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# SOME SELENOUREAS, SELENAZOLONES, AND SELENAZOLES

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*Received October 14, 1952*

During the course of our investigations we have prepared various dialkyl and aryl substituted selenoureas and their derivatives. These compounds provide starting materials for the preparation of a number of selenium-bearing heterocyclic compounds. Their preparation can be carried out with little difficulty and the yields are excellent.

The synthetic method leading to the formation of the substituted selenourea involves the preparation of the alkyl or aryl cyanamide (carbodiimide in the case of the symmetrically substituted derivatives), followed by the addition of hydrogen selenide in ammoniacal solution. This method has been used by Haginiwa (1) and Zetzsche and Pinske (2). Condensation of the selenourea with an $\alpha$-halocarboxylic acid (A) leads to the formation of the 2-amino-4-selenazolone while the 2-aminoselenazole is formed when an $\alpha$-haloketone is used (B). With $\beta$-halocarboxylic acids there is formed a derivative of isoselenourea. The condensation of N, N-dimethylselenourea with $\beta$-bromopropionic acid, for example, gives $\beta$-Se-N,N-dimethylisoselenoureapropionic acid hydrobromide (C).

Undesirable selenium contamination which invariably occurs during the preparation of seleno-organics or upon their exposure to air or moisture, can be largely or completely eliminated. Any precipitated gray selenium is removed by filtration while the colloidal red selenium which forms upon isolation of the crystalline solid is removed by recrystallization from benzene, in which red selenium is completely soluble. In those cases where the material is insoluble in benzene, heating the contaminated material in benzene prior to addition of the recrystallizing solvent, will yield a colorless product.

## EXPERIMENTAL

*N,N-Dimethylselenourea.* Through a solution containing 37 g. (0.50 mole) of dimethylcyanamide[1] in 75 ml. of concentrated aqueous ammonia and 25 ml. of water, there was passed a slow stream of hydrogen selenide.[2, 3] The reaction was carried out at room temperature and the reaction flask was agitated at frequent intervals. The reaction was quite exothermic and after four to five hours, crystals of dimethylselenourea were formed. At this point, the generation of gas was terminated and the solution was cooled in an ice-bath. After the separation of the crystals by filtration, they were thoroughly washed with ice-cold water and 50% ethanol until they assumed a pale red or gray color. Recrystallization from water or ethanol gave colorless needles which slowly turned pink and then gray on standing. The

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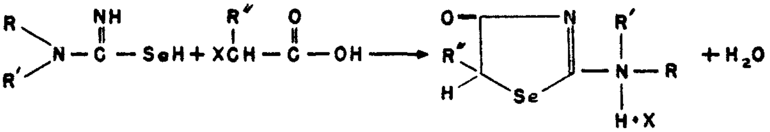
[1] The dimethyl- and diethyl-cyanamide were supplied by the American Cyanamid Company.

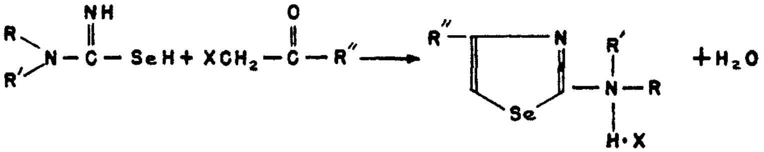
[2] Hydrogen selenide was generated by the action of dilute hydrochloric acid on aluminum selenide.

[3] Hydrogen selenide should be handled with all the precautions exercised in working with hydrogen sulfide. All manipulations should be carried out in a hood until the crystalline solid is isolated and washed.

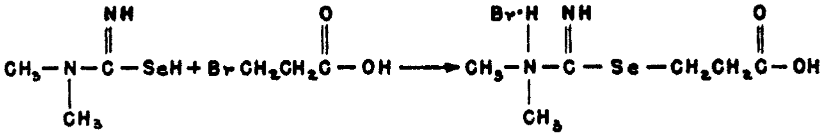
A.



B.

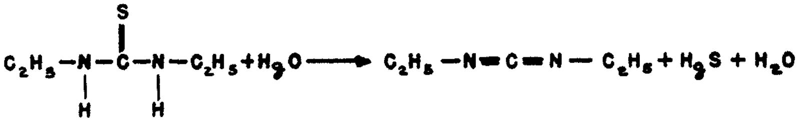


C.



$\mathrm{CH_3-\underset{CH_3}{\underset{|}{N}}-\overset{NH}{\overset{\|}{C}}-SeH+BrCH_2CH_2\overset{O}{\overset{\|}{C}}-OH \longrightarrow CH_3-\underset{CH_3}{\underset{|}{\overset{Br\cdot H}{\overset{|}{N}}}}-\overset{NH}{\overset{\|}{C}}-Se-CH_2CH_2\overset{O}{\overset{\|}{C}}-OH}$

D.



$\mathrm{C_2H_5-\underset{H}{\underset{|}{N}}-\overset{S}{\overset{|}{C}}-\underset{H}{\underset{|}{N}}-C_2H_5+H_2O \longrightarrow C_2H_5-N=C=N-C_2H_5+H_2S+H_2O}$

material was only slightly soluble in benzene, but recrystallization from this solvent yielded a stable form of N,N-dimethylselenourea, m.p. 169–170°, with decomposition. The yield was at least 75% on every trial.

*Anal.* Calc'd for $C_3H_8N_2Se$: C, 23.84; H, 5.34; N, 18.55.

Found: C, 23.5; H, 5.4; N, 18.6.

*N,N-Diethylselenourea.* To a solution of 40 ml. (0.35 mole) of diethylcyanamide in 50 ml. of ethanol was added 50 ml. of concentrated aqueous ammonia. The solution was warmed to 60° in a water-bath and maintained at this temperature throughout the course of the reaction. A slow stream of hydrogen selenide was passed through the solution for five hours during which time the vessel was frequently agitated. After this time the flask was cooled in ice and crystallization occurred. The crystalline material was filtered off and washed with ice-cold 50% ethanol. Recrystallization from benzene yielded 60–85% of beautiful rhomboids of N,N-diethylselenourea which melted at 80° and decomposed at 121–124°.

*Anal.* Calc'd for $C_5H_{12}N_2Se$: C, 33.52; H, 6.75; N, 15.64.
Found: C, 33.8; H, 6.9; N, 15.6.

*N,N'-Diethylselenourea.* Diethylcarbodiimide was prepared as shown in equation D. This is a slight modification of the method described by Schmidt, Lahde, and Hitzler (3). Into 300 ml. of dry, diethyl ether containing 100 g. of anhydrous calcium sulfate, was added 26.4 g. (0.20 mole) of N,N'-diethylthiourea and 86.5 g. (0.40 mole) of freshly precipitated, red mercuric oxide. The reaction vessel was sealed and the mixture was automatically agitated for 18 hours. The ether solution was then filtered off from the calcium sulfate and the mixture of mercuric oxide and mercuric sulfide. The solution was evaporated to 200 ml., made alkaline by the addition of 10 ml. of concentrated aqueous ammonia, and a slow stream of hydrogen selenide was passed through the solution for three hours. The solution was cooled in ice and the impure crystalline material was collected. Recrystallization from benzene gave 30–60% yields of beautiful, colorless leaflets of N,N'-diethylselenourea, m.p. 88–90°.

*Anal.* Calc'd for $C_5H_{12}N_2Se$: C, 33.52; H, 6.75; N, 15.64.
Found: C, 33.6; H, 6.9; N, 15.5.

*Phenylselenourea.* An alcoholic solution of phenylcyanamide was prepared by agitating a solution of 45 g. (0.3 mole) of phenylthiourea in 250 ml. of ethanol with 44.6 g. (0.2 mole) of lead oxide and 43.2 g. (0.2 mole) of freshly precipitated red mercuric oxide in the presence of anhydrous calcium sulfate for 24 hours. To the clear alcoholic solution, after removal of the residual matter, was added 20 ml. of concentrated aqueous ammonia. The solution was warmed to 50° and a stream of hydrogen selenide was passed through the solution for 2½ hours at this temperature. Crystals of phenylselenourea began to form at the end of two hours. The solution was cooled and the crystalline material was filtered off and washed with cold water. Recrystallization from water gave 40–60% yields of phenylselenourea in the form of pink needles, m.p. 176–178° with decomposition.

*4-Selenazolones.* To 9.4 g. (0.10 mole) of chloroacetic acid in 150 ml. of ethanol was added 15.1 g. (0.10 mole) of N,N-dimethylselenourea and the mixture was refluxed for an hour. The hot solution was filtered in order to remove any precipitated gray selenium. On cooling, colorless needles of 2-dimethylamino-4-selenazolone hydrochloride were formed. The yields were quantitative.

The reaction involved is shown in equation A. All of the derivatives listed in Table I were prepared as described. In general, the selenazolone would not recrystallize from alcohol; instead, the alcoholic solution was evaporated to a very small volume and the product was salted out with ether in the cold.

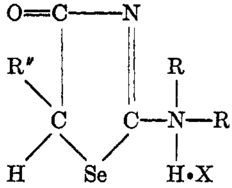
*Selenazoles.* In 50 ml. of ethanol were refluxed for one hour 6 g. (0.03 mole) of phenylselenourea and 3 g. (0.03 mole) of chloroacetone. The hot solution was filtered and cooled. The addition of ether brought about the separation of a heavy oil (2-phenylamino-4-methylselenazole) which was removed with a separatory-funnel. Heating 5 g. of this oil with 5 g. of picric acid and refluxing in 400 ml. of ethanol caused the separation of a heavy yellow precipitate. Recrystallization from 95% alcohol gave soft, bright yellow needles of 2-phenylamino-4-methylselenazole picrate.

This was the general method of preparation, but in some cases, the hydrochloride precipitated directly upon the addition of ether. The reaction involved is shown in equation B. A tabulation of the other selenazoles that were prepared is given in Table II.

*β-Se-N,N-Dimethylisoselenoureapropionic acid hydrobromide.* To a solution of 15.3 g. (0.10 mole) of β-bromopropionic acid in 100 ml. of ethanol was added 15.1 g. (0.10 mole) of N,N-dimethylselenourea. The solution was refluxed for 45 minutes, filtered to remove the precipitated selenium, and cooled in an ice-bath. To the cool filtrate ether was slowly added to salt out the precipitate. The latter was taken up again in the minimum volume of hot alcohol, but the addition of ether to the cold solution was again necessary to salt out the grayish crystals of β-Se-N,N-dimethylisoselenoureapropionic acid hydrobromide which decomposed at 185–187°.

## TABLE I

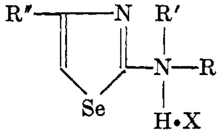
### DERIVATIVES OF 4-SELENAZOLONE



| R | R′ | R″ | X | M.P., °C. | ANALYSES | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Calc'd | | | Found | | |
| | | | | | C | H | N | C | H | N |
| $CH_3$ | $CH_3$ | H | Cl | 229–231, dec. | 26.4 | 4.0 | 12.3 | 26.5 | 4.2 | 12.4 |
| $CH_3$ | $CH_3$ | $CH_3$ | Cl | 211–212 | 29.8 | 4.6 | 11.6 | 29.8 | 4.6 | 12.1 |
| $CH_3$ | $CH_3$ | $C_2H_5$ | Br | 201–205, dec. | 28.0 | 4.4 | 9.3 | 28.4 | 4.4 | 9.5 |
| $C_2H_5$ | $C_2H_5$ | H | Cl | 204–206, dec. | 32.9 | 5.1 | 11.0 | 33.0 | 5.1 | 11.2 |
| $C_2H_5$ | $C_2H_5$ | $CH_3$ | Cl | 203–205 | 35.6 | 5.6 | 10.4 | 35.7 | 5.7 | 10.5 |

## TABLE II

### DERIVATIVES OF SELENAZOLE



| R | R′ | R″ | X | M.P., °C. | ANALYSES | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Calc'd | | | Found | | |
| | | | | | C | H | N | C | H | N |
| $CH_3$ | $CH_3$ | $CH_3$ | Cl | 121–124 | 31.9 | 4.9 | 12.4 | 30.8 | 5.1 | 12.2 |
| $CH_3$ | $CH_3$ | $CH_3$ | Picrate | 176–178, dec. | 34.5 | 3.1 | 16.7 | 34.6 | 3.1 | 16.9 |
| $C_2H_5$ | $C_2H_5$ | $CH_3$ | — | oil | | | | | | |
| $C_2H_5$ | $C_2H_5$ | $CH_3$ | Picrate | 166–167[a] | | | | | | |
| $C_6H_5$ | H | $CH_3$ | — | oil | | | | | | |
| $C_6H_5$ | H | $CH_3$ | Picrate | 204–206, dec. | 41.2 | 2.8 | 15.0 | 41.8 | 2.8 | 15.2 |

[a] Haginiwa (1) reported m.p. 165° for this compound.

*Anal.* Calc'd for $C_6H_{13}BrN_2O_2Se$: C, 23.70; H, 4.31; N, 9.22.
Found: C, 23.8; H, 4.2; N, 9.0.

*β-Se-N,N-Diethylisoselenoureapropionic acid hydrobromide.* To 15.3 g. (0.10 mole) of β-bromopropionic acid was added 17.9 g. (0.10 mole) of N,N-diethylselenourea and the mixture was heated over a steam-bath. The diethylselenourea slowly dissolved (about one hour) and a clear, thick syrup was formed. Ethanol was slowly added until the syrup dissolved and the heating was continued for an hour. The solution was filtered, cooled in ice, and ether was added and the syrup separated out. The mixture was cooled at −10° overnight and crystallization was induced by scratching with a glass rod. The filtrate was decanted from the crystalline mass which was powdered and heated in an equal volume of ethyl acetate. Ethanol was then added until solution was effected. The solution was then cooled in ice and the addition of ether brought about recrystallization. The final product was obtained as in the form of colorless crystals, m.p. 129–131°.

*Anal.* Calc'd for $C_8H_{17}BrN_2O_2Se$: C, 28.93; H, 5.16; N, 8.44.
Found: C, 28.9; H, 5.0; N, 8.4.

## SUMMARY

Several new selenoureas have been prepared by the reaction of a substituted cyanamide or carbodiimide in ammoniacal solution with hydrogen selenide. Pure, selenium-free materials can be prepared by treatment with benzene. These compounds undergo condensation reactions with $\alpha$-halocarbonyl compounds to yield various heterocyclic selenium-bearing derivatives.

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