

A new Synthesis of 6-Selenoctic Acid and a Related Compound

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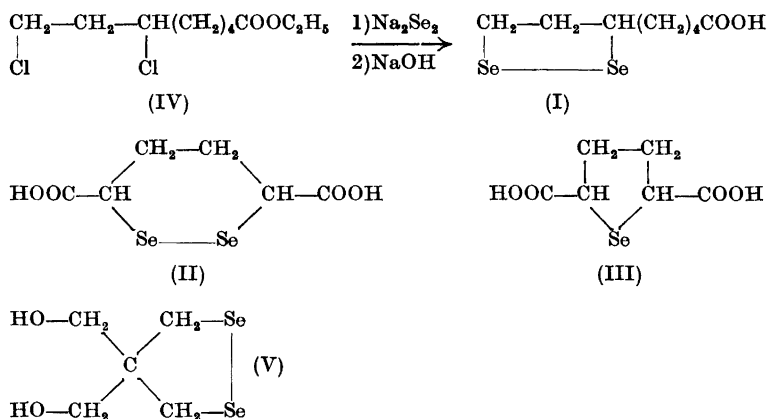
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Recently the author described the synthesis of 6-selenoctic acid (I) in this journal¹. As this substance had not been characterized before and since operations with cyclic selenium compounds are not easy, the author then applied a method of synthesis analogous to one used in the preparation of 6-thioctic acid². The method involved the synthesis of 6,8-dibenzylselenooctanoic acid from ethyl 6,8-dichlorooctanoate followed by reductive cleavage with sodium in liquid ammonia and oxidation with air. In this way 6-selenoctic acid was obtained in fair yield, and some of its properties could be determined. It now seemed advisable to look for other synthetic methods.

The simplest of all methods for preparing organic diselenides is the alkylation of alkali diselenides. As pointed out by Fredga³, however, this method fails to give the six-membered cyclic diselenide 1,2-diselenane-3,6-dicarboxylic acid (II) when α,α' -dibromo adipic acid is treated with potassium diselenide. In this case the reaction leads to the five-membered cyclic monoselenide tetrahydroselenophene-2,5-dicarboxylic acid (III) and elementary selenium. When ethyl 6,8-dichlorooctanoate (IV) is treated with sodium diselenide, however, only a small amount

of elementary selenium remains after the reaction, and ring closure takes place to form 6-selenoctic acid. In a similar way reaction between 2,2-(bisiodomethyl)propanediol-1,3 and sodium diselenide gives the cyclic compound 4,4-(bishydroxymethyl)-1,2-diselenolane (V).

From the point of view of steric strain in the cyclic diselenides it seems difficult to explain why the five-membered rings seem to form more easily than the six-membered. The presence of the carboxylic groups in the vicinity of the bromine atoms in dibromo adipic acid possibly complicates the reaction. A preliminary experiment with dibromoglutaric acid and sodium diselenide points in this direction. It must be borne in mind that α -halogen substituted carboxylic acids (contrary to other halogen compounds) completely oxidize sodium ditelluride to elementary tellurium, the acid being reduced to the unsubstituted fatty acid⁴. In view of the possible oxidative action of the halogen compounds towards the alkali diselenide it seems advisable to use chlorine compounds whenever possible. It must be pointed out that 6-selenoctic acid is obtained in better yield than 4,4-(bishydroxymethyl)-1,2-diselenolane, which may be due to the fact that a chlorine compound was used in the preparation of the former and an iodine compound for the latter. Backer and Winter also got only a low yield of 4-phenyl-4-methyl-1,2-diselenolane when phenyl methyl dibromopropane was treated with potassium diselenide. The chief products were elementary selenium and a hydrocarbon.⁵ When complications of these kinds occur the second method worked out by



Fredga, *viz.* hydrolysis of selenocyanates must be recommended³. In this way, Fredga obtained 1,2-diselenane-3,6-dicarboxylic acid, and Backer and Winter 4-phenyl-4-methyl-1,2-diselenolane and 4,4-dimethyl-1,2-diselenolane⁵.

6-Selenoctic acid has its characteristic UV-peak at 442 m μ as can be seen from Fig. 1, curve 1. The spectrum of 4,4-(bis-hydroxymethyl)-1,2-diselenolane is closely related as well as that of 1,2-diselenolane itself⁶. Non-cyclic diselenides absorb at about 310 m μ ⁷. Whether the shoulder at about 300 m μ in the spectra of the five-membered ring compounds is due to the presence of a small amount of polymer in the solution or to a hitherto unrecognized band cannot be answered at present. After standing over night the spectrum of the solution of 6-selenoctic acid did not change significantly. When 6-selenoctic acid was treated with NaBH₄, the absorption band at 442 m μ disappeared, indicating complete reduction to the selenol (Fig. 1 curve 2). 1,2-Dithiolane derivatives are said not to be reduced by sodium borohydride⁸. When the reduced solution was allowed to stand in the air for about one hour, oxidation to 6-selenoctic acid occurred, as seen from Fig. 1 curve 3. A complete report of the UV and IR spectra of diselenides is to be published in *Arkiv Kemi*. Preparation of optically active 6-selenoctic acid is planned.

Experimental: 6-Selenoctic acid. Sodium diselenide solution was prepared by dissolving 2.17 g of sodium formaldehydesulphoxylate (Rongalite C), 1.47 g of sodium hydroxide and 2.91 g of selenium in 30 ml of water in a nitrogen atmosphere. 4.43 g of ethyl 6,8-dichlorooctanoate dissolved in 30 ml of ethanol was added dropwise and the reaction mixture stirred for 90 min, the temperature being kept at 60–70°. 1.47 g of sodium hydroxide in 25 ml of water was added and stirring and warming continued for 5 h. After standing over night the mixture was acidified with 6 N hydrochloric acid. The product was taken up in 50 ml of chloroform. This extract was dried with sodium sulphate and the solvent removed in vacuum. The residue was extracted with boiling *n*-hexane, and when this solution cooled, the crude 6-selenoctic acid separated (m. p. 86–89°). The yield was about 25 % but it seems possible to increase it. After recrystallization from *n*-hexane, the product melted at 89–90.5°.

4,4-(Bishydroxymethyl)-1,2-diselenolane. The sodium diselenide solution was prepared as above, and the calculated quantity of 2,2-

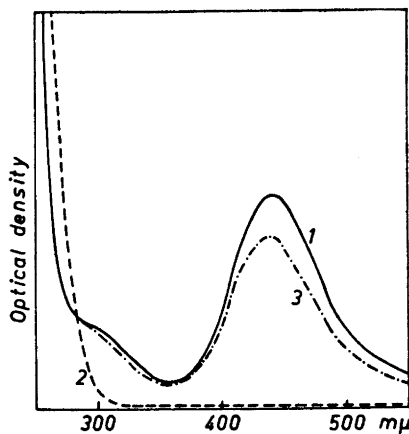


Fig. 1. Light absorption of 1) 6-selenoctic acid in ethanol, 2) 6-selenoctic acid reduced with NaBH₄, 3) the reduced solution after 1 h exposure to air.

(bisiodomethyl)-propanediol-1,3 dissolved in ethanol was added. After 5 h reflux, the mixture was extracted with 3 × 50 ml of ether. The extract was dried with sodium sulphate and the ether evaporated. The residue was boiled with some petroleum ether to remove impurities and then recrystallized twice from benzene. The product crystallized in long dark red needles m. p. 133–135°. (Found: Se 59.8. Calc. 60.6.) Yield 8 %.

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