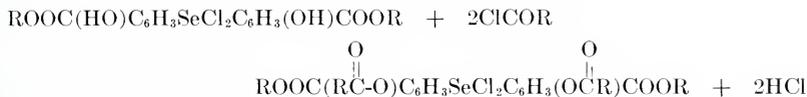


SELENIUM DERIVATIVES OF SALICYLIC ACID

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Phenols react, as a rule, with acid chlorides to form acylated derivatives. Attempts were made to acylate the phenolic group upon the dialkyl 5,5'-selenodisalicylate Se-dichlorides, prepared by Nelson, Schroeder, and Bunting¹ according to the following reaction:



The reaction did not take place and the original material was recovered.

Attempts were then made to acylate the phenolic groups in 5,5'-selenodisalicylic acid prepared according to Morgan and Burstall.² Warming with acetic anhydride in the presence of concentrated sulphuric acid, boiling with acetyl chloride, and boiling with glacial acetic acid failed to produce acylation.

This raised some question as to the structure of the compounds, since the seleno esters gave no ferric chloride phenol test, but the acid, on the other hand, gave the test. Also the fact that the selenium oxychloride, being an acid chloride, might have acted on the phenolic group instead of the fifth hydrogen on the ring, in the preparation of the selenium compounds, needed to be considered. This would give compounds of the same empirical formula, but their structure would be entirely different.

Nelson and Baker³ prepared 5,5'-selenodisalicylic acid from dimethyl 5,5'-selenodisalicylate Se-dichloride indicating that the two compounds had analogous structures. This did not show the position of the selenium. However, in this work, an attempt to prepare 5,5'-selenodisalicylic acid Se-dibromide by the action of bromine in chloroform solution upon 5,5'-selenodisalicylic acid gave 3,5-dibromo salicylic acid, which indicates that the selenium was attached to the ring.

Attempts at methylation of dimethyl 5,5'-selenodisalicylate with dimethyl sulphate in alkaline solution were unsuccessful.

An attempt to prepare trimethyl 5,5',5''-selenotrisalicylate Se-chloride by treating dimethyl 5,5'-selenodisalicylate Se-dichloride with methyl salicylate in the presence of anhydrous aluminum chloride gave dimethyl 5,5'-selenodisalicylate.

The treatment of dimethyl 5,5'-selenodisalicylate Se-dichloride with sodium cyanide resulted only in hydrolysis with the formation of dimethyl 5,5'-selenodisalicylate Se-dihydroxide melting at 137°.

¹ Nelson, Schroeder, and Bunting: *J. Am. Chem. Soc.* 55, 801. 1933.

² Morgan and Burstall: *J. Chem. Soc.* 3260. 1928.

³ Nelson and Baker: *J. Am. Chem. Soc.* 56, 467. 1934.

Experimental

The selenium oxychloride and salicylic acid used in this work were obtained from the J. T. Baker Chemical Company and not further purified. The methyl salicylate was obtained from the Mallinckrodt Chemical Company. Analysis for selenium was carried out according to the method of Shaw and Reid,⁴ 5,5'-selenodisalicylic acid was prepared according to the method of Morgan and Burstall, and dimethyl 5,5'-selenodisalicylate Se-dichloride was prepared according to the method of Nelson, Schroeder, and Bunting.

Acetylation of dimethyl 5,5'-selenodisalicylate Se-dichloride.

Twenty-five g. of dimethyl 5,5'-selenodisalicylate Se-dichloride was treated with a large excess (25 g.) of acetyl chloride and boiled for several hours. No reaction took place.

Acetylation of 5,5'-selenodisalicylic acid.

Twenty-five g. of 5,5'-selenodisalicylic acid was refluxed with 100 cc. of acetyl chloride for 24 hours, but no reaction occurred. In another attempt 25 g. of the acid was refluxed with 100 cc. of glacial acetic, and still another was refluxed with 100 cc. of acetic anhydride. The final attempt was to warm the acid gently with 50 cc. of acetic anhydride in which 10 cc. of concentrated sulphuric acid had been dissolved. In each case the original product, 5,5'-selenodisalicylic acid was obtained.

3,5-Dibromosalicylic acid.

Ten per cent excess of bromine in chloroform solution was added to a chloroform solution of 5,5'-selenodisalicylic acid and warmed until the evolution of HBr ceased. The chloroform was evaporated and the solid washed with ether and recrystallized from hot water. M. pt. 223° C. Mixed melting point with the 3,5-dibromosalicylic acid prepared by the action of bromine upon salicylic acid was unchanged.

Dimethyl 5,5'-selenodisalicylate.

In an attempt to prepare trimethyl-5,5',5''-selenotrisalicylate Se-chloride, 6.5 g. of methyl salicylate was added to 20 g. of dimethyl-5,5'-selenodisalicylate Se-dichloride in the presence of 12 g. of anhydrous aluminum chloride. This reaction was carried out in anhydrous ether and warmed until evolution of HCl ceased. The solid material was separated and boiled with 200 cc. of water in which 10 cc. of conc. HCl had been dissolved. The resulting solid was recrystallized several times from benzene. M. pt. 158° C. Yield 45%.

	Selenium
Calc. for C ₁₆ H ₁₄ O ₆ Se.....	20.8%
Found.....	20.6%

Dimethyl 5,5'-selenodisalicylate was prepared by the method of Nelson, Schroeder, and Bunting. M. pt. 158° C. A mixed melting point of the two products was constant.

For more complete identification, dimethyl 5,5'-selenodisalicylate Se-dibromide was prepared by adding a 10% excess of bromine in chloro-

⁴ Shaw and Reid: J. Am. Chem. Soc. 49, 2330. 1927.

form solution to chloroform solutions of each of the compounds. The m. pt. of each was 143° C., and the mixed melting point remained constant.

Attempt to methylate Dimethyl 5,5'-selenodisalicylate.

Twenty-five and three-tenths g. of dimethyl 5,5'-selenodisalicylate was treated with 22.6 g. of dimethyl sulphate in 125 cc. of H₂O containing 20 g. of NaOH. After standing 30 minutes another equal portion of dimethyl sulphate was added and the mixture refluxed for an hour. After cooling and acidifying with HCl, 5,5'-selenodisalicylic acid was precipitated. After recrystallization from dilute alcohol it melted at 272° . A mixed melting point was unchanged.

Dimethyl 5,5'-selenodisalicylate Se-dihydroxide.

Twenty-two and six-tenths g. of dimethyl 5,5'-selenodisalicylate Se-dichloride was treated with 4.9 g. of NaCN in 100 cc. of H₂O. The mixture was kept cold in an ice bath and stirred for two hours. The color turned from cream to white. The white solid was extracted with water to remove NaCN, filtered and recrystallized several times from water. M. pt. 137° C. Yield 15%. A mixed melting point with dimethyl 5,5'-selenodisalicylate Se-dihydroxide, m. pt. 137° C., prepared according to Nelson, Schroeder, and Bunting remained constant.

Summary

1. Attempts to acylate dimethyl 5,5'-selenodisalicylate Se-dichloride or 5,5'-selenodisalicylic acid were unsuccessful.
2. The position of selenium on the ring of 5,5'-selenodisalicylic acid and its derivatives has been demonstrated.
3. Saponification occurred when dialkyl 5,5'-selenodisalicylate was treated with dimethyl sulphate in alkaline solution.
4. Dimethyl 5,5'-selenodisalicylate was formed when dimethyl-5,5'-selenodisalicylate Se-dichloride was treated with methyl salicylate in the presence of anhydrous aluminum chloride.
5. Dialkyl 5,5'-selenodisalicylate Se-dichlorides yield the corresponding dihydroxides upon treatment with sodium cyanide solution.