iodide analysis[4] gave 72.4% bromine (theory 71.4%), showing all four bromines active.

Some Factors Influencing the Rate of Formation of Naphthalene Tetrabromide.—When 0.01 mole of naphthalene in 20.00 ml. of carbon tetrachloride was brominated under anhydrous conditions with 0.01 mole of bromine in 10.00 ml. of the same solvent in a darkened laboratory at room temperature, 5.1 ± 1% of the active bromine was found by the sodium iodide analysis. The presence of 0.029 g. of iodine did not change this percentage. Photobromination of 0.01 mole of the hydrocarbon in 20.00 ml. of carbon tetrachloride on a water-bath and under a 6″ mercury arc at 3″ distance with 10.00 ml. of molar bromine-carbon tetrachloride solution, during three hours, resulted in the formation of 21.1 ± 2% of active bromine; cooling the reaction to 0° and using a 2″ arc at 2″ for seventy minutes gave 61.0 ± 5% of active bromine.

With the aid of a Universal Spectrophotometer, Model 14, the effect of wave length on the formation of naphthalene tetrabromide has been determined. When 0.005 mole of naphthalene in 5.00 ml. carbon tetrachloride was brominated for twenty minutes at 41° with 10.00 ml. of half molar bromine solution in the same solvent under anhydrous conditions at 6000, 5250, 3700 Å. and no irradiation, the percentages of active bromine by sodium iodide analyses were respectively, 23.8 ± 0.2, 11.0 ± 1, 1.3 and 0%.

Rates of Formation of Bromine Addition Compounds with Other Condensed Ring Hydrocarbons.—The rates of formation of bromine addition compounds under dark-room conditions were carried out on 0.01 mole quantities of the hydrocarbons in 20.00 ml. carbon tetrachloride at 0° for a period of eighteen hours; 10.00 ml. of bromine-carbon tetrachloride solutions (molar) were added under anhydrous conditions. Sodium iodide analyses yielded the following percentages of active bromine: phenanthrene 55.2 ± 3%, naphthalene 11.2 ± 0.1% and diphenylmethane 2.0 ± 2%. Fluorene, benzene and diphenyl gave no active bromine even though the solutions were kept cold to prevent decomposition of any addition compounds during the treatment with sulfite and evaporation of the carbon tetrachloride. The addition of 0.029 g. iodine to the above reactions did not change by more than 2% the rates of bromine addition.

Since anthracene is insoluble in carbon tetrachloride 0.005 mole of this hydrocarbon was dissolved in 50.00 ml. of carbon disulfide, and the dark room brominations made with 10.00 ml. of half-molar bromine in the same solvent. Naphthalene solutions of the same strength were used for comparison. The results showed the presence of 13.0 ± 1.2% bromine with anthracene but none with naphthalene.

The photobrominations were carried out in carbon tetrachloride under anhydrous conditions at 0° with a 2″ arc at 2″ for sixty minutes; sodium iodide analyses indicated the following active bromine present: phenanthrene 84.1 ± 2%, naphthalene 55.3%, diphenyl 1% and benzene 1%. When 0.005 mole of anthracene and naphthalene were photobrominated in 50.00 ml. of carbon disulfide under similar conditions, they gave 74.0 ± 2% and 69.0% active bromine, respectively. These results demonstrate conclusively that larger amounts of active bromine addition products of the hydrocarbons are formed in photobromination than in dark room bromination.

Acknowledgments.—The authors are happy to acknowledge the helpful suggestions made by Dr. E. Emmet Reid in this research. Financial assistance was received from the Office of Naval Research.

Summary

1. Measurements have been made on the rates of formation of active bromine addition compounds under photo and dark room brominations of some condensed ring hydrocarbons.

2. Naphthalene tetrabromide has been prepared in 30% yield by photobromination.

GREENVILLE, SOUTH CAROLINA RECEIVED JUNE 6, 1949

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[4] Sampey, Blitch and King, THIS JOURNAL, **70**, 2606 (1948).

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF THE JOHNS HOPKINS UNIVERSITY]

The Structure of Diphenylthiocarbazone (Dithizone)[1]

BY ALSOPH H. CORWIN AND GEORGE R. JACKSON[2,3]

Introduction

The compound diphenylthiocarbazone, known as "dithizone," is well known in analytical chemistry because of its colorimetric reactions with traces of metals. A search of the literature will show, however, that no direct attempt has been made to prove the structure arbitrarily assigned to it by Emil Fischer.[4a,b]

Because of increasing interest in dithizone derivatives, it was deemed advisable to attempt a structural determination of diphenylthiocarbazide, from which would follow the structure of its oxidation product, dithizone.

Diphenylthiocarbazide is prepared by the reaction of phenylhydrazine with carbon disulfide. In ether or benzene, the phenylhydrazine salt of phenyldithiocarbazic acid precipitates.[5,6] Heating this salt to 90–100° drives off hydrogen sulfide and leaves behind diphenylthiocarbazide. Treating this with alcoholic potassium hydroxide produces dithizone, for which the following equation has been proposed[4a]

$$2C_6H_5NHNH\underset{\overset{\|}{S}}{C}NHNHC_6H_5 \longrightarrow$$

I

$$C_6H_5N{=}N\underset{\overset{\|}{S}}{C}NHNHC_6H_5 + C_6H_5NH_2 + C_6H_5NHNH\underset{\overset{\|}{S}}{C}NH_2$$

II

III

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[1] From the doctoral dissertation of G. R. Jackson, The Johns Hopkins University.

[2] Chemical Foundation Fellow, 1942–1943; Standard Oil Company of Indiana Fellow, 1946–1947.

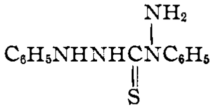
[3] Present address: Chemistry Department, Western Reserve University, Cleveland, Ohio.

[4] (a) E. Fischer, *Ann.*, **190**, 114 (1878); (b) **212**, 320 (1882).

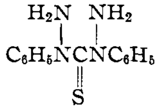
[5] Grummitt and Stickle, *Ind. Eng. Chem., Anal. Ed.*, **14**, 953 (1942).

[6] Billman and Cleland, THIS JOURNAL, **65**, 1300 (1943).

On the basis of analysis, structure I was assigned to diphenylthiocarbazide. Structures IV and V should be considered as alternatives, however.


$C_6H_5NHNH\underset{\underset{S}{\|}}{C}\overset{\overset{NH_2}{|}}{N}C_6H_5$

IV


$C_6H_5\overset{\overset{H_2N}{|}}{N}\underset{\underset{S}{\|}}{C}\overset{\overset{NH_2}{|}}{N}C_6H_5$

V

These differ from Fischer's structure with respect to the point of attachment of the nitrogens to the carbon. Compound IV would be formed by the α,β condensation of carbon disulfide with phenylhydrazine, compound V by the β,β condensation.

The structural investigation of diphenylthiocarbazide (I) is divided into two parts; (1) the reduction to phenylthiosemicarbazide and (2) the investigation of the structure of the latter compound which has been formulated as III but for which the alternative β formulation has not been excluded.

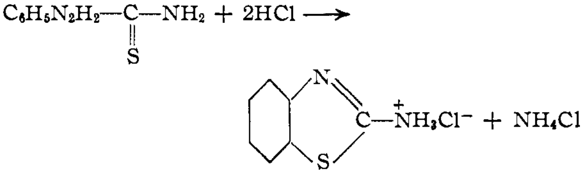
Upon reduction with stannous chloride and hydrochloric acid,[7] diphenylthiocarbazide gave one mole of aniline and one mole of phenylthiosemicarbazide. The reduction was also performed catalytically, using Raney nickel. The reaction stopped after one mole of hydrogen was consumed and additional shaking had no effect. The products were again aniline and phenylthiosemicarbazide.

Since compound V cannot yield the S=C—NH_2 grouping on reduction, the reductions show that one half of the diphenylthiocarbazide molecule has the structure C_6H_5—NH—NH—C, an observation which excludes formula V. The problem is thus reduced to that of ascertaining the structure of phenylthiosemicarbazide.

Phenylthiosemicarbazide was prepared from phenylhydrazine hydrochloride and ammonium thiocyanate according to the procedure given by Fischer and Besthorn,[8] but since the compound obtained from the reduction and the synthetic product both decomposed on heating, mixed melting points could not be used to establish identity. Proof of identity was obtained by the mixed solubility method, using the absorption in the ultraviolet as the criterion of solubility.

Reductions of phenylcarbazide with tin in hydrochloric acid, zinc in glacial acid, zinc in hydrochloric acid and sodium hydrosulfite were tried, but only starting material was recovered in each case.

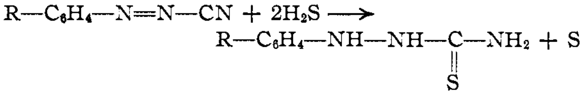
The acid used in the stannous chloride reductions was approximately 5 normal. It was found that when concentrated hydrochloric acid was used, with or without the reducing agent, 2-aminobenzothiazole hydrochloride was formed according to the equation



Thus it was found that strong reducing agents had no effect on phenylthiosemicarbazide, and concentrated hydrochloric acid converted it to 2-aminobenzothiazole, which did not conclusively prove the structure. The resistance of this class of hydrazine derivatives toward reduction will be investigated further.

Aqueous cyanide solutions will react with diazonium salts to precipitate colored compounds referred to as diazocyanides, the reaction differing from the normal coupling reaction in that the solution must remain acid during the addition.[9,10] It has generally been accepted that the structure of the aromatic diazocyanides is of the form R—C_6H_4—N=N—CN, and that labile and stable isomers which have been isolated represent *syn* and *anti* forms of this general structure.

The substituted benzene diazocyanides are easily converted to the thioamides by treatment with hydrogen sulfide. Either the *syn* or the *anti* form of the diazocyanide may be used


$$R—C_6H_4—N=N—CN + 2H_2S \longrightarrow R—C_6H_4—NH—NH—\underset{\underset{S}{\|}}{C}—NH_2 + S$$

When a diazotized solution of aniline was treated with aqueous potassium cyanide at −5° a red, unstable oil was obtained. The ether extract was treated with hydrogen sulfide. The product obtained melted with decomposition at 200° and had all the physical properties of the phenylthiosemicarbazide obtained from the reduction of diphenylthiocarbazide.

If the structure of benzenediazocyanide is accepted as $C_6H_5N=NCN$, the C–N–N–C grouping is established. From the reaction with H_2S it follows that the structure of phenyl thiosemicarbazide is $C_6H_5NHNH\underset{\underset{S}{\|}}{C}NH_2$. This observation excludes formula IV and thus establishes Fischer's formulation of the structure of diphenylthiocarbazide.

A simple formulation of the mechanism of the condensation between phenylhydrazine and carbon disulfide is rendered improbable by the observation that this condensation does not proceed in the absence of air. It might be postulated that the catalytic effect of air is due to the fact that the essential reagent is a free radical.

To shed some light on the mechanism of the condensation, the reaction of cyanogen bromide with phenylhydrazine was studied in ether and in aqueous solution at different acidities.

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[7] Fierz-David, "Technologie der Textilfasern," Julius Springer, Berlin, 1926, Vol. III, p. 660.

[8] Fischer and Besthorn, *Ann.*, **212**, 316 (1882).

[9] Gabriel, *Ber.*, **12**, 1637 (1879).

[10] Hantzsch and Schultze, *ibid.*, **28**, 666 (1895).

Pelazzari and Tivoli[11] have shown that cyanogen halides react with phenylhydrazine to give cyanophenylhydrazines. In ether β-cyanophenylhydrazine is formed. This is an unstable oil which forms a reasonably stable hydrochloride. Ammonium hydrosulfide converts this to β-phenylthiosemicarbazide. Water, on the other hand, converts it to β-phenylsemicarbazide. We have established the identity of the β-phenylthiosemicarbazide by intercomparison with material prepared according to Fischer's method.[8]

If the reaction between phenylhydrazine and cyanogen bromide is carried out in aqueous solution using a twofold excess of phenylhydrazine, two products are formed. The first is β-cyanophenylhydrazine. The main product is an isomer, α-cyanophenylhydrazine. This reacts with ammonium hydrosulfide to give α-phenylthiosemicarbazide, decomposing at 153°, and with water to give α-phenylsemicarbazide.

We have found that both α and β substitutions can occur in aqueous solution. At *p*H 0.6 the yield was quite low but more than half of the product was β-phenylsemicarbazide obtained from the β-isomer and less than half was α. At *p*H 3.5 the yield was higher and the proportion was much greater in favor of the α-isomer. At *p*H 5.6 the yield of α-isomer appears to be still higher but the results are complicated by the fact that a secondary reaction, perhaps polymerization, sets in. These condensations must be regarded as anomalous since the β-position of phenylhydrazine should be the more reactive in the case of the free base while increasing salt formation should either block the reaction or should favor condensation in the α-position. The contrary results observed show the need for an investigation of the mechanism of the reaction.

Experimental

Preparation and Purification of Diphenylthiocarbazide.—The procedure given by Grummitt and Stickle[5] was followed for the preparation of crude diphenylthiocarbazide. When crystallized from alcohol in the manner directed, the crystals obtained are slate-gray in color. It is necessary to wash these crystals with three portions of benzene to obtain an "almost colorless product." Attempts to purify the slate-gray material by means of further recrystallizations from alcohol do not give a better looking product.

A much more satisfactory method of purification consists of heating 95% alcohol to boiling, pouring it on the crude carbazide, and filtering hot. On cooling, the crystals are invariably snow white, except if one uses as starting material the slate-gray product referred to above. This method consumes more alcohol than the other but a product suitable for analysis is obtained.

Anal. Calcd. for $C_{13}H_{14}N_4S$: C, 60.41; H; 5.47. Found: C, 60.35; H, 5.43.

It was found that the crude diphenylthiocarbazide consists of two materials, one of which is extremely soluble in alcohol. This can be extracted from the main product by boiling with benzene, in which diphenylthiocarbazide is very slightly soluble. The suspension is filtered hot and on cooling the second product comes out as a white, amorphous mass. The yield averaged 10 g. for 54 g. of phenylhydrazine. Further investigations on this substance are in progress.

Reduction of Diphenylthiocarbazide with Stannous Chloride.—A solution of 10 g. of $SnCl_2 \cdot 2H_2O$ in 20 cc. of concentrated hydrochloric acid was added to a mixture of 10 g. of diphenylthiocarbazide and 60 cc. of water. This was stirred for fifteen minutes at room temperature, heated on the steam-bath for three hours with stirring, and then allowed to cool. The crystalline product was filtered, mixed with 50 cc. of water and filtered again. This was repeated with another 50-cc. portion of water, and finally the product was washed with 25 cc. of water. The crystals remaining were sucked as dry as possible and recrystallized once from 95% ethanol, to obtain 6.0 g. (95% of theoretical) of material melting with decomposition sharply at 200°.

To recover the aniline, hydrogen sulfide was passed into the combined filtrates from above until precipitation ceased, and the tin sulfides removed and washed with water containing a little hydrochloric acid. Ammonium sulfide was then added to complete the precipitation of tin. This was filtered and washed as before. The filtrate was made strongly basic and extracted five times with 50–75 cc. portions of ether. The ether was then removed from the combined extracts and finally pale yellow aniline was collected, b. p. 183–183.5°. This was acetylated to give a derivative melting at 113.5–114°. The yield of aniline was 3.1 cc. or 86% of the theoretical.

Catalytic Hydrogenation.—Three cubic centimeters of Raney nickel catalyst was added to 4 g. of pure diphenylthiocarbazide in 200 cc. of 95% ethanol. The diphenylthiocarbazide did not dissolve completely. The suspension was placed on the shaker and hydrogen was introduced under a pressure of 50 lb. p.s.i. After forty-five minutes no hydrogen had been absorbed. Five cubic centimeters more catalyst was added at this point and shaking was resumed. Hydrogen was absorbed rapidly and after two hours the theoretical amount for one mole had been taken up. The hydrogenation was allowed to continue overnight but no more hydrogen was absorbed.

The catalyst was filtered off and phenylthiosemicarbazide was isolated as a white crystalline solid melting with decomposition at 200°. Aniline was isolated as acetanilide, m. p. 113.5–113.8°.

Spectrophotometric Identification of Phenylthiosemicarbazide.—Saturated solutions were made of the substance prepared by reduction of diphenylthiocarbazide and by synthesis from phenylhydrazine and ammonium thiocyanate by mixing 350 mg. of material with 10 cc. of 95% ethanol. A solution saturated with respect to both compounds was also made by mixing 350 mg. of each compound with 10 cc. of 95% alcohol. These were allowed to stand for three hours before measurements were begun, to insure complete equilibration. The absorptions of the three solutions at 312 mμ were 29.2, 29.0 and 29.4, proving the identity of the two compounds.

Attempted Reductions of Phenylthiosemicarbazide. 1. **Tin and Hydrochloric Acid.**—One gram of phenylthiosemicarbazide was added to a solution of 10 cc. of concentrated hydrochloric acid and 10 cc. of water. To this was added 2 g. of mossy zinc and the mixture heated on the steam-bath. The phenylthiosemicarbazide did not go into solution and was recovered on cooling.

2. **Zinc and Glacial Acetic Acid.**—One gram of phenylthiosemicarbazide was added to 10 cc. of glacial acetic acid and warmed until it went into solution. This was heated on the steam-bath for two hours with zinc dust. The excess zinc dust was filtered off and water added to the acetic acid solution, at which time almost 1 g. of starting material crystallized.

3. **Zinc and Hydrochloric Acid.**—One gram of phenylthiosemicarbazide was mixed with 10 cc. of concentrated hydrochloric acid and 10 cc. of water, and zinc dust added. Hydrogen was evolved but the phenylthiosemicarbazide was recovered unchanged.

4. **Sodium Hydrosulfite.**—A mixture of 1 g. of phenylthiosemicarbazide, 5 cc. of water, and 2 g. of sodium hydrosulfite was heated on the steam-bath for two hours, the

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[11] Pelazzari and Tivoli, *Gazz. chim. ital.*, **22**, 226 (1892); Pelazzari, *ibid.*, **37**, 611 (1907).

phenylthiosemicarbazide remaining suspended in the colorless solution the entire time. When cooled, washed with water, and dried, more than 0.9 g. of starting material was recovered.

Preparation of 2-Aminobenzothiazole from Phenylthiosemicarbazide.—Four grams of phenylthiosemicarbazide was added to 40 cc. of concentrated hydrochloric acid and heated on the steam-bath for two hours. On cooling, the hydrochloride crystallized. The free base obtained by neutralizing the hydrochloride was recrystallized from water to give white shining platelets which melted reversibly at 130–131°. Warming with acetic anhydride and recrystallizing from alcohol produced thick prisms melting sharply at 187°. The acetyl derivative of 2-aminobenzothiazole is reported as melting at 186–187° and 2-aminobenzothiazole as melting at 130–131°.[12]

Preparation of 1-Phenylthiosemicarbazide from Benzenediazocyanide.—Almost water-white aniline was prepared by fractional distillation of aniline which had been twice steam distilled, collecting the fraction coming over at 181.5–182° (uncor.). A mixture of 28 cc. of this aniline, 90 cc. of concentrated hydrochloric acid and 180 cc. of water was cooled to −5° and a solution of 21 g. of sodium nitrite in 60 cc. of water slowly added until diazotization was complete. Then 350 cc. of ether that had been freshly distilled from a weakly acidic ferrous sulfate solution to remove peroxides was slowly added, keeping the temperature below 0°. To this was slowly added a solution of 39 g. of potassium cyanide in 75 cc. of water, the mixture being well stirred and the temperature maintained below 0°. When addition was complete, the mixture was poured into a large separatory funnel and the aqueous portion separated and discarded. Preliminary tests showed that the crude diazocyanide decomposed on warming to room temperature so it was not isolated. The ether extract was quickly cooled in an ice-bath and hydrogen sulfide passed through. The red solution turned dark very slowly, and then suddenly changed to light straw color. The crude precipitate melted with decomposition over a wide range from 185–195°. After recrystallizing from alcohol once a pure product was obtained which melted with decomposition sharply at 200°.

The same product was obtained when the ether extract from the diazonium mixture was dried with sodium sulfate before introducing the hydrogen sulfide, and since there was a considerable loss due to adsorption on the sodium sulfate, this step was omitted. The best yield of pure 1-phenylthiosemicarbazide was approximately 20 g., or 40% of theoretical.

Reaction between Phenylhydrazine and Cyanogen Bromide at Various Acidities. 1. **At *p*H 0.6.**—A mixture of 2.8 g. of phenylhydrazine hydrochloride (0.02 mole), 5 g. of sodium bisulfate and 3 g. of sodium sulfate was dissolved in 50 cc. of water to give a solution whose *p*H was observed to be 0.6. Two and two-tenths grams (0.02 mole) of cyanogen bromide in 5 cc. of 95% ethanol was added slowly. After standing for fifteen minutes the solution was warmed slightly and then allowed to cool. A crop of 0.4 g. of α-cyanophenylhydrazine in the form of thin white platelets was obtained. The filtrate was again warmed for a few minutes and then thoroughly cooled. 0.4 g. of the hydrolysis product of β-cyanophenylhydrazine, β-phenylsemicarbazide, was obtained. On evaporation an additional 0.2 g. of this substance was obtained.

2. **At *p*H 3.5.**—A mixture of 2.8 g. of phenylhydrazine hydrochloride and 15 g. of sodium sulfate was dissolved in 100 cc. of water giving a solution whose *p*H was 3.5. Two and two-tenths grams of cyanogen bromide in 5 cc. of 95% ethanol was added slowly. After standing four hours the crystals of α-cyanophenylhydrazine were removed, washed with water and dried, yield 0.8 g. The filtrate was evaporated to two-thirds of its original volume and allowed to cool. The precipitate was 1.0 g. additional α-isomer. Upon further evaporation and cooling 0.7 g. of β-phenylsemicarbazide was obtained.

3. **At *p*H 5.6.**—A mixture of 2.8 g. of phenylhydrazine hydrochloride and 15 g. of sodium acetate was dissolved in 100 cc. of water to give a solution whose *p*H was 5.6. Two and two-tenths grams of cyanogen bromide was added as before. An abundant white precipitate of α-cyanophenylhydrazine came down almost immediately. Within a few minutes this started to turn yellow and after thirty minutes it was almost completely transformed to tar.

Reaction of Phenylhydrazine with Carbon Disulfide with and without Air.—A solution of 10 cc. of phenylhydrazine in 40 cc. of benzene was added to each of two 100-cc. three-neck flasks equipped with stirrers and condensers. Three and two-tenths cubic centimeters of carbon disulfide was dropped into each with stirring, producing a light-yellow, practically solid sludge. The third neck of flask A was then plugged but air was not excluded. Nitrogen was introduced through the third neck of flask B to remove air. Both were heated on steam cones and B was continually swept with nitrogen. It was necessary to make periodic additions of benzene to B to compensate for evaporation. Parallel observations are recorded.

Time, min.	Flask A (with air)	Flask B (with nitrogen)
15	Thick suspension	Yellow solution
30	H_2S being evolved	Green color. Trace of H_2S
35	H_2S	No H_2S. Removed to icebox
50	Solution H_2S still evolved	Cooling overnight gave no ppt.
120	H_2S test negative, heavy ppt.; removed to icebox; obtained solid mass of diphenylthiocarbazide	Next day air admitted, white ppt. formed slowly

Summary

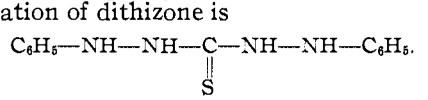
1. Diphenylthiocarbazide has been reduced catalytically and chemically to produce aniline and phenylthiosemicarbazide, proving that one half of the molecule has the grouping C_6H_5—NH—NH—C.

2. Attempts to reduce phenylthiosemicarbazide to thiourea and aniline were unsuccessful.

3. 1-Phenylthiosemicarbazide obtained from benzene diazocyanide and hydrogen sulfide was found to be identical to the phenylthiosemicarbazide obtained from the reduction of diphenylthiocarbazide.

4. Assuming that benzene diazocyanide is $C_6H_5N{=}N{-}CN$, it follows that phenylthiosemicarbazide and therefore diphenylthiocarbazide have the C—N—NC grouping of benzene diazocyanide.

5. From this evidence it is concluded that the structure of diphenylthiocarbazide used in the preparation of dithizone is



$$C_6H_5{-}NH{-}NH{-}\underset{\underset{S}{\|}}{C}{-}NH{-}NH{-}C_6H_5.$$

BALTIMORE 18, MD. RECEIVED APRIL 18, 1949

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[12] Hugershoff, *Ber.*, **36**, 3134 (1903).