1,4-Disubstituted-5-Iminotetrazolines

One gram of the iminotetrazoline hydrochloride is mixed with 1.4 g. of potassium hydroxide in 5 ml. of water and 1 ml. of ethanol. The solution is extracted successively with 10 ml. and 5 ml. of ether. The combined ether layers are dried over sodium carbonate. After evaporating the ether the residual, liquid base is treated with half its volume of phenylisothiocyanate and the mixture is heated for 1-5 minutes on a steam bath. The crude product is washed with 5 ml. of petroleum ether and 5 ml. of 50% isopropyl alcohol. The phenylthioureas are recrystallized from 75% isopropyl alcohol.

It was necessary to cool the washed product with dry ice to cause crystallization in the preparation of the phenylthioureas derived from the 3-phenylpropyl and 2-phenylethyl substituted tetrazolines.

The addition of half a gram of Norite was necessary in purifying the derivatives of the p-nitrobenzyl, m-nitrobenzyl and 3-phenylpropyl substituted tetrazolines.

Formulae, melting points and analyses are given in Table III.

1-(2-Cyclohexylethyl)-4-Aralkyl-5-Iminotetrazolines

The iminotetrazoline bases were prepared as follows: 2 g. of the hydrochloride are treated with 1 g. of potassium hydroxide, 5 ml. of water and 20 ml. of ether. The mixture is refluxed on a steam bath until both layers are clear. After cooling, the ether layer is separated and the water layer extracted with 10 ml. of ether. The combined ether layers are dried over sodium carbonate and the ether evaporated under reduced pressure on a steam bath. The residual oils were cooled with ice or dry ice to cause crystallization when necessary. No

1. The first step in the process of the investigation is to determine the scope of the problem.

2. The second step is to identify the causes of the problem.

3. The third step is to develop a plan of action to address the problem. This plan should be based on the findings of the investigation and should take into account the resources available. The plan should also be flexible enough to allow for changes as more information is gathered. The fourth step is to implement the plan. This involves putting the plan into action and monitoring the progress. The fifth step is to evaluate the results. This involves comparing the actual results with the expected results and determining whether the plan was effective. If the plan was not effective, then the process should be repeated.

6. The sixth step is to report the findings. This involves preparing a report that summarizes the findings of the investigation and the recommendations for action. The report should be clear, concise, and easy to understand. The seventh step is to follow up on the recommendations. This involves ensuring that the recommendations are implemented and that the problem is resolved.

8. The eighth step is to review the process. This involves evaluating the effectiveness of the investigation process and making any necessary improvements.

1. (a) The first step in the process of the investigation is to determine the scope of the problem.

The first step in the process of the investigation is to determine the scope of the problem. This involves identifying the problem and determining its extent. The second step is to identify the causes of the problem. This involves gathering information about the problem and analyzing it to determine the causes. The third step is to develop a plan of action to address the problem. This plan should be based on the findings of the investigation and should take into account the resources available. The plan should also be flexible enough to allow for changes as more information is gathered. The fourth step is to implement the plan. This involves putting the plan into action and monitoring the progress. The fifth step is to evaluate the results. This involves comparing the actual results with the expected results and determining whether the plan was effective. If the plan was not effective, then the process should be repeated.

TABLE III

Phenylthioureas Derived from 1-(2-Cyclohexylethyl)-4-Aralkyl-5-Iminotetrasolines



R	Formula	MP, °C	χ_d		χ_M		χ_{OL}	
			Calc.	Found	Calc.	Found	Calc.	Found
Benzyl	$C_{23}H_{28}N_6S$	139.0	139.5	19.98	20.04	7.62	7.34	-
o-Chlorobenzyl	$C_{23}H_{27}ClN_6S$	117.5	118.5	18.47	18.69	7.05	7.04	7.79
p-Chlorobenzyl	$C_{23}H_{27}ClN_6S$	128.0	128.5	18.47	18.64	7.05	7.06	7.79
2,4-Dichlorobenzyl	$C_{23}H_{26}Cl_2N_6S$	115.0	115.5	17.17	17.34	6.55	6.63	14.49
3,4-Dichlorobenzyl	$C_{23}H_{26}Cl_2N_6S$	144.0	145.0	17.17	17.25	6.55	6.58	14.49
p-Nitrobenzyl	$C_{23}H_{27}N_7O_2S$	133.5	134.5	21.06	21.02	6.89	6.88	-
m-Nitrobenzyl	$C_{23}H_{27}N_7O_2S$	129.0	129.5	21.06	21.24	6.89	7.01	-
3-Phenylpropyl	$C_{25}H_{32}N_6S$	112.5	113.5	18.73	18.67	7.15	7.08	-
2-Phenylethyl	$C_{24}H_{30}N_6S$	86.5	87.0	19.34	19.49	7.38	7.17	-

Analyses by Micro-Tech. Laboratories, Skokie, Illinois.

*Uncorrected

1. The first part of the document is a list of names and addresses of the members of the committee.

1.	Mr. J. H. Smith	123 Main St.	Springfield, Mass.
2.	Mr. J. H. Smith	123 Main St.	Springfield, Mass.
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20.	Mr. J. H. Smith	123 Main St.	Springfield, Mass.

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could be ascertained from the investigation conducted in the
 laboratory. (The Bureau was unable to identify the 2,4,6-trinitro-
 benzene and the 2,4-dinitrobenzene identified in the laboratory.
 Petroleum ether was used to remove the benzene, 2,4-dinitro-
 benzene and 2,4,6-trinitrobenzene from the mixture.
 Benzene, 2,4-dinitrobenzene, and 2,4,6-trinitrobenzene were
 identified in the mixture.

TABLE IV

1-(2-Cyclohexylethyl)-4-Aralkyl-5-Iminotetrazolines



R	Formula	MP (a) °C	C		H		N		Cl	
			Calc.	Found	Calc.	Found	Calc.	Found	Calc.	Found
Benzyl	$C_{16}H_{23}N_5$	120.0	121.0	67.33	-	8.12	-	24.54	-	-
o-Chlorobenzyl	$C_{16}H_{22}ClN_5$	58.0	59.0	60.08	60.41	6.93	7.05	21.90	21.72	11.09 11.26
p-Chlorobenzyl	$C_{16}H_{22}ClN_5$	52.5	53.5	60.08	59.89	6.93	6.78	21.90	21.73	11.09 11.32
2,4-Dichlorobenzyl	$C_{16}H_{21}Cl_2N_5$	69.5	70.5	54.24	54.13	5.98	5.92	19.77	19.90	20.02 20.11
3,4-Dichlorobenzyl	$C_{16}H_{21}Cl_2N_5$	94.5	95.0	54.24	54.33	5.98	6.05	19.77	19.76	20.02 20.02
p-Nitrobenzyl	$C_{16}H_{22}N_6O_2$	108.0	109.0	58.16	58.13	6.71	6.91	25.44	25.59	- -
m-Nitrobenzyl	$C_{16}H_{22}N_6O_2$	83.5	84.5	58.16	58.43	6.71	6.68	25.44	25.30	- -
3-Phenylpropyl	$C_{18}H_{27}N_5$	(b)	68.97	-	8.68	-	22.35	-	-	-
2-Phenylethyl	$C_{17}H_{25}N_5$	50.0	50.5	68.19	68.18	8.42	8.23	23.39	23.23	- -

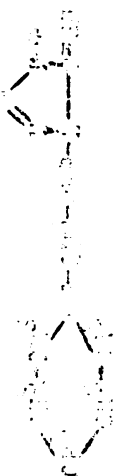
Analyses by Micro-Tech. Laboratories, Skokie, Illinois.

(a) Uncorrected.

(b) Could not be obtained as a solid.

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1. The first of the two main parts of the paper is devoted to a study of the properties of the function $f(x)$ defined by the equation $f(x) = \int_0^x f(t) dt$. It is shown that $f(x)$ is a continuous function of x and that it satisfies the differential equation $f'(x) = f(x)$. The second part of the paper is devoted to a study of the properties of the function $g(x)$ defined by the equation $g(x) = \int_0^x g(t) dt$. It is shown that $g(x)$ is a continuous function of x and that it satisfies the differential equation $g'(x) = g(x)$.

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SUMMARY

2020-2021

1. The preparation and properties of a new monosubstituted 5-amino-tetrazole have been described.
2. The preparation and properties of a series of 1-(2-cyclohexylethyl)-4-alkyl-5-aminotetrazolines and their hydrochlorides have been described.
3. The monoalkylation of a 1-substituted-5-aminotetrazole to give a 1-~~4~~-disubstituted-5-aminotetrazoline has been discussed.
4. A proof of structure for the 1-(2-cyclohexylethyl)-5-aminotetrazole has been described.

1. The production and distribution of a new commodity is described.

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1. J. H. Van Vleet, *Journal of the National Medical Association*, 44: 100, 1950.

2. J. H. Van Vleet, *Journal of the National Medical Association*, 44: 100, 1950.

3. J. H. Van Vleet, *Journal of the National Medical Association*, 44: 100, 1950.

4. J. H. Van Vleet, *Journal of the National Medical Association*, 44: 100, 1950.

5. J. H. Van Vleet, *Journal of the National Medical Association*, 44: 100, 1950.

6. J. H. Van Vleet, *Journal of the National Medical Association*, 44: 100, 1950.

7. J. H. Van Vleet, *Journal of the National Medical Association*, 44: 100, 1950.

8. J. H. Van Vleet, *Journal of the National Medical Association*, 44: 100, 1950.

9. J. H. Van Vleet, *Journal of the National Medical Association*, 44: 100, 1950.

10. J. H. Van Vleet, *Journal of the National Medical Association*, 44: 100, 1950.

LITERATURE CITED

1. J. H. Van Vleet, *Journal of the National Medical Association*, 44: 100, 1950.

2. J. H. Van Vleet, *Journal of the National Medical Association*, 44: 100, 1950.

3. J. H. Van Vleet, *Journal of the National Medical Association*, 44: 100, 1950.

4. J. H. Van Vleet, *Journal of the National Medical Association*, 44: 100, 1950.

5. J. H. Van Vleet, *Journal of the National Medical Association*, 44: 100, 1950.

6. J. H. Van Vleet, *Journal of the National Medical Association*, 44: 100, 1950.

7. J. H. Van Vleet, *Journal of the National Medical Association*, 44: 100, 1950.

8. J. H. Van Vleet, *Journal of the National Medical Association*, 44: 100, 1950.

9. J. H. Van Vleet, *Journal of the National Medical Association*, 44: 100, 1950.

10. J. H. Van Vleet, *Journal of the National Medical Association*, 44: 100, 1950.

SECRET

1. E. F. Elslager, T. F. Reutner, and J. C. Paters, Abstracts of Papers Presented at the Meetings of the American Chemical Society, Dallas, Texas, 7M (April 1956)
2. J. Thiele, Ann., 270, 54 (1892)
3. J. Thiele, and H. Ingle, Ann., 287, 232-265 (1895)
4. R. M. Herbst, and D. Percival, J. Org. Chem., 19, 439 (1954)
5. A. Hantzsch, and A. Vagt, Ann., 314, 339-369 (1901)
6. R. Stolle, Ber., 62, 1118-26 (1929)
7. R. Stolle, J. prakt. Chem., 134, 282-309 (1932)
8. R. Stolle, J. prakt. Chem., 124, 261-300 (1900)
9. R. Stolle, Ber., 55, 1237-97 (1922)
10. J. von Braun, and W. Keller, Ber., 65, 1677 (1932)
11. R. M. Herbst, C. Roberts, and E. Harvill, J. Org. Chem., 16, 139 (1951)
12. K. Schmidt, Ber., 57, 704 (1924)
13. W. Garbrecht, and R. M. Herbst, J. Org. Chem., 18, 1014 (1953)
14. R. M. Herbst, Abstracts of Papers Presented at the Meetings of the American Chemical Society, Dallas, Texas, 7M (April 1956)
15. Organic Reactions, ed., Roger Adams, et. al., John Wiley and Sons, Inc., New York (1946) Vol. III, p. 310
16. W. Garbrecht, and R. M. Herbst, J. Org. Chem., 18, 1003 (1953)
17. F. R. Benson, Chem. Revs., 41, 1 (1947)
18. Beilstein, Prager-Jacobson, B XII, p. 13
19. DuPont, Explosives Division
20. Eastman Kodak Reagent
21. L. Birkhofer, Ber., 75, 429 (1942)
22. K. Wilson, unpublished work

1. J. L. ... (1911) ...
2. ... (1912) ...
3. ... (1913) ...
4. ... (1914) ...
5. ... (1915) ...
6. ... (1916) ...
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17. ... (1927) ...
18. ... (1928) ...
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20. ... (1930) ...
21. ... (1931) ...
22. ... (1932) ...

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