

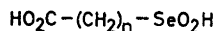
Some Long-chain ω -Carboxy Alkyl Seleninic Acids and α,ω -Alkyl Diseleninic Acids

ERIK REBANE

Chemical Institute, University of Uppsala, Uppsala, Sweden

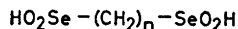
The syntheses of two long-chain ω -carboxy alkyl seleninic acids (I–II) and three long-chain α,ω -alkyl diseleninic acids (III–V) from the corresponding diselenides or selenocyanates are described. Some short remarks are made on their properties and on the methods of preparation.

After the discovery, by Schwarz and Foltz,¹ that selenium is an essential part of the nutritionally important Factor 3, organic selenium compounds have attracted increased interest from the biological point of view, and the biological activity of many selenium compounds, among them a number of short-chain ω -carboxy alkyl seleninic acids, has been investigated.^{2,3} As long-chain ω -substituted alkyl seleninic acids do not appear to have been described in the literature, it was considered of interest to extend the work to some compounds of this type in connection with studies on long-chain alkyl mono-seleninic acids.⁴ In this paper the preparation and properties of two ω -carboxy alkyl seleninic acids (I) and (II) and three α,ω -alkyl diseleninic acids (III)–(V) are reported.



I: $n=10$

II: $n=12$



III: $n=10$

IV: $n=12$

V: $n=14$

The most convenient methods for the preparation of aliphatic seleninic acids involve an oxidation of certain selenium containing compounds, especially diselenides and selenocyanates.⁵ Hydrogen peroxide in different solvents⁶ and dilute or concentrated nitric acid⁷ are the oxidizing agents frequently used.

The ω -carboxy alkyl seleninic acids (I) and (II) were prepared from the corresponding diselenides (in the case of the acid (II) the corresponding di-

seleno diethyl ester, being available,⁹ was used), the oxidations being performed at 50° with dilute nitric acid. Concentrated nitric acid seemed to cause some decomposition of the diselenides even at room temperature. The acid (II) was also prepared from ω -carbethoxy-dodecyl selenocyanate, obtained from the corresponding bromoester⁹ and potassium selenocyanate. The hydrolysis of the terminal carbethoxy group in the case of this acid may be performed either before the oxidation of the diselenide or selenocyanate group (the corresponding diseleno-dicarboxylic acid being the expected product) or after it. According to the first method an acid hydrolysis ought to be preferable because diseleno-dicarboxylic acids are known not to be very stable in alkaline solution.⁸ However, because the hydrolysis in acid solution of diethyl ω, ω' -diselenodidodecanecarboxylate has also been found to cause partial decomposition,⁹ the alternative method, mentioned above, for preparation of the acid (II) was chosen. Both alkaline and acid hydrolyses of the thus obtained ω -carbethoxy dodecyl seleninic acid were tried; the latter seemed to give somewhat purer products. In this case isolation of the intermediate ester obtained may not be necessary and the hydrolysis may be carried out by addition of some water to the acid reaction mixture after complete oxidation of the selenocyanate group, followed by warming. The temperature during this last step was not allowed to exceed 50°.

The α, ω -alkyl diseleninic acids (III)–(V) have been prepared from the corresponding pure diselenocyanates, obtained from the corresponding dibromides and potassium selenocyanate. Details about these selenocyanates, which do not appear to have been described previously in the literature, are given in the experimental part. For their oxidation fuming nitric acid had to be used, and the reaction was carried out first at room temperature and then completed at about 60°. The diseleninic acids obtained were most conveniently isolated in the form of their hydronitrates. The yields were good. The free acids (III)–(V) were then obtained by suspending their pure nitric acid compounds in warm water, the minimum amount of methanol added to give a clear solution followed by neutralization of the nitric acid with sodium hydroxide. After cooling, the diseleninic acids (III)–(V) separated in a pure state as thin white glistening flakes.

The ω -carboxy alkyl seleninic acids (I) and (II) and the α, ω -alkyl diseleninic acids (III)–(V) are all white crystalline solids which can, if necessary, be rather easily purified by recrystallizations from dilute methanol or dilute acetone. The two functional groups in these acids of course increase their solubility in polar solvents as compared with the monoseleninic acids of the same chain length. For instance the solubility of 1,10-decyl diseleninic acid (III) in water, determined as described earlier,⁴ is almost three times greater (0.022 g/100 ml solution, 25°) than that of decyl seleninic acid⁴ and about four times greater than that of the corresponding dicarboxylic acid.¹⁰

The acids (I)–(V) all seem to be quite stable substances in the pure state at room temperature and no change in appearance has been observed even after long standing. The storage of these acids as their hydronitrates, also rather easily obtainable in the pure state, which is often convenient in the case of short-chain seleninic acids,⁵ seems therefore to be of no special advantage here. Both the carboxy alkyl seleninic acids and the alkyl diseleninic acids

and their hydronitrates described here melt with simultaneous decomposition. The rate of heating has some influence on the melting points, specially in the case of the diseleninic acids (III)–(V). The melting points given for the acids (I)–(V) were obtained according to the following method: the apparatus was preheated to 10° below the preliminary melting point found previously and the temperature was then raised at the rate of 3°/min near the melting point.

EXPERIMENTAL

All melting points are uncorrected. The infrared spectra were recorded with a Perkin-Elmer model 237 spectrophotometer. The selenium analyses were carried out according to Fredga.¹¹

12-Carbethoxy-dodecyl selenocyanate. 4.29 g ethyl ω -bromotridecanoate⁹ and 2.30 g potassium selenocyanate in 50 ml dry acetone were refluxed for 4.5 h. The acetone was then distilled off, 50 ml water was added to dissolve the potassium bromide and the mixture was extracted with 3 \times 30 ml ether. After drying over magnesium sulfate and evaporation of the ether 3.80 g (82 %) of a brownish oil was obtained, crystallizing after cooling. After one recrystallization from petroleum ether (cooling in a freezing-mixture was necessary) an almost colorless product, m.p. 20–21.5°, was obtained. (Found: Se 22.76. Calc. for C₁₆H₂₂NO₂Se: Se 22.79).

1,10-Decyl diselenocyanate. 15.00 g 1,10-decyl dibromide and 17.00 g potassium selenocyanate similarly gave 14.51 g (83 %) of an oil, crystallizing after cooling. One recrystallization from dilute methanol followed by one from petroleum ether (b.p. 60–71°) gave large colorless glistening flakes, m.p. 34–35°. (Found: Se 44.97. Calc. for C₁₂H₂₀N₂Se₂: Se 45.07).

1,12-Dodecyl diselenocyanate. 2.15 g 1,12-Dodecyl dibromide and 3.30 g potassium selenocyanate in 35 ml dry acetone gave 2.25 g (91 %) of a slightly yellowish product m.p. 46–48°. One recrystallization (at –14°) from 150 ml petroleum ether (b.p. 60–71°) gave thin colorless glistening flakes, m.p. 47–48°. (Found: Se 41.66. Calc. for C₁₄H₂₄N₂Se₂: Se 41.74).

1,12-Dodecyl dibromide was prepared by bromination of dodecane-1,12-diol,¹² yield 90 %, m.p. 37.5–38.5°.

Dodecane-1,12-diol was obtained by reduction of diethyl decane-1,10-dicarboxylate with lithium aluminium hydride,¹³ yield 96 %, m.p. 80–81° (from benzene).

Diethyl decane-1,10-dicarboxylate was prepared from the corresponding acid according to Brändström,¹⁴ the acid being obtained from decane-1,10-dibromide *via* the dinitrile.

1,14-Tetradecyl diselenocyanate. 1.98 g 1,14-Tetradecyl dibromide and 2.34 g potassium selenocyanate gave 2.05 g (91 %) of an almost colorless product, m.p. 54–55.5°. One recrystallization from petroleum ether (b.p. 60–71°) gave colorless glistening flakes, m.p. 56–57°. (Found: Se 38.67. Calc. for C₁₆H₂₈N₂Se₂: Se 38.85).

1,14-Tetradecyl dibromide was prepared by bromination of 1,14-tetradecane diol,¹² yield 78 %, m.p. 48–49° (from alcohol).

1,14-Tetradecane diol was obtained by reduction of diethyl 1,12-dodecane dicarboxylate⁹ with lithium aluminium hydride,¹³ yield 68 %, m.p. 84–85° (from benzene).

10-Carboxy-decyl seleninic acid (I). To a suspension of 0.21 g ω,ω' -diseleno-diundecanoic acid¹⁵ in 1 ml water was added dropwise, with shaking, 1 ml concentrated nitric acid followed by 0.5 ml fuming nitric acid at room temperature. After 5 min at this temperature the mixture was warmed with occasional shaking to 50°. The oxidation proceeded smoothly and was complete after 25 min. 2 ml warm water was added to the pale yellow homogeneous reaction mixture, the solution filtered and allowed to cool. 0.24 g (84 %) hydronitrate of (I) in the form of thin glistening flakes was obtained, m.p. 102–104° (decomp.). (Found: equiv. wt. 120.0. Calc. for C₁₁H₂₃NO₂Se: equiv. wt. 120.1).

The free acid (I) was obtained by suspending the hydronitrate in water heating to about 50° and adding a few drops of methanol to give a clear solution. Then sodium hydroxide was added to pH 3 and after cooling (I) separated as glistening flakes, m.p. 116–117° (decomp.). (Found: Se 26.29; equiv. wt. 149.1. Calc. for C₁₁H₂₂O₄Se: Se 26.56;

equiv. wt. 148.6). IR-absorption in the region expected for oxygenated selenium groups (KBr-phase): 890 cm^{-1} (w), 790 cm^{-1} (s), 690 cm^{-1} (s).

12-Carboxy-dodecyl seleninic acid (II). To 0.65 g 12-carbethoxy-dodecyl selenocyanate was added 0.5 ml fuming nitric acid and after 5 min at room temperature, the mixture was kept at 50° for 15 min. Then 10 ml water and sodium hydroxide to about pH 3 was added and after cooling the precipitate was filtered, 0.53 g (80%), m.p. $74-80^\circ$. After one recrystallization from dilute acetone 12-carbethoxy-dodecyl seleninic acid had m.p. $80-81^\circ$. (Found: equiv. wt. 350.5. Calc. for $\text{C}_{18}\text{H}_{30}\text{O}_4\text{Se}$: equiv. wt. 353.4).

This ester was also prepared by oxidizing diethyl ω,ω' -diseleno-di-tridecanoate⁹ with dilute nitric acid at 50° .

0.36 g of this ethyl ester in 15 ml 10% nitric acid and 5 ml acetone was kept at 50° overnight. 0.28 g of a product, m.p. $95-98^\circ$ (decomp.) (probably a mixture of (II) and its hydronitrate) was obtained. One recrystallization from dilute acetone gave 0.18 g glistening flakes, m.p. $120.5-121.5^\circ$ (decomp.). (Found: Se 24.09; equiv. wt. 163.4. Calc. for $\text{C}_{13}\text{H}_{22}\text{O}_4\text{Se}$: Se 24.27; equiv. wt. 162.7). IR-absorption in the region expected for oxygenated selenium groups (KBr-phase) 890 cm^{-1} (w), 790 cm^{-1} (s), 695 cm^{-1} (s), 685 cm^{-1} (s).

(II) dissolved in nitric acid (concentrated nitric acid-water, 2:1 by volume) gave after cooling 12-carboxy-dodecyl seleninic acid hydronitrate, m.p. $103-106^\circ$ (decomp.). (Found: equiv. wt. 128.6. Calc. for $\text{C}_{13}\text{H}_{27}\text{NO}_7\text{Se}$: equiv. wt. 129.4).

1,10-Decyl diseleninic acid (III). To 2.82 g 1,10-decyl diselenocyanate was added 1.5 ml fuming nitric acid and the mixture was kept at room temperature for 10 min with occasional shaking; another 1.5 ml fuming nitric acid was then added and the temperature was raised to 60° for 20 min. About twice its volume of water was then added to the mixture, followed by heating to give a clear, somewhat yellowish, solution. After cooling 3.40 g (86%) of the dihydronitrate of (III) was obtained, m.p. $127-128.5^\circ$ (decomp.). (Found: equiv. wt. 124.0. Calc. for $\text{C}_{10}\text{H}_{24}\text{N}_2\text{O}_{10}\text{Se}_2$: equiv. wt. 122.6).

(III) was obtained from this dihydronitrate by dissolving it in warm dilute methanol and adding sodium hydroxide to pH 3-4. After cooling 2.20 g of the free seleninic acid (III) was obtained, the melting point after another recrystallization from dilute methanol being $125-126^\circ$ (decomp.). (Found: Se 43.27; equiv. wt. 183.7. Calc. for $\text{C}_{10}\text{H}_{22}\text{O}_4\text{Se}_2$: Se 43.36; equiv. wt. 182.1). IR-absorption in the region expected for oxygenated selenium groups (KBr-phase) 835 cm^{-1} (s), 810 cm^{-1} (s), 670 cm^{-1} (s), 660 cm^{-1} (s).

1,12-Dodecyl diseleninic acid (IV). 1.30 g 1,12-dodecyl diselenocyanate was oxidized with 2.5 ml fuming nitric acid. After complete reaction 7.5 ml concentrated nitric acid and 7.5 ml water were added and the mixture heated until a clear solution was obtained. After cooling 1.63 g (92%) dihydronitrate of (IV) was obtained, m.p. $131-132^\circ$ (decomp.). (Found: equiv. wt. 128.8. Calc. for $\text{C}_{12}\text{H}_{28}\text{N}_2\text{O}_{10}\text{Se}_2$: equiv. wt. 129.6).

Neutralization of the nitric acid and one recrystallization from 50% methanol gave (IV) as thin glistening flakes, m.p. $136-137^\circ$ (decomp.). (Found: Se 40.13; equiv. wt. 196.6. Calc. for $\text{C}_{12}\text{H}_{26}\text{O}_4\text{Se}_2$: Se 40.26; equiv. wt. 196.1). IR-absorption in the region expected for oxygenated selenium groups (KBr-phase) 840 cm^{-1} (s), 810 cm^{-1} (s), 675 cm^{-1} (s), 665 cm^{-1} (s).

1,14-Tetradecyl diseleninic acid (V). Oxidation of 1.36 g 1,14-tetradecyl diselenocyanate with 2.5 ml fuming nitric acid gave 1.64 g (90%) of dihydronitrate of (V), m.p. $129-130^\circ$ (decomp.). (Found: equiv. wt. 135.8. Calc. for $\text{C}_{14}\text{H}_{32}\text{N}_2\text{O}_{10}\text{Se}_2$: 136.6). From this dihydronitrate 1.04 g (V) as glistening flakes was obtained, m.p. $137-138^\circ$ (decomp.). (Found: Se 37.31, equiv. wt. 209.6. Calc. for $\text{C}_{14}\text{H}_{30}\text{O}_4\text{Se}_2$: Se 37.57; equiv. wt. 210.2). IR-absorption in the region expected for oxygenated selenium groups (KBr-phase) 830 cm^{-1} (s), 810 cm^{-1} (s), 675 cm^{-1} (s), 665 cm^{-1} (s).

Acknowledgements. I wish to express my sincere gratitude to Professor Arne Fredga for his kind interest and all the facilities he has put at my disposal. A grant from the *Faculty of Mathematics and Natural Sciences*, University of Uppsala, is gratefully acknowledged. I also wish to thank Mr. R. Kumar, who has corrected the language in the manuscript.

REFERENCES

1. Schwarz, K. and Foltz, C. M. *J. Am. Chem. Soc.* **79** (1957) 3292.
2. Agenäs, L-B. *Acta Chem. Scand.* **19** (1965) 764.
3. Schwarz, K. *Federation Proc.* **20** (1961) 666.
4. Rebane, E. *Arkiv Kemi* **26** (1967) 345.
5. Houben-Weyl, *Methoden der organischen Chemie*, Stuttgart 1955, Vol. 9, pp. 1129–1151.
6. Fredga, A. *J. prakt. Chem.* (2) **123** (1929) 142.
7. Backer, H. J. and van Dam, W. *Rec. Trav. Chim.* **48** (1929) 1291.
8. Fredga, A. *Uppsala Universitets Årsskrift* **1935: 5**, p. 84.
9. Rebane, E. *Arkiv Kemi* **20** (1962) 204.
10. Walker, J. and Lumsden, J. S. *J. Chem. Soc.* **79** (1901) 1202.
11. Fredga, A. *Uppsala Universitets Årsskrift* **1935: 5**, p. 16.
12. *Org. Syn. Coll. Vol. II*, 1961, p. 246.
13. Nyström, R. F. and Brown, W. G. *J. Am. Chem. Soc.* **69** (1947) 1198.
14. Brändström, A. *Arkiv Kemi* **1** (1950) 481.
15. Fredga, A. and Lindgren, A. *Acta Chem. Scand.* **15** (1961) 938.

Received December 5, 1966.