hydrogenation, the most active form being produced when the fusion temperature is 600°.

2. The importance of knowing the exact purity of the catalyst used for the reductions has been demonstrated. Ferrous chloride accelerates the reduction of aromatic aldehydes which contain a free hydroxyl group but not those which do not have this group.

3. The importance of considering the nature of the substances to be reduced when studying promoters has been demonstrated. The reduction of successive portions of benzaldehyde is accelerated by shaking with oxygen. On the other hand, the reduction of maleic acid is not so accelerated but is actually slowed.

4. Comparison of platinum and palladium oxides as catalysts in the reduction of various aromatic aldehydes and maleic acid shows that they have approximately the same activity.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, YALE UNIVERSITY]

RESEARCHES ON AMINES. IX. SOME CHEMICAL PROPERTIES OF AMINO-ACETO-PHENYLANILIDE

BY ERWIN B. KELSEY

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In previous publications,[1] the writer, with A. J. Hill, described the preparation of isothiocyano-acetanilide and certain of its nucleus substituted derivatives. It has been shown that such mustard oils are unstable and rearrange at once into substituted normal thiohydantoins.

$$RNHCOCH_2NCS \longrightarrow R\overline{N{-}CS{-}NHCH_2CO}.$$

This paper deals with the attempts to synthesize isothiocyano-aceto-ethylanilide, $C_6H_5N(C_2H_5)COCH_2NCS$, and isothiocyano-aceto-phenylanilide, $(C_6H_5)_2NCOCH_2NCS$, since in mustard oils of this type, normal thiohydantoin formation through intramolecular change is rendered impossible.

The methods of synthesis described in the previous papers[2] were again employed, and the chloro-anilides successively converted into the corresponding primary amine, dithiocarbamate, and carbo-ethoxy-dithiocarbamate. Although the writer was unable to obtain either of the isothiocyanates named above, certain unusual and interesting facts have been brought to light, as follows.

1. Chloro-aceto-ethylanilide reacts rapidly with aqueous or alcoholic

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[1] Johnson, Hill and Kelsey, THIS JOURNAL, **42,** 1711 (1920). Hill and Kelsey, *ibid.*, **44,** 2357 (1922).

[2] Hill and Kelsey, *ibid.*, **42,** 1704 (1920).

ammonia yielding only the tertiary amine—the tri-(phenylethylamide) of triglycol-amidic acid: $(C_6H_5N(C_2H_5)COCH_2)_3N$.

2. Carbo-ethoxy-amino-aceto-phenylanilide does not decompose in the usual manner to yield the isothiocyano derivative. Instead, the breakdown is much more profound, and definite products could not be isolated.

3. Amino-aceto-phenylanilide dithiocarbamate is very unstable, and rapidly loses hydrogen sulfide, forming the thio-urea. But the mercury and silver salts of this acid are extremely stable, and decomposed only at such elevated temperatures that no definite products were isolated.

Experimental Part

The Preparation of Chloro-aceto-ethylanilide, $C_6H_5C_2H_5NCOCH_2Cl$ and Chloro-aceto-phenylanilide, $(C_6H_5)_2NCOCH_2Cl$.—One molecular proportion of the appropriate amine was dissolved in a convenient quantity of benzene and a slight excess of 2 *N* sodium hydroxide solution was then added, followed by 1.25 molecular proportions of chloro-acetyl chloride. The latter was introduced drop by drop with vigorous agitation, the mixture being kept well cooled. Chloro-aceto-ethylanilide was soluble in benzene and was obtained by tapping off the benzene layer, evaporating the benzene, and distilling the residual oil under reduced pressure. The anilide was obtained as a colorless, sirupy liquid boiling at 188° (35 mm.); yield, 89%. In a cooling mixture it partly solidified to white needles.

Analyses. Calc. for $C_{10}H_{12}ONCl$: N, 7.07. Found: 7.14, 7.13.

Chloro-aceto-phenylanilide was also soluble in warm benzene and was obtained by tapping off the benzene layer, evaporating to small volume and letting the anilide crystallize. It usually separated as very large, red crystals with a blue fluorescence. After recrystallization from alcohol it was obtained as colorless plates; yield, about 60%.

The Action of Aqueous and of Alcoholic Ammonia upon Chloro-aceto-ethylanilide. The Tri(phenylethylamide) of Triglycol-amidic Acid. $(C_6H_5N(C_2H_5)COCH_2)_3N$.—Twenty-five g. of chloro-aceto-ethylanilide was placed in a flask with 500 cc. of concd. aqueous ammonia. The anilide was not soluble, and after a few days began to solidify. The reaction was allowed to continue for 15 days. The solid thus obtained was purified by dissolving in alcohol and adding water, which precipitated it as a heavy, colorless oil that soon solidified to colorless crystals melting at 119°.

Analyses. Calc. for $C_{30}H_{36}O_3N_4$: N, 11.20. Found: 11.37, 10.94.

Many other runs were made, in which the concentration of the ammonia and the time of reaction were varied, but no product other than the tertiary amine was isolated. The yield was quantitative.

Thirty g. of chloro-aceto-ethylanilide was dissolved in 600 g. of alcoholic ammonia and allowed to react for 13 days. Almost all of the alcohol was then removed under reduced pressure and the residue poured into water. An oil separated which on cooling partly solidified. The crystals were filtered and dried, after which the solid melted at 89.5°. Since the amount of crystalline material was very small, no effort was made to purify it.

Analyses. Calc. for $C_{30}H_{36}O_3N_4$: N, 11.20. Found: 10.89, 10.96.

A portion of the remaining oil was carefully dried; this then contained 10.92% of nitrogen. Neither the crystals nor the oil showed any basic properties and both were unquestionably the tertiary amine previously described. Alcoholic ammonia always yielded the amine in the liquid form, which never crystallized completely.

The Action of Alcoholic Ammonia on Chloro-aceto-phenylanilide. Amino-aceto-phenylanilide. $(C_6H_5)_2NCOCH_2NH_2$.—Thirty g. of chloro-aceto-phenylanilide was treated with 1200 cc. of alcoholic ammonia (saturated at 10°), and the mixture allowed to stand at room temperature for four days. The anilide was not readily soluble in the alcoholic ammonia, but usually disappeared after 24 hours. At the end of the reaction period almost all of the alcohol was evaporated under reduced pressure and the residue poured into a large volume of water. This precipitated an oil (the secondary amine, $[(C_6H_5)_2NCOCH_2]_2NH$) which soon solidified to a gummy mass. This was filtered, and the filtrate evaporated to dryness, leaving the hydrochloride of the primary base; yield, 27 g., or 90%. It was very soluble in water and alcohol and crystallized in colorless needles. The nitrate of the amine was difficultly soluble in water and crystallized in plates melting with decomposition at 211–214°.

Analyses. Calc. for $C_{14}H_{14}ON_2.HCl$: N, 10.67. Found: 10.95, 10.85.

The free amine was obtained by dissolving the pure hydrochloride in warm water and adding a slight excess of concd. sodium hydroxide solution. This precipitated a light yellow oil heavier than water, which was removed and washed with water. This oil was very soluble in alcohol, practically insoluble in ether, chloroform, or benzene and very sparingly soluble in water. It was a strong base, rapidly changing litmus. An attempt was made to purify this base by vacuum distillation, and at 10 mm. a few cc. of distillate collected, although decomposition was marked.

Analysis. Calc. for $C_{14}H_{14}ON_2$: N, 12.39; calc. for $C_{14}H_{14}ON_2.H_2O$: 11.47. Found: 11.31.

It is noteworthy that the analysis indicates a monohydrate, even after distillation at high temperature. A sample of the oil was kept in a vacuum desiccator over sulfuric acid for two months, when it solidified to long, silky needles, which melted at 53–55°. This anhydrous base was readily soluble in ether.

Analyses. Calc. for $C_{14}H_{14}ON_2$: N, 12.39. Found: 12.49, 12.62.

The preparation of this base was many times repeated using time intervals from 4 to 20 days, without materially affecting the amount formed. The average yield of base (as the hydrochloride) was 93%.

The Di-(diphenylamide) of Diglycol-amidic Acid. $[(C_6H_5)_2NCOCH_2]_2NH.HCl$.—The gummy solid, obtained by pouring into water the partially evaporated alcoholic liquor from the experiment described above, could not be directly purified. It was readily soluble in alcohol, but did not separate. It was, therefore, dissolved in a very little alcohol, and hydrogen chloride passed into the solution. This caused the separation of the hydrochloride in glistening, white plates, which were sparingly soluble in alcohol. This salt melted, with some decomposition, at 240–245°. The average yield—from 30 g. of chloro-anilide—was 4.25 g. Although the free base could not be isolated in pure condition, it was fairly strong, as was proved by causing it to react with certain acid chlorides.

Analyses. Calc. for $C_{28}H_{25}O_2N_3.HCl$: N, 8.91. Found: 8.81, 8.81.

The Action of Aqueous Ammonia on Chloro-aceto-phenylanilide.—Ten g. of chloro-aceto-phenylanilide was placed with 200 cc. of concd. aqueous ammonia in a sealed bottle. Since the anilide is difficultly soluble in water, reaction proceeded very slowly, but after some time the substance began to lose its crystalline appearance. At the end of two years, the remaining solid was filtered off and dried. The substance was extremely soluble in alcohol, but separated as a gummy oil. On saturating the alcoholic solution with hydrogen chloride, a substance separated in glistening, white plates that melted, with some decomposition, at 240–245°, thus identifying the compound as the hydrochloride of the di-(diphenylamide) of diglycol-amidic acid, described above. The yield was nearly quantitative.

Carbo-ethoxy-amino-aceto-phenylanilide. $(C_6H_5)_2NCOCH_2NHCOOC_2H_5$.—Five g. of thoroughly dried amino-aceto-phenylanilide was suspended in benzene and 3 g. ($1^1/_8$ molecular equivalents) of ethyl chloroformate rapidly added, followed by slightly more than one molecular equivalent of 2 *N* sodium hydroxide solution. After the mixture had been agitated for a few minutes the benzene layer was tapped off and allowed to evaporate spontaneously. Six g. of a crystalline solid remained, which corresponds to a 90% yield. This solid was excessively soluble in benzene, separating in the form of long, silky needles that became quite brittle when dry. After two crystallizations the compound melted at 64–65°.

Analyses. Calc. for $C_{17}H_{18}O_3N_2$: N, 9.40. Found: 9.24, 9.16.

This condensation was tried using an ether solution of the amine. On evaporating the solvent a heavy, colorless oil was left which did not crystallize even after standing in a vacuum for a long time, or when seeded with some of the solid previously obtained. Repetitions of the preparation always yielded the oil from ether solution and the solid from benzene. The oil was not further investigated.

Aceto-amino-aceto-phenylanilide. $(C_6H_5)_2NCOCH_2NHCOCH_3$.—Five g. of thoroughly dried amino-aceto-phenylanilide was suspended in benzene and 2.6 g. ($1^1/_2$ molecular equivalents) of acetyl chloride rapidly added, followed by slightly more than one molecular equivalent of 2 *N* sodium hydroxide solution. The benzene layer was drawn off and evaporated to dryness leaving 6 g. of the aceto derivative—practically a quantitative yield. This compound was extremely soluble in alcohol and benzene. For analysis it was twice crystallized from 5% alcohol, from which it separated as colorless needles melting at 157–158°.

Analyses. Calc. for $C_{16}H_{16}O_2N_2$: N, 10.45. Found: 10.69, 10.29.

Chloro-aceto-amino-aceto-phenylanilide, $(C_6H_5)_2NCOCH_2NHCOCH_2Cl$, **and Benzoylamino-aceto-phenylanilide,** $(C_6H_5)_2NCOCH_2NHCOC_6H_5$, were prepared by methods analogous to that used in the synthesis of the acetyl derivative. The chloro-acetyl derivative was obtained after two crystallizations from alcohol as colorless needles melting at 117–118°; yield, 38%.

Analyses. Calc. for $C_{16}H_{15}O_2N_2Cl$: N, 9.26. Found: 9.35, 9.56.

The benzoyl derivative was also crystallized from alcohol and obtained as colorless needles melting at 182°; yield, 85%.

Analyses. Calc. for $C_{21}H_{18}O_2N_2$: N, 8.48. Found: 8.39, 8.25.

Benzoyl-di-(diphenylamide) of Diglycol-amidic Acid. $[(C_6H_5)_2NCOCH_2]_2NCOC_6H_5$.—Six g. of the hydrochloride of di-(diphenylamide) of diglycol-amidic acid was suspended in 30 cc. of acetone. One molecular equivalent of 2 *N* sodium hydroxide was added and the mixture warmed until the acetone layer was clear. Three g. of benzoyl chloride was slowly added, while the mixture was shaken, followed by slightly more than one molecular proportion of 2 *N* sodium hydroxide solution, and the whole allowed to stand overnight. The acetone layer was then removed and evaporated nearly to dryness. An oil separated which partially solidified on standing. After two crystallizations from dil. alcohol the compound was obtained as colorless, glistening crystals melting at 200°; yield of pure product, 5 g., or 74%. It is very soluble in acetone, and moderately so in alcohol.

Analyses. Calc. for $C_{35}H_{29}O_3N_3$: N, 7.79. Found: 7.88, 7.62.

Amino-aceto-phenylanilide Dithiocarbamate. $(C_6H_5)_2NCOCH_2NHCSSH.NH_2CH_2CON(C_6H_5)_2$.—Twenty g. of amino-aceto-phenylanilide hydrochloride was dissolved in a little hot water, the solution decolorized with boneblack, and the base freed by the addition of a slight excess of concd. sodium hydroxide solution. The oil thus freed was drawn off, twice washed with water, and dissolved in 25 cc. of alcohol; 4.3 g. ($1^1/_2$ molecular equivalents) of carbon disulfide was then added, causing an immediate exothermic reaction with separation of a heavy oil that soon solidified to a granular mass. This solid was filtered off, washed and dried at room temperature; yield, 13 g., or 65%. The compound seemed quite stable in air and did not discolor on drying. It was very difficultly soluble in ethyl acetate, and quite soluble in alcohol, but decomposed extensively when dissolved in the latter. For analysis, a "crude" sample was carefully washed with alcohol and ether and dried at 40°. This sample was pure white, apparently microcrystalline, and strongly pyro-electric. When its melting point was taken in the usual manner it sintered noticeably at 150–153°, but did not really melt until a temperature of 260° was reached. (See next reaction.) When suddenly thrust into a bath heated to 150–155°, the compound melted, but instantly decomposed, giving off hydrogen sulfide.

Analyses. Calc. for $C_{29}H_{28}O_2N_4S_2$: N, 10.60; S, 12.13. Found: N, 10.63, 10.83; S, 12.03.

The preparation of the dithiocarbamate was several times repeated with an average yield of 65%.

The Behavior of Amino-aceto-phenylanilide Dithiocarbamate toward Heat; its Conversion into Symmetrical Amino-aceto-phenylanilide-thio-urea. $(C_6H_5)_2NCOCH_2NHCSNHCH_2CON(C_6H_5)_2$.—In the preceding discussion it was mentioned that the dithiocarbamate was quite soluble in hot alcohol. Such a solution always smelled strongly of hydrogen sulfide, and on standing deposited tiny, pale yellow crystals. These crystals were extremely insoluble in organic solvents and melted, with previous discoloring and some decomposition, at 260°. Analyses show this compound to be the thio-urea.

Analyses. Calc. for $C_{29}H_{26}O_2N_4S$: N, 11.33; S, 6.48. Found: N, 11.23, 11.18; S, 6.21.

The thio-urea was so insoluble that it was not found possible to purify any of it. However, in the preparation described above, it crystallized very slowly from a large volume of alcohol, and must, therefore, have been practically pure. This preparation was several times repeated, with identical results. The thio-urea was also prepared by a different method, namely, by the action of thiophosgene on amino-aceto-phenylanilide; this will be discussed later.

Carbo-ethoxy-amino-aceto-phenylanilide Dithiocarbamate. $C_2H_5OOCSCSNHCH_2CON(C_6H_5)_2$.—Twenty-five g. of amino-aceto-phenylanilide dithiocarbamate was suspended in 350 cc. of ether and 6.7 g. ($1^1/_3$ molecular equivalents) of ethyl chloroformate added. The mixture was allowed to stand in the cold for 24 hours, after which it was gently boiled for an hour. The ether solution was then yellow, and the solid more crystalline in appearance than originally. The solid was filtered off and washed with ether, the washings being added to the original filtrate. If the reaction had proceeded quantitatively, this residue would have weighed 10 g.; it actually weighed 11 g. and was almost completely water-soluble, indicating that it contained practically nothing but amino-aceto-phenylanilide hydrochloride.

When the ether filtrate was evaporated, 15 g. of a light yellow oil was obtained, which is 1 g. in excess of the amount required by calculation. This oil became quite viscous as it cooled, and after 36 hours had almost entirely solidified in the form of tiny, nearly white crystals. These were quite gummy, so they were dissolved in alcohol, in which the substance was extremely soluble, and the solution was cooled in a freezing mixture. By this treatment several g. of very pale yellow needles was obtained, which sintered at 101° and melted slowly with slight decomposition at 112–115°. Owing to the small amount of material, and its excessive solubility, no further purification was attempted.

Analyses. Calc. for $C_{18}H_{18}O_3N_2S_2$: N, 7.48. Found: 7.26, 7.28.

This preparation was several times repeated, and practically quantitative yields of the ester and the amine salt were obtained in each case. Usually, however, the carbo-ethoxy derivative was obtained as a viscous oil which solidified partly, or not at all. It could not be vacuum-dried, as some decomposition set in. After long standing in a desiccator the oil frequently became so viscous that it could not be poured out of the container. It had a faint aromatic odor.

The Behavior of Carbo-ethoxy-amino-aceto-phenylanilide Dithiocarbamate on Distillation.—Sixteen g. of this ester was placed in a small distilling flask and the pressure above it was reduced. Decomposition took place readily, and at first the pressure could not be reduced below 70 mm. As the decomposition became less, the flask was slowly heated in an oil-bath to an external temperature of 120° and the pressure reduced to 30 mm. After $2^1/_2$ hours, decomposition seemed at an end; a dark liquid remained which solidified to a black tar. No distillate was collected during the decomposition even with the receiver ice-cooled. The tar was soluble in alcohol, but formed again unchanged. It gave none of the reactions characteristic of mustard oils, and no definite compound could be isolated from it.

The Action of Silver Nitrate on Amino-aceto-phenylanilide Dithiocarbamate.—Fifteen g. of amino-aceto-phenylanilide dithiocarbamate was added to a warm solution of 5 g. of silver nitrate in 50 cc. of water. A heavy, orange precipitate formed, which at once darkened. The solution was warmed just below the boiling point for 20 minutes. During this heating a faint odor of carbon disulfide was noticed, but no hydrogen sulfide could be detected, even with lead acetate paper. The precipitate was filtered and washed with hot water. On cooling the filtrate, which was perfectly colorless, beautiful white plates separated. These proved to be amino-aceto-phenylanilide nitrate, which was difficultly soluble in water and melted at 211–214°. The precipitate of the silver salt appeared quite stable. It was insoluble in all common reagents, but dissolved slightly in hydrochloric acid, being precipitated unchanged by addition of water. If the double decomposition reaction had proceeded quantitatively, 11 g. of this silver salt and 9 g. of the amine nitrate would have been formed. The weights actually obtained were 11 g. and 8 g., respectively.

This preparation was repeated without heating the solution and the silver salt filtered, extracted with hot alcohol and dried at a low temperature. The substance was thus obtained as an amorphous, brown powder. Some impurity was evidently present, as nitrogen analysis was 1.25% low. However, the corresponding mercury salt was obtained in the pure condition.

The Effect of Heat on Silver Amino-aceto-phenylanilide Dithiocarbamate.—Eleven g. of the crude air-dried silver salt was placed in a small distilling flask provided with a receiving tube, and subjected to a vacuum of 20 mm. The flask was then slowly heated in an oil-bath. There was no visible decomposition until an external temperature of 220° was reached. Some gas (of the odor of hydrogen sulfide) was then evolved, and the pressure rose to 23 mm. for a short time. Finally, with the oil-bath at 250–255°, a yellow oil distilled and solidified in the receiver. The total time of heating was one hour. The solid which distilled was crystallized from alcohol and melted at 54°; yield, 2 g. It was diphenylamine.

The residue in the flask weighed 7 g. and consisted of a black tar which responded to none of the usual mustard oil tests.

The Action of Mercuric Chloride on Amino-aceto-phenylanilide Dithiocarbamate.—A mixture of 25 g. of the dithiocarbamate with a cold solution of 7 g. of mercuric chloride in 300 cc. of alcohol was shaken for one-half hour. A heavy, somewhat gelatinous precipitate formed, and coagulated in part during the shaking. This was filtered off, washed with hot alcohol, and dried at room temperature; yield, 18 g., or 95%.

The salt darkened on drying, but appeared quite stable. No odor of hydrogen sulfide could be detected when small portions were boiled with water.

Sixteen g. of this mercury salt was placed in a small distilling flask provided with a receiver, and a flask containing concd. sodium hydroxide solution in dil. alcohol placed in the system. A vacuum of 50 mm. was obtained and the substance slowly heated in an oil-bath. Decomposition began at the external temperature of 155°, the contents of the flask blackened, and partially melted. After one and one-half hours the heating was stopped. There had been no distillate, but a very little solid sublimed and collected in the side arm—probably diphenyl amine. The caustic solution through which the gases of decomposition had been passed gave a strong sulfur test. The odor of carbon disulfide was noticed at the pump outlet during distillation. The residue in the flask consisted of a black tar, which gave no tests for a mustard oil with the customary reagents.

After negative results in the mustard oil test, the flask was again sealed, the vacuum restored, and the whole heated to 285°. Even at this temperature, there was no distillate, and after the system had cooled, tests for a mustard oil were again negative. The residue in the flask was not entirely carbonized, as it burned violently in air.

The Action of Hydrochloric Acid on Amino-aceto-phenylanilide Dithiocarbamate.—To a mixture of 20 g. of amino-aceto-phenylanilide dithiocarbamate and 75 cc. of warm alcohol (30°), was added saturated alcoholic hydrochloric acid a little at a time until all of the salt dissolved. The solution was decolorized with bone black and set aside for some hours. A faint odor of carbon disulfide was detected, but no hydrogen sulfide. After a short time a white solid crystallized. This was filtered off and identified as amino-aceto-phenylanilide hydrochloride. The amount recovered was 12 g., which is slightly in excess of that calculated.

To the filtrate was added 4.9 g. (the calculated quantity) of mercuric chloride, which readily dissolved. The resulting solution was allowed to evaporate spontaneously and yielded several grams of colorless, heavy crystals. These were pulverized thoroughly, washed with alcohol and dried at room temperature. The salt became somewhat green on drying. Analysis indicates that it was the mercuric salt of amino-aceto-phenylanilide dithiocarbamic acid, $[(C_6H_5)_2NCOCH_2NHCSS]_2Hg$.

Analyses. Calc. for $C_{30}H_{26}O_2N_4S_4Hg$: N, 6.98. Found: 6.83, 6.87.

In view of the ease with which the dithiocarbamate decomposed in alcohol solution, evolving hydrogen sulfide and forming the thio-urea, the stability of the silver and mercury salts is most remarkable.

The Action of Thiophosgene on Amino-aceto-phenylanilide.—To a solution of 13 g. (3 molecular equivalents) of amino-aceto-phenylanilide, which had been vacuum-dried for some months, in 100 cc. of ether, was slowly added 2.1 g. (1 equivalent) of thiophosgene diluted with 25 cc. of ether. A somewhat exothermal reaction took place with separation of a heavy oil which partly crystallized. The mixture was allowed to stand for 24 hours. The ether layer was then removed and on evaporating left a viscous oil (about 0.5 g.). This oil did not appear to react with ammonia, aniline, ethyl alcohol or hydrogen chloride and was therefore presumably neither mustard oil nor unchanged amine. The solid residue was extremely insoluble and could not be crystallized. After repeated extraction with hot alcohol it was obtained as a fine-white crystalline powder melting at 258–260°, the same temperature as the melting point of the thio-urea previously mentioned. The difference in color is undoubtedly due to a difference in the state of division of the two samples.

Analyses. Calc. for $C_{29}H_{26}O_2N_4S$: N, 11.33. Found: 11.61, 11.42.

Summary

1. The compounds formed by the reaction of alcoholic ammonia on chloro-aceto-ethylanilide and chloro-aceto-phenylanilide have been identified and certain of their derivatives prepared.

2. Attempts to convert amino-aceto-phenylanilide into the corresponding isothiocyanate were unsuccessful.

3. The anomalous behavior of amino-aceto-phenylanilide dithiocarbamate toward mercury and silver salts has been noted.

NEW HAVEN, CONNECTICUT

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF COLUMBIA UNIVERSITY, No. 444]

RESEARCHES ON SELENIUM ORGANIC COMPOUNDS
III. THE PREPARATION OF A SELENIUM DERIVATIVE OF CINCHOPHEN TYPE

BY MARSTON TAYLOR BOGERT AND HORACE H. HOPKINS

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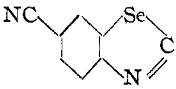
Introductory

Bogert and Abrahamson[1] have described the synthesis of 2-phenylbenzothiazole-6-carboxylic acid from 2-phenyl-6-aminobenzothiazole, and have pointed out its structural relationship to Cinchophen (Atophan) and the possibility of its possessing useful physiological properties.

Pending the carrying out of pharmacological tests on the sulfur compound, it seemed to us worth while to prepare the analogous selenium compound, so that the properties of the two might be compared, and this brief contribution records that synthesis. As was the case with the sulfur compound, so here too it was found impossible to obtain either the nitrile or the free acid in crystalline form, and final purification was accomplished through the methyl ester.

Experimental Part

2-Phenyl-6-cyano-benzoselenazole,  was prepared from the corresponding 6-amino derivative[2] by the Sandmeyer reaction. From 10 g. of the amine, 12 g. of crude nitrile was obtained in the form of a brownish powder, which decomposed at 145–150° with previous sintering, and which defied all attempts to crystallize it. By repeated solution in alcohol and re-precipitation with water, it was

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[1] Bogert and Abrahamson, THIS JOURNAL, **44**, 826 (1922).

[2] Bogert and Chen, *ibid.*, **44**, 2355 (1922).