

**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.

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

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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).

isothiocyanato-acetanilide by a method which precluded the formation of a normal thiocyanate, and observed that the substance was so unstable that it immediately isomerized into the normal thiohydantoin. This confirmed from a new standpoint, in the specific case of chloro-acetanilide and potassium thiocyanate, that the mustard oil cannot be the primary product of the reaction, otherwise the normal, and not the pseudothiohydantoin would be formed.

Beckurts and Frerichs<sup>4</sup> have recently stated that potassium thiocyanate acts upon certain chloro-anilides, (chloro-aceto-*p*-anisidide, chloro-aceto-*p*-chloro-anilide, and chloro-aceto-*m*-toluidide), to give, as primary products, unstable *isothiocyanates* which rearrange into *normal thiocyanates* and the latter into aryl thiohydantoin.

In the present investigation the writers have again utilized the method of procedure described in their previous paper and have converted Beckurts' chloro-anilides successively into the corresponding primary amines, dithiocarbamates, carbethoxy-dithiocarbamates, and finally the isothiocyanates, and have observed that the latter are so unstable that they rearrange immediately into normal 2-thiohydantoin. In other words, Beckurts and Frerichs could not have been dealing with isothiocyanates, as the primary products of their reactions, but on the contrary, with the changes shown by this laboratory to be characteristic for the interaction of chloro-acetanilides and potassium thiocyanate.

That the writers' compounds were normal thiohydantoin was shown, first, by their conversion into the corresponding oxyhydantoin, and second, by the synthesis of the latter from the urethanes of the general formula,  $\text{RNHCOCH}_2\text{NHCOOC}_2\text{H}_5$ . Further, a comparison of the melting points of these thiohydantoin with those of the pseudothiohydantoin described by Beckurts and Frerichs demonstrates that they are not identical. For example, 1-*p*-chlorophenyl-2-thiohydantoin melts at 225–227°; 1-*p*-methoxyphenyl-2-thiohydantoin at 207–209°, and 1-*m*-tolyl-2-thiohydantoin at 187°. The melting points assigned by Beckurts and Frerichs to the corresponding pseudothiohydantoin are 213°, 184° and 161°, respectively.

Some interesting derivatives of both the thio- and oxyhydantoin have also been prepared during this work.

The writers are now engaged in an investigation of amines of the general formula  $\text{R}'\text{R}''\text{N}.\text{COCH}_2\text{NH}_2$  ( $\text{R}'$  = aromatic;  $\text{R}''$  = aliphatic or aromatic), from which it is hoped that stable mustard oil combinations may be prepared, since, in this type, normal thiohydantoin formation, through intramolecular change, is rendered impossible by the substitution of the amide hydrogen by  $\text{R}'$  and  $\text{R}''$ .

<sup>4</sup> Beckurts and Frerichs, *Arch. Pharm.*, **253**, 233 (1915).

### Experimental Part

Chloro-aceto-*p*-chloro-anilide,  $\text{ClC}_6\text{H}_4\text{NHCOCH}_2\text{Cl}$ , chloro-aceto-*p*-anisidide,  $\text{CH}_3\text{OC}_6\text{H}_4\text{NHCOCH}_2\text{Cl}$ , and chloro-aceto-*m*-toluidide,  $\text{CH}_3\text{C}_6\text{H}_4\text{NHCOCH}_2\text{Cl}$  were prepared in accordance with the general procedure described by Jacobs and Heidelberger.<sup>5</sup>

One molecular proportion of the amine was dissolved in a convenient quantity of benzene and a slight excess of 2 *N* sodium hydroxide as then added, followed by  $1\frac{1}{3}$  moles of chloro-acetyl chloride. The latter was introduced drop by drop with vigorous agitation, the mixture being cooled below 60°. Chloro-aceto-*p*-anisidide was soluble in the warm benzene and was obtained by pouring off the benzene layer and allowing the anilide to crystallize. It separated in large well-formed crystals, melting at 90°, and was used without further purification. The yield was 90%. Chloro-aceto-*m*-toluidide and chloro-aceto-*p*-chloro-anilide were practically insoluble in benzene and separated at once in very small white needles, which were filtered, dried and used without further purification. The yield in each case was very nearly quantitative.

**The Action of Alcoholic Ammonia upon Chloro-aceto-*p*-chloro-anilide.** Amino-aceto-*p*-chloro-anilide,  $\text{ClC}_6\text{H}_4\text{NHCOCH}_2\text{NH}_2 \cdot \text{H}_2\text{O}$ .—One hundred g. of chloro-aceto-*p*-chloro-anilide<sup>6</sup> was dissolved in 2.5 liters of alcoholic ammonia (saturated at 10°) and allowed to stand at room temperature for a period of 6 days. The alcohol was then evaporated under reduced pressure until ammonium chloride began to separate in quantity. At this point the remaining liquid was poured into 500 cc. of cold water. This precipitated an oil (the secondary amine,  $(p\text{-ClC}_6\text{H}_4\text{NHCOCH}_2)_2\text{NH}$ ) which soon crystallized in fine, white needles. These were removed by filtration, and the filtrate evaporated to a volume of about 150 cc., and then saturated with ammonia. After standing a short time, the free primary amine crystallized in stout needles. The amine was best purified by crystallization from water, from which it was obtained in the form of stout, transparent needles which contained 1 molecule of water of crystallization. The yield was 65 g. The pure substance melted at 81° and was very soluble in alcohol or acetone, less soluble in water, and insoluble in ether or benzene. Its aqueous solution gave a basic reaction with litmus, and absorbed carbon dioxide quite readily.

*Analyses.* Calc. for  $\text{C}_8\text{H}_9\text{N}_2\text{OCl} \cdot \text{H}_2\text{O}$ : N, 13.83;  $\text{H}_2\text{O}$ , 8.89. Found: N, 13.75, 13.74;  $\text{H}_2\text{O}$ , 9.10, 9.09.

After removal of the water of crystallization the amine melted at 64°. The anhydrous base could not be crystallized from any solvent, although it crystallized from its own melt in slender colorless needles.

**B. The Di-(*p*-chlorophenylamide) of Diglycolamidic Acid,  $[\text{Cl} \cdot \text{C}_6\text{H}_4 \cdot \text{NH} \cdot \text{COCH}_2]_2 \cdot \text{NH}$ .**—The solid, obtained by pouring the partially evaporated alcoholic liquor from the above experiment into water, was purified by crystallization from acetone, followed by two crystallizations from glacial acetic acid, and finally, one from alcohol. The crude product could not be purified by crystallization from 95% alcohol directly, as it contained some impurity with which it formed mixed crystals. After this purification the compound was obtained in the form of long, colorless needles which melted at 170–171°.

*Analyses.* Calc. for  $\text{C}_{16}\text{H}_{16}\text{O}_2\text{N}_3\text{Cl}_2$ : N, 11.94. Found: 11.76, 11.90.

The secondary amine is very soluble in alcohol, acetone, ethyl acetate, and glacial acetic acid, but is insoluble in water, ether, or benzene. If a concentrated alcoholic solution is saturated with hydrogen chloride, the difficultly soluble hydrochloride is precipitated in white plates which decompose at a high temperature without melting.

<sup>5</sup> Jacobs and Heidelberger, *J. Biol. Chem.*, **21**, 104 (1915).

<sup>6</sup> Compare Ref. 3, p. 1704.

**Carbethoxy-amino-aceto-*p*-chloro-anilide**,  $C_6H_4.NHCO.CH_2.NH.COOC_2H_5$ .—Eight g. of thoroughly dried amino-aceto-*p*-chloro-anilide was suspended in 200 cc. of benzene; 6.3 g. ( $1\frac{1}{3}$  moles) of ethyl chloroformate was then rapidly added, followed by slightly more than 1 mole of 2 *N* sodium hydroxide solution. After standing for an hour the insoluble material was filtered, triturated with water, and crystallized from 95% alcohol, from which the urethane separated in fine, colorless needles which melted at 198°. The yield was 10 g. or 90%. The compound is readily soluble in alcohol or acetone, very sparingly soluble in ether and hot water, and insoluble in benzene.

*Analyses.* Calc. for  $C_{11}H_{13}O_3N_2Cl$ : N, 10.92; Cl, 13.82. Found: N, 10.70; Cl, 13.71.

**Benzoyl-amino-aceto-*p*-chloro-anilide**,  $C_6H_4.NH.CO.CH_2NH.CO.C_6H_5$ .—Five g. of amino-aceto-*p*-chloro-anilide was suspended in 100 cc. of benzene, and 4.9 g. ( $1\frac{1}{3}$  moles) of benzoyl chloride was rapidly added, followed by a slight excess of 2 *N* sodium hydroxide. The mixture was agitated for 10 minutes, and then allowed to stand for an hour. The insoluble material was filtered, thoroughly triturated with water, and crystallized from 95% alcohol, in which it was rather sparingly soluble. The substance melted slowly at 217–218°. The yield was 7 g., or 90%.

*Analyses.* Calc. for  $C_{15}H_{15}O_2N_2Cl$ : N, 9.71. Found: 9.53, 9.47.

**Amino-aceto-*p*-chloro-anilide Dithiocarbamate**,  $C_6H_4.NHCOCH_2NH_2.SHCS.NHCH_2CONHC_6H_4Cl$ .—Forty g. (2 moles) of the primary amine was dissolved in 150 cc. of 95% alcohol, and this solution was kept at a temperature of about 30° during the addition of 123 g. ( $1\frac{1}{2}$  moles) of carbon disulfide. After standing for a short time the dithio salt began to separate in white, granular lumps. The reaction mixture was finally cooled in ice, the product filtered and triturated very thoroughly with water to remove any unchanged amine. Following this treatment, it was washed successively with small amounts of alcohol and ether, and finally dried at room temperature. The yield was 37 g. or 77%.

The salt was rather unstable. When moderately heated, or even when allowed to stand exposed to the air for a few hours, it turned a delicate pink and the odor of hydrogen sulfide was plainly perceptible. On this account the salt was always freshly prepared for reactions in which it was to be used.

It was best crystallized from warm water, from which it separated in minute plates of light salmon color. When heated in a capillary tube, it commenced to decompose at 125–130°, turned deep red and gave off hydrogen sulfide and, therefore, showed no sharp melting point. When very rapidly heated, it melted at 155° to a yellow liquid which almost instantly underwent decomposition. The salt was fairly soluble in alcohol and acetone, difficultly soluble in water, and practically insoluble in ether, petroleum ether, and benzene.

*Analyses.* Calc. for  $C_{17}H_{18}O_2N_4Cl_2S_2$ : N, 12.58. Found: 12.48, 12.27.

**Carbethoxy-amino-aceto-*p*-chloro-anilide Dithiocarbamate**,  $C_2H_5OOCSCSNH.CH_2CONHC_6H_4Cl$ .—Thirty g. of amino-aceto-*p*-chloro-anilide dithiocarbamate was finely pulverized and suspended in 350 cc. of dry ether; 9.7 g. of ethyl chloroformate was then rapidly added. There was an immediate reaction, and the ether layer became pale yellow. The reaction mixture was then allowed to stand for 60 hours at room temperature, with very frequent agitation during the first 12 hours in order to prevent caking. At the end of this time, the insoluble residue was pure white and more crystalline in appearance than the original material, while the ether solution had assumed a bright yellow color.

The suspension was filtered, the residue washed repeatedly with small amounts of fresh ether, and the washings added to the original filtrate. If the reaction had proceeded quantitatively, the *residue* would have weighed 15 g. but we obtained 24 g.

of a mixture consisting of amino-aceto-*p*-chloro-anilide hydrochloride, unchanged dithiocarbamate, and the urethane,  $\text{ClC}_6\text{H}_4\text{NHCOCH}_2\text{NHCOOC}_2\text{H}_5$ .

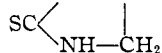
When the ether solution was evaporated, a residue remained consisting of a yellow oil, which soon solidified to light yellow crystals which melted with decomposition at  $103^\circ$ . This crystalline material, after drying at room temperature, weighed 11 g., and was identified as a mixture of the carbethoxy-dithiocarbamate and the urethane of amino-aceto-*p*-chloro-anilide.

The small amount of urethane contaminating the carbethoxy-dithiocarbamate was apparently formed by the decomposition of the latter according to the following equation.  $\text{C}_7\text{H}_5\text{OOCSCSNHCH}_2\text{CONHC}_6\text{H}_4\text{Cl} \rightarrow \text{C}_2\text{H}_5\text{OOCNHCH}_2\text{CONHC}_6\text{H}_4\text{Cl} + \text{CS}_2$ .

Analyses of the reaction product gave results low in sulfur and correspondingly high in nitrogen, for, owing to the instability of the ester, its complete separation was very difficult from the contaminating urethane, *p*- $\text{ClC}_6\text{H}_4\text{NHCOCH}_2\text{NHCOOC}_2\text{H}_5$ .

*Analysis.* Calc. for  $\text{C}_{12}\text{H}_{13}\text{O}_3\text{N}_2\text{S}_2\text{Cl}$ : N, 8.42. Found: 9.01.

**The Behavior of Carbethoxy-amino-aceto-*p*-chloro-anilide Dithiocarbamate on Distillation; its Conversion into 1-(*p*-chlorophenyl)-2-thiohydantoin,**



Nine g. of the air-dried ester was placed in a distilling flask which was connected to a small, ice-cooled receiver, and this in turn with a bulb containing a strong solution of sodium hydroxide in 50% alcohol. The system was evacuated to a pressure of 40 mm., and the flask heated in an oil-bath to a temperature of  $140\text{--}145^\circ$  (external), when decomposition set in and soon became so brisk that a part of the vacuum was lost. A small quantity of a colorless distillate collected in the receiver and the contents of the flask turned to a dark brown mass. After the decomposition was over, the vacuum was restored and the heating continued for 15 minutes. The products of the reaction were investigated as follows.

The caustic alkali solution, through which the gases of decomposition were passed during destructive distillation, was evaporated to small volume on the water-bath in order to remove the alcohol. The residual aqueous solution gave a strong test for sulfur, indicating that carbon oxysulfide or carbon disulfide had been evolved during distillation.

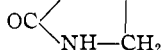
The distillate which collected in the receiver boiled at  $78^\circ$  under normal pressure and yielded iodoform with sodium carbonate and iodine, and acetaldehyde by oxidation with potassium dichromate and sulfuric acid. The distillate was, therefore, ethyl alcohol. The total amount collected was 1 g. or 77%.

The residue in the flask was dark brown, and of somewhat resinous appearance. The customary tests for a mustard oil gave negative results. A small portion, however, when digested with alkaline lead acetate, gave a precipitate of lead sulfide. The entire residue was warmed with a small amount of alcohol, which dissolved out the resinous material. These highly colored alcoholic liquors were filtered and the residual solid purified by crystallization from fresh alcohol. The yield was 4 g., corresponding to 60%.

The product was soluble in 95% alcohol and glacial acetic acid, very soluble in acetone, very difficultly soluble in hot water, and practically insoluble in ether, benzene and toluene. For analysis, it was crystallized from 95% alcohol, from which it separated in pale yellow, fluffy needles, which melted, with decomposition, at  $225\text{--}227^\circ$ . These properties are not in accord with those of the pseudothiohydantoin obtained by Beckurts and Frerichs by the interaction of potassium thiocyanate and chloro-aceto-*p*-chloro-anilide.

*Analyses.* Calc. for  $\text{C}_9\text{H}_7\text{ON}_2\text{SCl}$ : N, 12.38; S, 14.15. Found: N, 12.55, 12.36; S, 14.07.

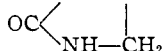
**The Desulfurization of 1-(*p*-chlorophenyl)-2-thiohydantoin:** 1-(*p*-Chlorophenyl)hydantoin,  $\text{ClC}_6\text{H}_4\text{N}-\text{CO}-$ Three g. of 1-(*p*-chlorophenyl)-2-thiohydantoin was



digested on the water-bath for 3 hours with a solution of 6 g. of chloro-acetic acid in 50 g. of water. At the end of this time, nearly all of the hydantoin had dissolved. The solution was filtered, and evaporated to  $\frac{2}{3}$  its original volume when, on cooling, a white solid separated. This was filtered, washed with water and purified by crystallization from 95% alcohol. It was quite soluble in alcohol of this strength, and also in water, and crystallized from either in well defined, colorless needles which melted at  $174^\circ$ . The yield was 1 g. or 37%.

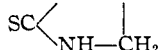
*Analysis.* Calc. for  $\text{C}_9\text{H}_7\text{O}_2\text{N}_2\text{Cl}$ : N, 13.31. Found: 13.39.

**The Conversion of Carboxy-amino-aceto-*p*-chloro-anilide into 1-(*p*-Chlorophenyl)hydantoin,**  $\text{ClC}_6\text{H}_4\text{N}-\text{CO}-$ Ten g. of the urethane was dissolved in a



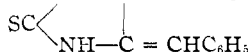
warm solution of 2.1 g. (1 mole) of potassium hydroxide in 100 cc. of 95% alcohol, and allowed to stand at room temperature for  $3\frac{1}{2}$  days. A white, crystalline solid separated from the solution in considerable quantity. A small amount of this solid was removed, and when examined qualitatively, was found to contain potassium, indicating that it was presumably the alkali salt of the hydantoic acid. At the end of the reaction period, the solution was made distinctly acid with an alcohol solution of hydrogen chloride and, after removal of the precipitated potassium chloride, the filtrate was evaporated to small volume. On cooling, a white solid crystallized. This substance was repeatedly crystallized from water, and finally melted at  $174^\circ$ . It proved to be identical with the 1-*p*-chloro-phenyl-hydantoin previously obtained by the desulfurization of the corresponding thiohydantoin, for a mixture of the two samples melted unchanged at  $174^\circ$ .

**The Action of Mercuric Chloride on Amino-aceto-*p*-chloro-anilide Dithiocarbamate.** The Preparation of 1-(*p*-Chlorophenyl)-2-thiohydantoin,  $\text{ClC}_6\text{H}_4\text{N}-\text{CO}-$



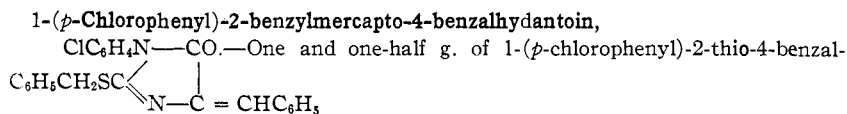
Twenty-five g. (2 moles) of amino-aceto-*p*-chloro-anilide dithiocarbamate was added to a solution of 6.9 g. (1 mole) of mercuric chloride in 200 g. of water. A white precipitate of the mercury salt at once separated. On warming, this precipitate rapidly blackened, and hydrogen sulfide was copiously evolved. The mixture was heated gently until the evolution of hydrogen sulfide had ceased. When the reaction was over the solution was cooled, and the precipitate filtered and repeatedly extracted with small portions of hot alcohol. The alcoholic liquors, when cooled, deposited crystals of 1-(*p*-chloro-phenyl)-2-thiohydantoin, which melted at  $225-227^\circ$  (with decomposition). A sample of this product melted unchanged when mixed with a sample of the hydantoin obtained by the previously described method.

**1-(*p*-Chlorophenyl)-2-thio-4-benzalhydantoin,**  $\text{ClC}_6\text{H}_4\text{N}-\text{CO}-$ Four g. (1 mole)



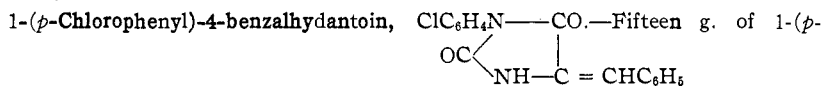
of 1-(*p*-chlorophenyl)-2-thiohydantoin, 3.8 g. (2 moles) of benzaldehyde, 13 g. of fused sodium acetate, and 50 g. of glacial acetic acid were gently boiled on an oil-bath for 4 hours. The hot solution was then poured into a large volume of water. A pale yellow, amorphous solid immediately separated. This product was filtered, dried and purified by crystallization from 95% alcohol. It was very sparingly soluble in the latter solvent, and crystallized in long, fluffy, pale yellow needles, which melted at  $257^\circ$ . The yield was quantitative.

*Analyses.* Calc. for  $\text{C}_{13}\text{H}_{11}\text{ON}_2\text{SCl}$ : N, 8.90. Found: 8.98, 8.79.



hydantoin was dissolved in a solution of sodium ethylate prepared by dissolving 0.12 g. (1 mole) of sodium in 50 cc. of absolute alcohol; 0.6 g. (1 mole) of benzyl chloride was rapidly added to the alkaline solution of the thiobenzalhydantoin. After the solution had stood for a few minutes, a solid began to separate, and the alcohol solution became solid. After an hour, the precipitate was filtered, triturated with water in order to remove the sodium chloride, and finally purified by crystallization from 95% alcohol. It was extremely insoluble in this solvent, and crystallized in pale lemon-yellow needles which melted at 176.5°. The yield obtained was 1.05 g., or 55%.

*Analyses.* Calc. for  $\text{C}_{23}\text{H}_{17}\text{ON}_2\text{SCl}$ : N, 6.92. Found: 6.96, 6.85.



chlorophenyl)hydantoin, 8 g. of benzaldehyde (a slight excess), 60 g. of fused sodium acetate and 180 g. of glacial acetic acid were gently boiled together for 6 hours. The solution was then poured into 1000 g. of water. The material which was thereby precipitated was filtered, washed with water and purified by crystallization from 95% alcohol, after which it melted at 274°. The compound was insoluble in alcohol and only sparingly soluble in glacial acetic acid. It crystallized in long, pale yellow needles. The yield was 8 g., or 38%.

*Analyses.* Calc. for  $\text{C}_{16}\text{H}_{11}\text{O}_2\text{N}_2\text{Cl}$ : N, 9.38. Found: 9.20, 9.60.

**The Action of Alcoholic Ammonia upon Chloro-aceto-*p*-anisidide. A. Amino-aceto-*p*-anisidide,  $\text{CH}_3\text{OC}_6\text{H}_4\text{-NH.CO.CH}_2\text{.NH}_2$ .**—A slight modification of the usual procedure was employed in the preparation of this amine. It was found advantageous to substitute sodium hydroxide for ammonia in order to liberate the free amine from its hydrochloride. The former was precipitated as an oil, which could be easily separated from the aqueous layer. After standing for a short time, this oil crystallized in stout needles.

The amine is very soluble in water, alcohol, acetone and ethyl acetate, but practically insoluble in ether or benzene. It is best crystallized from 25% alcohol from which it separates in silky needles which melt at 98–99°; yield, 73%. This amine is not hydrated.

*Analyses.* Calc. for  $\text{C}_9\text{H}_{12}\text{O}_2\text{N}_2$ : N, 15.55. Found: 15.51, 15.12.

**B. The Di-(*p*-methoxyphenylamide) of Diglycolamidic Acid,  $(\text{CH}_3\text{OC}_6\text{H}_4\text{NH.COCH}_2)_2\text{.NH}$ .**—This secondary amine was obtained in a manner similar to that used for the isolation of the chlorine analog. It is readily purified by crystallization from 30% alcohol from which it can be obtained in small plates, or in long, flat, colorless needles. Both forms melt at the same temperature, namely, 143°. It is extremely soluble in alcohol, acetone and ethyl acetate, but almost insoluble in water, benzene and ether. When an alcoholic solution of the base is saturated with hydrogen chloride, the corresponding hydrochloride is obtained in the form of glistening plates.

*Analyses.* Calc. for  $\text{C}_{18}\text{H}_{21}\text{O}_4\text{N}_3$ : N, 12.24. Found: 12.09, 12.06.

**C. The Tri-(*p*-methoxyphenylamide) of Triglycolamidic Acid,  $(\text{CH}_3\text{OC}_6\text{H}_4\text{NH.COCH}_2)_3\text{.N}$ .**—In one experiment, it accidentally happened that the alcohol was not fully saturated with ammonia, and therefore a relatively large amount of the secondary amine was formed. When this was crystallized from alcohol, a small amount of another substance was isolated, which after repeated crystallization from 95% alcohol melted at

192–193°. This was identified as the tertiary amine. It is quite difficultly soluble in alcohol, and insoluble in water. It crystallizes from alcohol in very small, heavy, white plates.

*Analyses.* Calc. for  $C_{27}H_{30}O_6N_4$ : N, 11.07, Found: 11.17, 11.25.

**Carbethoxy-amino-aceto-*p*-aniside**,  $CH_3OC_6H_4.NH.CO.CH_2NH.COOC_2H_5$ .—The transformation of amino-aceto-*p*-aniside into carbethoxy-amino-aceto-*p*-aniside was very nearly quantitative. After trituration with water the reaction product was crystallized from 95% alcohol from which it separated in large colorless plates which melted at 154°. This urethane is very soluble in alcohol, but insoluble in water and benzene.

*Analyses.* Calc. for  $C_{12}H_{16}O_4N_2$ : N, 11.11. Found: 11.15, 11.49.

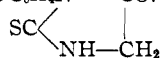
**Amino-aceto-*p*-aniside-dithiocarbamate**,  $CH_3OC_6H_4NHC(O)CH_2NH_2SHCSNH_2.CH_2.CO.NHC_6H_4OCH_3$ .—This compound is more stable than the previously described *p*-chloro derivative. It is quite soluble in water, fairly soluble in warm alcohol, acetone and ethyl acetate, but insoluble in ether and benzene. It crystallizes from 95% alcohol in broad, thin, colorless blades which are frequently of considerable length. It reddens in a capillary tube at 130°, and decomposes at 140–145° with evolution of hydrogen sulfide. Fifty-two g. of the carbamate was obtained from 50 g. of the amine.

*Analyses.* Calc. for  $C_{19}H_{24}O_4N_4S_2$ : N, 12.84; S, 14.69. Found: N, 12.60, 12.68; S, 14.93.

**Carbethoxy-amino-aceto-*p*-aniside Dithiocarbamate**,  $C_2H_5OOCSCSNHCH_2CO.NHC_6H_4OCH_3$ .—The weight of the air-dried substance, obtained from 50 g. of amino-aceto-*p*-aniside dithiocarbamate by the usual procedure, was 26 g. This crude material did not show a sharp melting point, but on the contrary decomposed at a temperature of 120°. It proved to be the desired carbethoxy compound, in which there was a small amount of the urethane ( $CH_3OC_6H_4.NHCO.CH_2NHCOOC_2H_5$ ). Owing to the instability of the carbethoxy compound in almost all solvents it was very difficult to obtain in a state of analytical purity and thereby free of the contaminating urethane.

*Analyses.* Calc. for  $C_{13}H_{16}O_4N_2S_2$ : N, 8.53. Found: 9.33, 9.51.

**Behavior of Carbethoxy-amino-aceto-*p*-aniside Dithiocarbamate on Distillation; its Conversion into 1-(*p*-methoxy phenyl)-2-thiohydantoin**,  $CH_3OC_6H_4N—CO—$



Twenty-six g. of the ester was subjected to distillation in an apparatus similar to that described in connection with the *p*-chloro compound. The compound underwent decomposition at 130°, the system being evacuated to a pressure of 40 mm. Sulfur compounds and ethyl alcohol were identified as products of the decomposition, the latter being recovered to an extent of 81%.

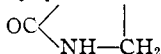
The residue in the flask failed to respond to the customary mustard oil tests. It was triturated with a small amount of warm alcohol to remove resinous material, and a yellow crystalline residue thereby obtained. The weight of the latter was 16 g., corresponding to 85%. It was purified for analysis by crystallization from alcohol. The hydantoin separated from this solvent in light yellow needles which melted at 207–209°. The properties of this compound are not in accord with those given by Beckurts and Frerichs for the pseudothiohydantoin obtained from the interaction of potassium thiocyanate and chloro-aceto-*p*-aniside. It is moderately soluble in 95% alcohol and glacial acetic acid, very sparingly soluble in hot water, and practically insoluble in ether and benzene.

*Analyses.* Calc. for  $C_{10}H_{10}O_2N_2S$ : N, 12.61; S, 14.43. Found: N, 12.63, 12.67; S, 14.62.



This thiohydantoin was also prepared by the action of mercuric chloride upon amino-aceto-*p*-anisidide dithiocarbamate. Eight g. of the dithiocarbamate was added to a solution of 2.5 g. of mercuric chloride in 75 cc. of water. A heavy precipitate of the mercury salt formed at once but, upon warming, this became black and hydrogen sulfide was copiously evolved. The solution was warmed until the evolution of hydrogen sulfide had ceased. After cooling, the precipitate was filtered and then extracted repeatedly with hot alcohol. The solution, thus obtained, deposited crystals of 1-(*p*-methoxyphenyl)-2-thiohydantoin upon standing. This product melted unchanged at 207° when mixed with that obtained by the previously described method.

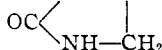
**The Desulfurization of 1-(*p*-Methoxyphenyl)-2-thiohydantoin.** 1-(*p*-Methoxyphenyl)hydantoin,  $\text{CH}_3\text{OC}_6\text{H}_4\text{N}-\text{CO}-$ —This compound was formed by digesting



3 g. of 1-(*p*-methoxyphenyl)-2-thiohydantoin with 6 g. of chloro-acetic acid in 50 g. of water. On evaporating the solution and cooling, it was obtained as white solid. The hydantoin crystallized from 20% alcohol in colorless needles which melted at 208°. The yield was 2 g., or 80%.

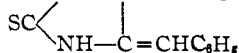
*Analyses.* Calc. for  $\text{C}_{10}\text{H}_{10}\text{O}_3\text{N}_2$ : N, 13.59. Found: 13.46, 13.48.

**The Conversion of Carbethoxy-amino-aceto-*p*-anisidide into 1-(*p*-Methoxyphenyl)-hydantoin,**  $\text{CH}_3\text{OC}_6\text{H}_4\text{N}-\text{CO}-$ —Three and one-half g. (87% yield) of the hydantoin



was obtained from 5 g. of the urethane. The former crystallized in well-defined needles melting at 208°, and also melted at this same temperature when mixed with the compound obtained from the desulfurization of 1-methoxyphenyl-2-thiohydantoin. The identity of the two was thereby established.

**1-(*p*-Methoxyphenyl)-2-thio-4-benzalhydantoin,**  $\text{CH}_3\text{OC}_6\text{H}_4\text{N}-\text{CO}-$ —Four g. of

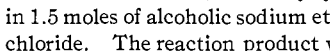


1-*p*-methoxyphenyl-2-thiohydantoin was condensed with benzaldehyde in the usual manner. The crude reaction product was crystallized from 95% alcohol, from which it separated in yellow plates melting at 203°. The yield was 5 g.

*Analyses.* Calc. for  $\text{C}_{17}\text{H}_{14}\text{O}_2\text{N}_2\text{S}$ : N, 9.03. Found: 9.09, 9.36.

**1-(*p*-Methoxyphenyl)-2-benzylmercapto-4-benzalhydantoin,**

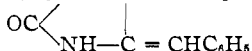
$\text{CH}_3\text{OC}_6\text{H}_4\text{N}-\text{CO}-$ —One and nine-tenths g. of the benzal hydantoin was dissolved



in 1.5 moles of alcoholic sodium ethylate and then treated with 1 g. ( $1\frac{1}{3}$  moles) of benzyl chloride. The reaction product was isolated in the usual manner and purified by crystallization from 95% alcohol in which it was difficultly soluble. It crystallized in slender needles of light yellow color, and melted at 174°. The yield was quantitative.

*Analyses.* Calc. for  $\text{C}_{24}\text{H}_{20}\text{O}_2\text{N}_2\text{S}$ : N, 7.00. Found: 6.97, 7.43.

**1-(*p*-Methoxyphenyl)-4-benzalhydantoin,**  $\text{CH}_3\text{OC}_6\text{H}_4\text{N}-\text{CO}-$ —The pure benzal



derivative was obtained by crystallization of the crude reaction product from 95% alcohol. The yield was 84%. This compound is soluble in acetic acid and very difficultly soluble in 95% alcohol, from which it crystallizes in long, pale yellow needles, melting at 238°.

*Analyses.* Calc. for  $\text{C}_{17}\text{H}_{14}\text{N}_2\text{O}_3$ : N, 9.52. Found: 9.33, 9.80.

**The Action of Alcoholic Ammonia upon Chloro-aceto-*m*-toluidide.** A. **Amino-aceto-*m*-toluidide**,  $\text{CH}_3\text{C}_6\text{H}_4\text{NH.CO.CH}_2\text{NH}_2\cdot\text{H}_2\text{O}$ .—The method employed for the preparation of the two previously described amines was used without any essential variation in procedure.

This amine is extremely soluble in water, alcohol, acetone and ethyl acetate, but practically insoluble in ether and benzene. It crystallizes from water or 95% alcohol in large transparent needles which contain 1 molecule of water of hydration. This hydrate melts at 74–75°. It is strongly basic, showing an alkaline reaction toward litmus, absorbing carbon dioxide from the air, and forming stable salts with acids; yield, 80–84%.

*Analyses.* Calc. for  $\text{C}_9\text{H}_{12}\text{N}_2\text{O}\cdot\text{H}_2\text{O}$ : N, 15.38;  $\text{H}_2\text{O}$ , 9.89. Found: N, 15.20, 15.39;  $\text{H}_2\text{O}$ , 10.12, 10.13.

The anhydrous amine may be obtained by allowing the hydrate to stand for a long time in a vacuum over sulfuric acid, or by heating it for an hour at 100°. It could not be crystallized from any solvent, but it crystallized from its own melt in well-defined, slender needles which melted at 54–55°.

*Analysis.* Calc. for  $\text{C}_9\text{H}_{12}\text{N}_2\text{O}$ : N, 17.07. Found: 16.66.

B. **The Di-(*m*-tolylamide) of Diglycolamidic Acid**,  $(\text{CH}_3\text{C}_6\text{H}_4\text{NH.COCH}_2)_2\text{NH}$ .—By reason of the insolubility of this amine in water, it could be isolated in a manner similar to that described in connection with the two previously mentioned secondary bases. It is very soluble in alcohol, acetone, ethyl acetate and glacial acetic acid, but practically insoluble in ether and benzene. It crystallizes from 50% alcohol in colorless needles (or plates under certain conditions) which melt at 136°. When a concentrated alcoholic solution is saturated with hydrogen chloride, the hydrochloride of the base precipitates in the form of platey white crystals.

*Analyses.* Calc. for  $\text{C}_{18}\text{H}_{21}\text{O}_2\text{N}_3$ : N, 13.50. Found: 13.29, 13.78.

**Benzoyl Amino-aceto-*m*-toluidide**,  $\text{CH}_3\text{C}_6\text{H}_4\text{NHCOCH}_2\text{NHCOC}_6\text{H}_5$ .—The crude benzoyl derivative was purified by crystallization from 95% alcohol, in which it is sparingly soluble and from which it separates in colorless needles melting at 186°. Seven g. of the pure compound was obtained from 5 g. of the amine.

*Analyses.* Calc. for  $\text{C}_{19}\text{H}_{19}\text{O}_2\text{N}_2$ : N, 10.45. Found: 10.55, 10.21.

**Carbethoxy-amino-aceto-*m*-toluidide**,  $\text{CH}_3\text{C}_6\text{H}_4\text{NHCOCH}_2\text{NHCOOC}_2\text{H}_5$ .—This urethane was purified by crystallization from benzene. The small prismatic crystals, thereby obtained, melted at 103°. This compound is very soluble in benzene, alcohol and ethyl acetate, but is very difficultly soluble in water and ether.

*Analyses.* Calc. for  $\text{C}_{12}\text{H}_{16}\text{O}_2\text{N}_2$ : N, 11.86. Found: 11.84, 12.03.

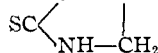
**Amino-aceto-*m*-toluidide Dithiocarbamate**,  $\text{CH}_3\text{C}_6\text{H}_4\text{NHCOCH}_2\text{NH}_2\cdot\text{SHCS.NH.CH}_2\text{CONHC}_6\text{H}_4\text{CH}_3$ .—The interaction of 100 g. of anhydrous amino-aceto-*m*-toluidide and 31 g. of carbon disulfide produced 105 g. (85%) of this carbamate. This reaction was conspicuously exothermic and it was, therefore, necessary to cool the solution in order to prevent evaporation of the solvent. The hydrated amine, under like conditions, also reacted smoothly with carbon disulfide, and in this case a 93% yield was obtained. For analysis it was purified by crystallization from ethyl acetate from which it separated in heavy, white, granular crystals which turned slightly pink upon standing. It is very soluble in alcohol and acetone, and difficultly soluble in ether, benzene and water. When warmed with the last named, it decomposes quite rapidly. When heated in a capillary tube, it suffers decomposition at 138°, with evolution of hydrogen sulfide.

*Analyses.* Calc. for  $\text{C}_{19}\text{H}_{21}\text{N}_4\text{O}_2\text{S}_2$ : N, 13.86; S, 15.85. Found: N, 13.88, 14.02; S, 15.20, 15.22.

**Carbethoxy-amino-aceto-*m*-toluidide Dithiocarbamate**,  $C_2H_5OOCSCSNHCH_2CO-NHC_6H_4CH_3$ .—The formation of this compound was attended with almost no side reactions, in contradistinction to the previously described *p*-chloro and *p*-methoxy homologs. One hundred g. of the dithiocarbamic acid salt gave 50 g. of ether-insoluble amino-aceto-*m*-toluidide hydrochloride and approximately 80 g. of the desired carbethoxy derivative. This was practically a quantitative partition of the normal reaction products. The carbethoxy compound is surprisingly stable as compared with the two homologs previously mentioned. A sample kept for several months underwent very little decomposition. It is rapidly decomposed by boiling water, but it may be crystallized from 95% alcohol without decomposition. It crystallizes from this solvent in well defined yellow needles, which decompose sharply at 113°.

*Analyses.* Calc. for  $C_{13}H_{16}O_3S_2N_2$ : N, 8.97; S, 20.53. Found: N, 8.95, 9.09; S, 20.36.

**The Behavior of Carbethoxy-amino-aceto-*m*-toluidide Dithiocarbamate on Distillation; its Conversion into 1-(*m*-Tolyl)-2-thiohydantoin**,  $CH_3C_6H_4N-CO-$



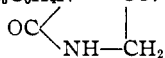
Fifty-eight g. of the ester was employed in this experiment. Decomposition of the ester took place at 120° (30 mm.) and, as in the other cases, both sulfur compounds and ethyl alcohol were identified in the distillate, the recovery of the latter being 7 g. or 83%. The solid residue in the flask gave no indications of the presence of an isothiocyanate. It was triturated with a small amount of alcohol and then crystallized from the same solvent. The hydantoin was obtained in the form of bright lemon-yellow needles, which melted at 187° with decomposition. The total amount of pure hydantoin resulting from this distillation was 18 g. or 47%.

The properties of this compound do not agree with those of the pseudothiohydantoin described by Beckurts and Frerichs. It is soluble in alcohol, acetone and glacial acetic acid, very sparingly soluble in water, and practically insoluble in ether and benzene.

*Analyses.* Calc. for  $C_{10}H_{10}ON_2S$ : N, 13.59; S, 15.55. Found: N, 13.71, 13.75; S, 15.75.

This thiohydantoin was also obtained from amino-aceto-*m*-toluidide-dithiocarbamate by warming 50 g. of the latter with a solution of 16.7 g. of mercuric chloride in 250 cc. of water. The usual procedure was then followed and 8.9 g. of 1-(*m*-tolyl)-2-thiohydantoin was obtained. A sample of this hydantoin melted at 187° with decomposition, and behaved similarly when mixed with the substance obtained by the preceding method.

**The Desulfurization of 1-*m*-Tolyl-2-thiohydantoin.** 1-(*m*-Tolyl) hydantoin,  $CH_3C_6H_4N-CO-$ —Seven g. of the thiohydantoin was digested for 6 hours with a solu-

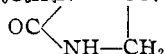


tion of 14 g. of chloro-acetic acid in 50 g. of water. The solution was filtered, evaporated to a sirupy consistency, and the crude hydantoin precipitated by the addition of 25 cc. of ether. It was purified for analysis by crystallization from 25% alcohol from which it separated in colorless needles which melted at 123°. The yield was 3.5 g., or 64%.

This hydantoin is very soluble in alcohol, less so in water, and insoluble in ether and benzene.

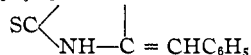
*Analyses.* Calc. for  $C_{10}H_{10}N_2O_2$ : N, 14.74. Found: 14.79, 14.90.

**The Conversion of Carbethoxy-amino-aceto-*m*-toluidide into 1-(*m*-Tolyl)hydantoin**,  $CH_3C_6H_4N-CO-$ —Twelve g. of the carbethoxy derivative was converted into the hy-



dantoin in accordance with the procedure described in connection with the *p*-chloro homolog. The reaction product was crystallized from dil. alcohol, and the pure hydantoin thus obtained weighed 4 g. This compound melted at 123° as did also a mixture of the same with the hydantoin obtained by the desulfurization of the corresponding thiohydantoin. The two compounds were, therefore, identical.

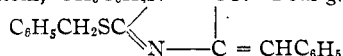
1-(*m*-Tolyl)-2-thio-4-benzalhydantoin,  $\text{CH}_3\text{C}_6\text{H}_4\text{N}-\text{CO}$ .—The reaction product



was purified by crystallization from 95% alcohol. It was sparingly soluble in this solvent, and crystallized in slender needles which melted at 183°. The yield from 10 g. of 1-*m*-tolyl-2-thiohydantoin was 13 g., or 91%.

*Analyses.* Calc. for  $\text{C}_{17}\text{H}_{14}\text{ON}_2\text{S}$ : N, 9.52. Found: 9.58, 9.84.

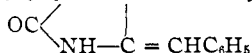
1-(*m*-Tolyl)-2-benzylmercapto-4-benzalhydantoin,  $\text{CH}_3\text{C}_6\text{H}_4\text{N}-\text{CO}$ .—Four g. of



the benzalhydantoin was alkylated in the usual manner with benzyl chloride. The crude mercapto derivative was crystallized from 95% alcohol, from which it separated in colorless, long, silky needles which melted at 145°. When this compound was recrystallized from alcohol, a mixture was obtained, consisting of the previously described needles, together with thin, yellow plates. This mixture was allowed to stand in alcohol for some hours after which it was noticed that all of the needles had disappeared. The entire preparation was repeated with identical results. The needles, therefore, seemed to be an unstable form of the mercapto compound which gradually passed into the stable form upon standing. Both forms melted at the same temperature, namely 145°. The yield was quantitative.

*Analyses.* Calc. for  $\text{C}_{24}\text{H}_{20}\text{N}_2\text{OS}$ : N, 7.29. Found: 7.12, 7.18.

1-(*m*-Tolyl)-4-benzalhydantoin,  $\text{CH}_3\text{C}_6\text{H}_4\text{N}-\text{CO}$ .—Twenty-two g. of the



hydantoin was digested with benzaldehyde under the conditions above described. The curdy yellow reaction product was crystallized from 95% alcohol in which it was sparingly soluble. When pure, it crystallized in broad needles of pale yellow color which melted at 214°. The yield was 18 g., or 56%.

*Analyses.* Calc. for  $\text{C}_{17}\text{H}_{14}\text{O}_2\text{N}_2$ : N, 10.07. Found: 10.02, 9.97.

#### The Behavior of Certain Secondary Amines with Acetone

An attempt was made to crystallize the secondary amine,  $(p\text{-ClC}_6\text{H}_4\text{NHCOCH}_2)_2\text{NH}$ , from acetone. The base dissolved readily, but after short heating, a solid crystallized from the hot solution. This material did not redissolve in any reasonable amount of the solvent. It was therefore filtered and examined. The weight of the new substance was practically equal to the weight of the secondary amine originally taken, but it melted at 250–251°, or nearly 100° higher than the amine, and was practically insoluble in alcohol and acetone. It was, however, readily soluble in glacial acetic acid but the material which crystallized from this solvent was *not* the high-melting substance, but the pure secondary amine. The preparation of this peculiar compound was several times repeated and identical results obtained. Owing to its insolubility in practically all solvents, a recrystallized sample could not be obtained and analyses were, therefore, made on a "crude" preparation. This sample was prepared from pure secondary amine and pure acetone. It appeared to be definitely crystalline and quite homogeneous, when examined under the microscope. The analytical data agree fairly well for a substance produced by the combination of two molecules of the secondary amine with one of acetone,  $[(\text{ClC}_6\text{H}_4\text{NHCOCH}_2)_2\text{NH}]_2 \cdot (\text{CH}_3)_2\text{CO}$ .

*Analyses.* Calc. for  $C_{16}H_{18}O_8N_6Cl_4$ : N, 11.02, Cl, 18.60. Found: N, 11.09, 11.11; Cl, 18.24.

A similar compound was obtained by boiling the di-(phenylamide) of diglycolamidic acid,  $(C_6H_5NHCOCH_2)_2NH$  with acetone for a short time. This substance could be crystallized from acetone, and was thus obtained in large blunt needles, which melted at  $166-167^\circ$  without decomposition. The melting point of the secondary base is  $141^\circ$ .

*Analyses.* Calc. for  $C_{35}H_{40}O_8N_6$ : N, 13.46. Found: 13.47, 13.41.

This reaction will be further investigated with the view of determining its generality, and also the structure of the molecular complexes formed thereby.

### Summary

1. Chloro-aceto-*p*-chloro-anilide, chloro-aceto-*p*-anisidide, and chloro-aceto-*m*-toluidide have been converted into the corresponding isothiocyanates by the method recently described by the writers.

2. These isothiocyanates are so unstable that they rearrange immediately into the isomeric normal 2-thiohydantoin.

3. The structure of these thiohydantoin has been established and characteristic derivatives prepared.

4. The investigations demonstrate that unstable mustard oils cannot be formed by the action of potassium thiocyanate on the above mentioned chloro-acetanilides, otherwise the final products of the reactions would be normal rather than pseudothiohydantoin.

NEW HAVEN, CONNECTICUT

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### NEW BOOKS

**Valenzkräfte und Röntgenspektren (Valence Forces and X-Ray Spectra).** By Dr. W. KOSSEL. Professor at the University of Kiel. Julius Springer, Berlin, 1921. 70 pp. 11 fig.  $22 \times 15$  cm.

The two sections of this pamphlet are based, respectively, on two articles which the author published in "Naturwissenschaften" in 1919 and 1920. In the first, the author shows how the over-emphasis of the study of the valence of a single element, namely carbon, has led to misconceptions. By coupling Abegg's ideas of homo- and hetero-valence with modern ideas as to the structure of the atom, the author endeavors to prove that the old Berzelius binary theory of molecular structure is valid. He is also able to derive on this basis ideas of valence and molecular structure which harmonize nicely with Werner's theories. In the second part, the author develops the Bohr theory of atomic structure, with particular reference to X-ray spectra, and draws numerous conclusions regarding the structure of atoms.

These essays are wonderfully clear, and are bound to be extremely interesting and stimulating to chemists. They make many complicated matters seem simple, and present many illuminating ideas.

<sup>7</sup> Hill and Kelsey, THIS JOURNAL, 42, 1704 (1920).