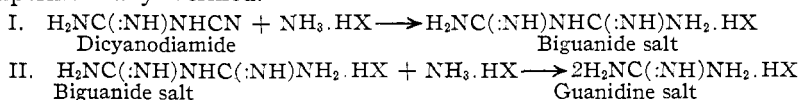
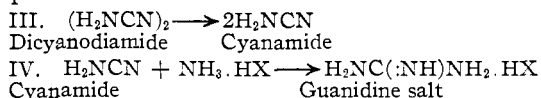


fused mixtures of dicyanodiamide and ammonium salts, is suggested and experimentally verified.



2. The mechanism previously suggested, postulating the depolymerization of dicyanodiamide in such fused mixtures is not capable of direct experimental verification.



3. The statement that biguanide salts are formed in such mixtures by de-ammonation of 2 molecules of guanidine salt (reverse of Reaction II, above) is shown to be very doubtful. The salt of biguanide is intermediate in the formation of guanidine salts in such fused mixtures, and is not a product of a side reaction.

4. It is shown that the reactions taking place in such fused mixtures cannot be offered as evidence against the cyanoguanidine structure for dicyanodiamide, and are rather in entire accord with it.

WASHINGTON, D. C.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF COLUMBIA UNIVERSITY]

## RESEARCHES ON SELENIUM ORGANIC COMPOUNDS.

### I. SYNTHESIS OF 2-METHYL-4-SELENOQUINAZOLONE, 2-PHENYL-BENZOSELENAZOLE, AND SOME DERIVATIVES OF THE LATTER<sup>1</sup>

BY MARSTON TAYLOR BOGERT AND YÜ-GWAN CHEN<sup>2</sup>

Received July 15, 1922

#### Introductory

Since metallic selenium is now available in considerable amount and at a reasonable price, it seemed to the authors an appropriate time to investigate somewhat further the possibilities of discovering organic selenium derivatives of service to mankind as drugs or dyes, or perhaps in still other fields.

The powerful physiological action of hydrogen selenide is well known. Valuable therapeutic properties have been claimed from time to time for various organic selenium compounds but, so far as we are aware, none of these substances are used in medicine to-day.

<sup>1</sup> The *o*-nitro-aniline used in this investigation was provided by the National Aniline and Chemical Co., and the selenium by the Baltimore Copper Smelting and Rolling Co., and we welcome this opportunity of expressing to them publicly our appreciation of their courtesy.

<sup>2</sup> Read at the Birmingham meeting of the American Chemical Society, April, 1922.

In so far as tinctorial properties are concerned, it is recognized that the effects of selenium are similar to those of sulfur, and that of the two the selenium derivatives generally show the deeper color, as will be noted immediately on comparing  $=CS$  with  $=CSe$  compounds, or  $-C-SH$  with  $-C-SeH$ , or  $-S=S-$  with  $-Se=Se-$ . The chief difficulty is likely to be encountered in the peculiar sensitiveness of selenium itself to light.

The investigations reported in the present paper relate to the synthesis and study of certain selenium heterocyclic compounds.

2-Methyl-4-selenoquinazolone can be obtained by an application of the methods developed in this laboratory for the synthesis of thioquinazolones,<sup>3</sup> but the compound is not very stable, slowly decomposing into 2-methyl-4-quinazolone and metallic selenium.

2-Phenyl-benzoselenazole is much more conveniently prepared, and in better yield, by heating benzalaniline rather than benzanilide<sup>4</sup> with selenium. On nitration, it yields either mono- or dinitro derivatives, according to the conditions. When the mononitro compound is reduced to the amine and the latter fused with potassium hydroxide, benzoic acid is formed as one of the cleavage products, but no nitrobenzoic acid. The amino, and hence the antecedent nitro group, therefore, must be in the benzene portion of the benzoselenazole nucleus and not in the 2-phenyl. As Bogert and Abrahamson<sup>5</sup> have proved that the analogous 2-phenyl-benzothiazole, under similar conditions, gives the 6-nitro derivative, it seems reasonable to assign a like position to the nitro and amino groups in this selenazole. In the case of the dinitro-selenazole, the most probable positions for the nitro groups would seem to us to be 4 and 6.

From both mono- and diamine, azo dyes have been prepared, and these show good fastness to acids, alkalies and light.<sup>6</sup>

### Experimental

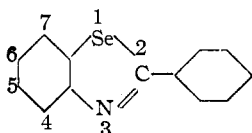
*o*-Amino-benzoselenamide,  $H_2N.C_6H_4.CSe.NH_2$ .—A solution of anthranilonitrile in absolute alcohol was saturated at  $0^\circ$  with dry hydrogen selenide and dry ammonia, and heated in a sealed tube for 10 hours at  $105-110^\circ$ . The tube was then opened and the liquid contents evaporated. After considerable concentration, a small amount of minute crystals was obtained, and these crystals after further recrystallization from water melted at  $116^\circ$  (corr.). The yield was poor, and the product rather unstable, so that no effort was made to prepare sufficient for analysis, since its use as initial material

<sup>3</sup> Bogert *et al.*, THIS JOURNAL, 25, 373 (1903).

<sup>4</sup> Fromm and Martin, *Ann.*, 401, 178 (1913).

<sup>5</sup> Bogert and Abrahamson, THIS JOURNAL, 44, 826 (1922).

<sup>6</sup> The following numbering for the benzothiazole nucleus is used throughout this article.



for the synthesis of the quinazolone offers no advantage over the process given below in which the final product sought is obtained in a single operation.

**2-Methyl-4-selenoquinazolone**,  $\overline{\text{NH.CSe.C}_6\text{H}_4\text{.N:C.CH}_3}$ .—Twenty g. of acetyl anthranilonitrile was dissolved in absolute alcohol, and dry hydrogen selenide and dry ammonia passed into the warm (60°) solution for 3 hours. On cooling, the quinazolone crystallized and was purified by recrystallization from dil. alcohol. Yield, about 10%.

In a second experiment, 10 g. of the nitrile was heated in a sealed tube at 110° with alcohol previously saturated at 0° with dry hydrogen selenide and dry ammonia. After 5 hours' heating, the tube was allowed to cool and the quinazolone which separated was recrystallized. Yield, about 16%.

Hydrogen selenide being rather unstable and not freely soluble in alcohol, it was replaced by freshly prepared sodium selenide. A solution of sodium hydroxide in absolute alcohol was treated first with a current of nitrogen, to displace all air in the solution and apparatus. Dry hydrogen selenide was then bubbled through the alcohol solution for 3 hours, and excess of this gas finally displaced again by nitrogen. The sodium selenide formed was collected and dried, first in an atmosphere of nitrogen, and finally in a vacuum over phosphoric anhydride. As thus prepared, it was colorless, but soon turned red on exposure to the air and became steadily darker. The only commercial "C. P." sodium selenide we could find on the market was black and practically useless for our purpose.

A mixture of 50 g. of this selenide and 20 g. of anthranilonitrile was heated to 115° in an atmosphere of nitrogen in a distilling flask, and 40 g. of acetic anhydride dropped in very slowly. The temperature was maintained at 110° for a half hour longer and then raised sufficiently to distil the acetic acid formed in the reaction. The whole operation required about an hour and a half. The quinazolone was dissolved out of the cooled reaction mixture by dil. aqueous sodium hydroxide solution, and re-precipitated from this clear alkaline extract by carbon dioxide, with the addition of a little common salt to aid the separation. The crude product was purified by crystallization from 25% alcohol; yield, 20 to 25%.

In another set of experiments, the mixture of anthranilonitrile, sodium selenide and acetic anhydride, was heated in sealed tubes for 3½ hours at 110–115°, but the yields were no better than when the reaction was carried out at atmospheric pressure.

The 2-methyl-4-selenoquinazolone obtained in these experiments crystallized from dil. alcohol in brownish needles or prisms, m. p. 213.5° (corr.). It dissolved easily in hot alcohol, but on concentration occasionally formed a sticky mass with a peculiar but not unpleasant odor. It was but slightly soluble in benzene or chloroform, practically insoluble in water, but readily soluble in aqueous alkalis, being re-precipitated from such solutions by carbon dioxide. On standing, exposed to light and air, it slowly decomposed with separation of finely divided metallic selenium and formation of 2-methyl-4-quinazolone.

A carefully purified sample was analyzed with the following results.

*Analyses.* Calc. for  $\text{C}_9\text{H}_8\text{N}_2\text{Se}$ : C, 48.38; H, 3.61; N, 12.55; Se, 35.46. Found: C, 48.45, 48.62; H, 3.82, 3.52; N, 12.51, 12.66; Se, 35.60, 35.42.

Busch, Lellmann and Stickel<sup>7</sup> produced thioquinazolones by the action of carbon disulfide upon *o*-amino-benzylamine, but attempts to carry out the analogous reaction with carbon diselenide were defeated by our inability to get this diselenide sufficiently pure, so that our products were always contaminated and difficult to handle.

The preparation of seleno-acetic acid from acetyl chloride and potassium hydrogen selenide proved equally unpromising and was abandoned.

<sup>7</sup> Busch, Lellmann and Stickel, *Ber.*, 19, 1605 (1886).

**2-Phenyl-benzoselenazole**,  $\text{Se.C}_6\text{H}_4\text{.N:C.C}_6\text{H}_5$ , was prepared first by Bauer,<sup>3</sup> from *o*-amino-selenophenol, and later by Fromm and Martin<sup>4</sup> from benzanilide and selenium. On repeating the latter process, we found the yields very poor (12–20%), and hence developed the following method.

A mixture of 106 g. of benzaldehyde and 93 g. of aniline, both freshly distilled, was heated at 120° for 2 hours until all water was driven off and a clear melt of benzal-aniline (m. p. 45°) obtained (yield theoretical). This clear melt was poured upon 160 g. of selenium dust contained in a Pyrex flask connected with an air condenser, and the mixture heated for 3 days to gentle boiling on a sand-bath. Hydrogen selenide was evolved freely during the reaction. When cold, the melt was pulverized, extracted with hot conc. hydrochloric acid, and the acid extracts filtered hot through glass wool. The filtrate was precipitated by pouring it into a large volume of cold water, and the precipitate crystallized from alcohol. Yield, 60%.

As thus prepared, it formed long, colorless needles, melting at 117.5° (corr.), in practical agreement with the melting-point (117°) reported by Fromm and Martin. It is insoluble in water; slightly soluble in cold methyl alcohol, ether, acetone, chloroform, acetic acid or anhydride, or nitrobenzene, more readily in hot; it dissolves readily in hot ethyl alcohol, ethyl acetate or carbon tetrachloride. It can be sublimed without difficulty, and has a faint but agreeable odor recalling that of the analogous sulfur compound ("Rosenkoerper").

**6-Nitro-2-phenyl-benzoselenazole**,  $\text{Se.C}_6\text{H}_3(\text{NO}_2)\text{.N:C.C}_6\text{H}_5$ .—Twenty-five g. of 2-phenyl-benzoselenazole was dissolved in 150 g. of conc. sulfuric acid at 5–10°. The clear solution was cooled below 0°, and a well-cooled mixture of 9.5 g. of conc. nitric and 15 g. of conc. sulfuric acids added slowly during 30 minutes with good stirring. This stirring was continued for 4 hours at the same temperature (below 0°), after which the solution was poured into 2 liters of ice water, the precipitate removed, crystallized first from acetic acid, decolorized by boiling in alcohol solution with animal charcoal, and finally crystallized from alcohol; yield, 95%.

The pure substance formed flattened, pale yellow needles, melting at 202.4° (corr.). It is practically insoluble in water; difficultly soluble in cold alcohol, acetic acid or anhydride, benzene, toluene, nitrobenzene or *o*-nitrotoluene and more readily soluble in the same solvents at their boiling-points.

*Analyses.* Calc. for  $\text{C}_{13}\text{H}_8\text{N}_2\text{O}_2\text{Se}$ : N, 9.24. Found: 9.36, 9.48.

**6-Amino-2-phenyl-benzoselenazole** was prepared from the foregoing substance by reduction with tin and hydrochloric acid, the yield being 75%. The compound crystallized from alcohol in fine, glistening, yellowish needles, melting at 201.2–202.3° (corr.). It is insoluble in water or ether, difficultly soluble in cold alcohol, benzene, toluene or nitrobenzene, but soluble in the same solvents when hot, and is moderately soluble in cold aniline.

*Analyses.* Calc. for  $\text{C}_{13}\text{H}_{10}\text{N}_2\text{Se}$ : C, 57.18; H, 3.69; N, 10.25. Found: C, 57.17, 57.00; H, 3.79, 3.85; N, 10.34, 10.42.

On fusion of this compound with potassium hydroxide, benzoic acid was obtained, being identified by its melting-point (121°), and by conversion into benzene, nitrobenzene and ethyl benzoate. The amino group, therefore, is not in the 2-phenyl nucleus and, reasoning from the experience of Bogert and Abrahamson<sup>5</sup> with the analogous thiazole, is most probably at Position 6.

**ACETYL DERIVATIVE.**—This occurred as colorless crystals, m. p. 188.1–188.7° (corr.); it is soluble in alcohol, ethyl acetate, amyl acetate, acetone or acetic acid, moder-

<sup>3</sup> Bauer, *Ber.*, **46**, 92 (1913).

ately soluble in toluene, and difficultly soluble or insoluble in ether, benzene or carbon disulfide.

*Analyses.* Calc. for  $C_{15}H_{12}N_2OSe$ : N, 8.88. Found: 8.92, 8.68.

**BENZAL DERIVATIVE.**—This was obtained from the amine and benzaldehyde, in alcoholic solution; yield, 90%. It forms yellow plates from carbon disulfide, melting at 156.7–157.6° (corr.); it is soluble in alcohol, ether, acetone, carbon tetrachloride or benzene and is difficultly soluble in ligroin.

*Analysis.* Calc. for  $C_{20}H_{14}N_2Se$ : N, 7.75. Found: 7.68.

**2-Phenyl-benzoselenazole-azo- $\beta$ -naphthol.**—On diazotizing the amine and coupling with  $\beta$ -naphthol in alkaline solution, in the customary manner, a deep red solution resulted, which was acidified with hydrochloric acid and treated with salt. The precipitated dye was crystallized from a mixture of alcohol and aniline and then appeared as a deep red powder, with a metallic luster, when rubbed; it melted at 284.2° (corr.). It dyed silk a fine pink.

*Analysis.* Calc. for  $C_{28}H_{16}ON_3Se$ : N, 9.81. Found: 9.75.

The diazotized amine was also combined with other ordinary couplers, with the following results.

Coupler.	Color of product.	Color of dyed silk.
Phenol	deep red	pale yellow
Resorcinol	purple	red
Pyrogallol	dark brown	gray
Salicylic acid	reddish	light brown
Dimethylaniline	orange	light yellow
<i>p</i> -Toluidine	light brown	.....
<i>p</i> -Nitro-aniline	light brown	.....
Sulfanilic acid	light brown	brownish
$\alpha$ -Naphthylamine	light brown	brownish

**Dinitro-2-phenyl-benzoselenazole.**—A solution of 25 g. of 2-phenyl-benzoselenazole in 150 g. of conc. sulfuric acid prepared at 5–10° was cooled below 0° and a well-cooled mixture of 9.5 g. of conc. nitric and 15 g. of conc. sulfuric acids added very slowly with mechanical stirring. After the mixture had been stirred for 2 hours at a temperature below 0°, another like amount of mixed acids (9.5 g. of nitric and 15 g. of sulfuric) was added gradually and the mixture was then heated at 100° for 2 hours. The solution was cooled, poured into 2 liters of ice water and the precipitate collected and purified by repeated crystallization from acetic acid; yield, 80%.

*Analyses.* Calc. for  $C_{18}H_7N_3O_4Se$ : N, 12.07. Found: 12.30, 12.12.

The recrystallized compound formed fine, pale yellow needles, melting at 246.8° (corr.); it was practically insoluble in water, soluble in hot alcohol, acetic acid or anhydride, nitrobenzene or *o*-nitrotoluene, but not readily soluble in these same solvents when cold. It is likely that the nitro groups will be found at Positions 4 and 6, but this point we have not had an opportunity of determining as yet.

**Diamino-2-phenyl-benzoselenazole**, obtained from the above by reduction with tin and hydrochloric acid, was crystallized first from alcohol and finally from pyridine, giving nearly colorless glistening needles, melting at 269–270.5° (corr.).

*Analyses.* Calc. for  $C_{18}H_{11}N_3Se$ : N, 14.6. Found: 14.4, 14.7.

**DIACETYL DERIVATIVE.**—This occurs as cubes from dil. alcohol, m. p. 239.5–240.5° (uncorr.).

*Analyses.* Calc. for  $C_{17}H_{15}O_2N_3Se$ : N, 11.3. Found: 11.43, 11.6.

**DIBENZAL DERIVATIVE.**—This was obtained as beautiful lustrous yellow plates from carbon disulfide, m. p. 186–187° (uncorr.).

*Analyses.* Calc. for  $C_{27}H_{19}N_3Se$ : N, 9.05. Found: 9.21, 9.34.

**Azo Dyes from the Diamine.**—The diamine was diazotized and combined in the customary way with the following couplers, giving some new selenium azo dyes.

Coupler.	Color of product.	Color of dyed silk.
Phenol	deep red	yellow
Resorcinol	dark purple	deep red
Pyrogallol	dark brown	gray
$\beta$ -naphthol	deep red	red
Salicylic acid	red	brown
Dimethylaniline	orange-red	yellow
<i>p</i> -Toluidine	brownish	brownish
<i>p</i> -Nitro-aniline	brownish	gray
Sulfanilic acid	brown	brown
$\alpha$ -Naphthylamine	yellow	yellow

### Summary

1. 2-Methyl-4-selenoquinazolone has been synthesized from anthranilnitrile by several different methods.
2. 2-Phenyl-benzoselenazole is obtained in better yield from benzal aniline than from benzanilide and selenium.
3. Its mono- and dinitro derivatives have been prepared and from them the corresponding amines.
4. The amine group in the mono-amine has been proved to be in the benzene portion of the benzothiazole nucleus.
5. From the amines, acetyl and benzal derivatives have been made, as well as azo dyes.

NEW YORK, N. Y.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, YALE UNIVERSITY]

## RESEARCHES ON THIOCYANATES AND ISOTHIOCYANATES. XV. THE NATURE OF THE INTRAMOLECULAR REARRANGEMENT OF ISOTHIOCYANATO-ACETANILIDES

BY ARTHUR J. HILL AND ERWIN B. KELSEY<sup>1</sup>

Received July 22, 1922

It has been shown by Wheeler and Johnson<sup>2</sup> and their colleagues that the primary products resulting from the interaction of the chloro-acetanilides and potassium thiocyanate are the normal thiocyanato-acetanilides, which rearrange into labile pseudothiohydantoins and the latter into stable isomers. Recently, the writers, in collaboration with Johnson,<sup>3</sup> prepared

<sup>1</sup> This paper is constructed from a dissertation presented by Erwin B. Kelsey to the Faculty of the Graduate School of Yale University, 1921, in candidacy for the degree of Doctor of Philosophy. (A. J. H.)

<sup>2</sup> Wheeler and Johnson, *Am. Chem. J.*, **28**, 121 (1902); *THIS JOURNAL*, **23**, 283 (1901); **25**, 483 (1903); **40**, 636 (1918).

<sup>3</sup> Johnson, *THIS JOURNAL*, **42**, 1711 (1920).