The Oxidation Products of Some Straight Chain

# Selenosubstituted Dicarboxylic Acids

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3,3'-Seleno-dipropionic acid (II) has been oxidised under various conditions. The product was found to be 4,4'-spirobi(4-selena-4-butanolide) (VI). Oxidation of 4,4'-seleno-dibutyric acid (III) and 5,5'-seleno-divaleric acid (IV) gave the corresponding selenoxides 4,4'-seleninyl-dibutyric acid (VIII) and 5,5'-seleninyl-divaleric acid (IX). The unsymmetrical analogue, 3,4'-seleno-propionic-butyric acid (V) gave the corresponding selenoxide 3,4'-seleninyl-propionic-butyric acid (X). The synthetic procedure and the spectra recorded are discussed.

Organic selenides are easily oxidised by a variety of common oxidising agents giving the corresponding selenoxides.[1] Being basic, these selenoxides add strong acids. Different salts have been prepared in this way [2,3] and a selenonium salt structure has been proposed for them.[3] It has been found that carboxylic acids also form salts of the same type.[4]

We thought the possibility of intramolecular reaction between a selenoxide group and carboxylic acid groups to be of interest; this paper deals with experiments on homologous ω,ω'-seleno-dicarboxylic acids in order to investigate the possible formation of spiro-selena-dilactones of the type shown in Scheme 1.
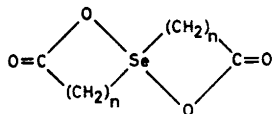
Scheme 1

Lesser and Weiss reported an aromatic analogue of this type [5] and we recently reinvestigated the structure.[6]

It has been reported that oxidation of low molecular weight ω,ω'-seleno-dicarboxylic acids give extremely unstable selenoxides which have not yet

been isolated.[7] By the choice of optimal reaction conditions it is possible that
these selenoxides may be isolated or compounds of the type shown in Scheme
1 formed by subsequent internal cyclisation. It is expected that the stability
of such compounds will depend to a great degree on the size of the rings.
Hydrogen peroxide in acetone or acetic acid, peracetic acid in acetic acid, or
dinitrogen tetroxide in dry ether were all found to be suitable oxidising agents.

Oxidation of seleno-diacetic acid (I) gave an unstable product which
decomposed immediately. The next homologue, 3,3′-seleno-dipropionic acid
(II) when oxidised under various conditions yielded a product of the type
shown in Scheme 1, while the next homologues, 4,4′-seleno-dibutyric acid
(III) and 5,5′-seleno-divaleric acid (IV) gave the corresponding selenoxides.
The unsymmetrical homologue 3,4′-seleno-propionic-butyric acid (V) also gave
the corresponding selenoxide.

The oxidation of II by hydrogen peroxide in acetone may be represented
by Scheme 2.
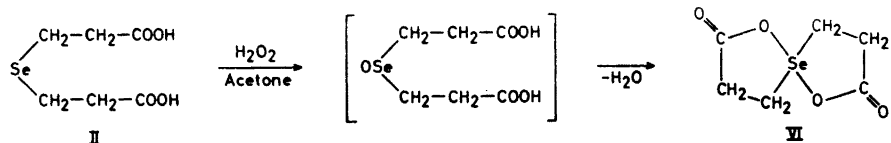
Scheme 2

The product VI was obtained as a white powder which rapidly precipitated
from the reaction mixture. Its low solubility in most solvents made it difficult
to purify. By using analytical grade II, the product VI was obtained in a
pure state, as verified by elemental analysis. The proposed structure of VI
is supported by the following alternative methods of formation.

The silver salt of II, suspended in dry chloroform, was treated with bromine
and a precipitate obtained. This product was found to be a mixture of silver
bromide and an organic compound. It was not possible to purify the latter
on account of its low solubility (Scheme 3).
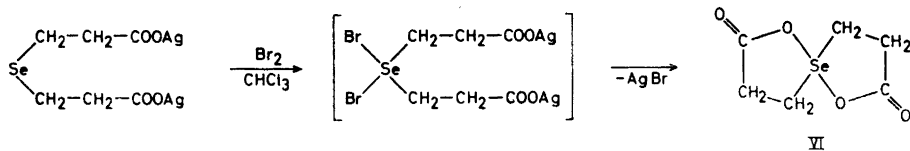
Scheme 3

A comparison of the infrared spectrum for this crude material with that
of pure VI obtained from the reaction in Scheme 2 showed beyond doubt that
identical products had been formed.

A reaction mixture containing 3,3′-seleno-dipropionic acid dibromide (VII),
prepared from II by the action of bromine in absolute ethanol, was treated

with sodium ethanolate. A precipitate was obtained containing sodium bromide and an organic material. The infrared spectra of this crude product and of pure VI were found to be superimposable, thus verifying the identity of the former (Scheme 4).

Scheme 4

The dibromide VII was synthesised,[8] and when treated with sodium ethanolate, it gave a product containing VI, as shown by infrared spectroscopy. The three reactions shown in Schemes 2 – 4 yield, without doubt, the same single organic product. The proposed structure for VI is supported strongly by the different methods of formation. Additional proofs for the structure are afforded by elemental analysis, equivalent weight determination by iodometric titration, and spectroscopical examinations of pure VI. The NMR-spectrum is of the general type A_2X_2, having two triplets at $\delta = 3.43$ and 4.27 ppm, which agrees well with the proposed structure.

Fig. 1. Infrared spectrum recorded for 4,4′-spirobi(4-selena-4-butanolide) (VI) in KBr-phase.

The infrared spectrum of pure VI (Fig. 1) was compared with that of pure II.[9] The following are the chief differences observed in the absorption spectra. The very characteristic broad band ascribed to strong intermolecular hydrogen bonds involving the O – H part of the carboxylic group overlaps the C – H

stretching vibration peak of the dicarboxylic acid II. In the case of VI (Fig. 1), only pure C — H stretching vibrations are observed in this range. It is of interest to note that four different peaks are obtained at 3020, 2970, 2930, and 2855 cm^{-1}. The latter two peaks occur at normal frequencies for stretching vibrations of a CH_2-group, while the former two occur at unusually high frequencies. Similar peaks have been reported earlier for small alicyclic rings.[10] The occurrence of four different peaks in the present spectrum may be explained by some type of intermolecular action. The carbonyl vibration gives one strong absorption band at 1675 cm^{-1} for VI whereas a doublet is observed in this range for II. Two new bands are observed for VI at 1035 and 895 cm^{-1}. The latter band occurs at the same frequency as the very characteristic band assigned to the SeO_2X_2 group.[11]

The infrared spectra recorded for 4,4'-seleninyl-dibutyric acid (VIII) and 5,5'-seleninyl-divaleric acid (IX) are given in Figs. 2 — 3, and differ much in character from the spectrum for VI (Fig. 1). The presence of a seleninyl group in VIII and IX gives rise to strong absorption peaks at 2480 and 1900 cm^{-1}. Infrared spectra recorded for 3-sulfinyl substituted carboxylic acids show similar broad peaks.[12-14] The occurrence of these intense absorption bands may consequently be caused by association between the seleninyl and carboxy
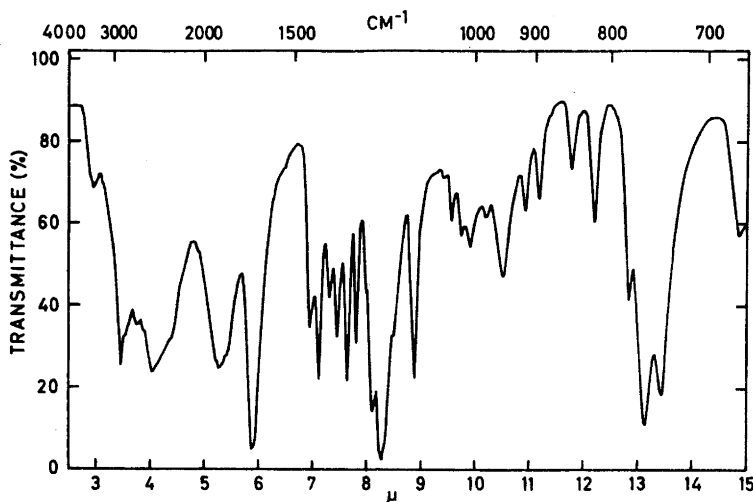

Fig. 2. Infrared spectrum recorded for 4,4'-seleninyl-dibutyric acid (VIII) in KBr-phase.

groups. An intense absorption band was also observed for VIII and IX at 757 cm^{-1}. This band, which has been ascribed to SeO stretching vibration, is seen in infrared spectra recorded for selenoxides.[3] Another intense absorption band, seen at 1280 — 1205 cm^{-1}, is also caused by the presence of a seleninyl group in the molecule. The unsymmetrical selenoxide X, obtained by the oxidation of V, was found to be very unstable and it was not possible to record any satisfactory infrared spectrum.
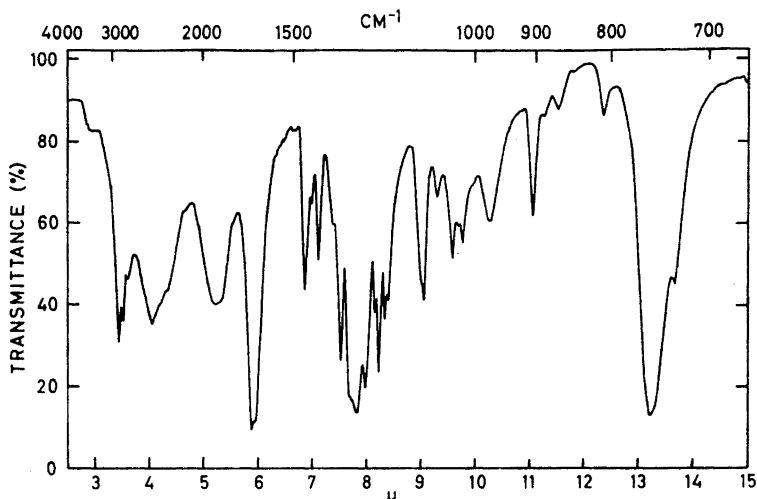
Fig. 3. Infrared spectrum recorded for 5,5′-seleninyl-divaleric acid (IX) in KBr-phase.

The mass spectrum recorded for VI does not contribute much towards proof of structure. A complex spectrum was obtained with no molecular fragment peak at m/e 224, but prominent peaks at m/e 226 and 306, corresponding to the molecular fragment peaks of 3,3′-seleno-dipropionic acid (II) and 3,3′-diseleno-dipropionic acid were found. In addition, a series of fragments was observed at mass numbers corresponding to elemental selenium, obviously formed by thermal decomposition of VI before ionisation.

The structure of VI was also investigated by means of ESCA measurements.[15] Owing to the few reference substances available, no satisfactory result was obtained. A hypothetical analogous structure for VI is the corresponding 3,3′-seleninyl-dicarboxylic anhydride (XI) shown in Scheme 5.

XI
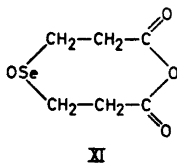
Scheme 5

When II was treated with acetic anhydride in an attempt to synthesise this compound, it was found that 3,3′-seleno-dipropionic anhydride (XII) was formed. It was not possible to purify the product owing to decomposition. Oxidation of the crude anhydride gave no well-defined product. This could be expected from the instability of this eight-membered ring. Thus,

the structure proposed for VI is supported both by chemical evidence and infrared spectroscopical investigations. The alternative structures for 4,4′-spirobi(4-selena-4-butanolide) may therefore be rejected.

EXPERIMENTAL

The NMR spectrum was recorded using a Varian Associates model A 60 spectrometer. The infrared spectra were recorded using a Perkin Elmer model 157 Infracord spectrophotometer. The selenium analyses were performed by a microanalytical method developed by Bengtsson [16] and very similar to that of Gould.[17] The melting points are uncorrected.

Oxidation of seleno-diacetic acid (I). A solution of 1.0 g (5 mmol) of seleno-diacetic acid [18] in 10 ml of acetone was prepared and 0.55 g (5 mmol) of 30 % hydrogen peroxide was added with cooling on ice. A vigorous reaction took place. The reaction mixture immediately turned cloudy and the colourless precipitate decomposed at once forming a yellowish solution. A similar result was obtained by use of acetic acid as solvent.

4,4′-Spirobi(4-selena-4-butanolide) (VI). a. Formation from silver 3,3′-seleno-dipropionate. To a suspension of 5.05 g (11.5 mmol) of silver 3,3′-seleno-dipropionate [19] in 20 ml of dry chloroform, 1.85 g (11.5 mmol) of bromine, dissolved in 20 ml of dry chloroform, was added dropwise. The reaction mixture was heated with stirring for 1 h. The solvent was removed by evaporation and the residue was extracted with ether to remove traces of 3,3′-seleno-dipropionic acid formed. The yellowish residue, insoluble in ether, darkened when exposed to light and in addition to silver bromide was found to contain an organic product. The two components could not be separated because of low solubility in organic solvents. The infrared spectrum recorded for the crude products was found to contain the same absorption peaks as shown in Fig. 1.

b. Formation from 3,3′-seleno-dipropionic acid (II). To a suspension of 2.25 g (10 mmol) of 3,3′-seleno-dipropionic acid [20] in 10 ml of absolute ethanol, 1.6 g (10 mmol) of bromine, dissolved in 10 ml of absolute ethanol, was added dropwise with stirring. A solution of sodium ethanolate, prepared from 0.5 g of sodium in 30 ml of absolute ethanol, was added dropwise to the reaction mixture, which was heated to reflux for 2 h. The solvent was removed by evaporation and the yellowish residue obtained was extracted with ether to remove soluble materials. The insoluble residue was found to contain sodium bromide and an organic product; it was not possible to separate the components because of low solubility in organic solvents. The infrared spectrum recorded for the crude products was found to contain the same absorption peaks as shown in Fig. 1.

c. Formation from 3,3′-dibromoseleno-dipropionic acid (VII). To a solution of 1.95 g (5 mmol) of 3,3′-dibromoseleno-dipropionic acid [8] in 20 ml of absolute ethanol, was added dropwise with stirring a solution of sodium ethanolate, prepared from 0.25 g of sodium in 15 ml of absolute ethanol. The reaction mixture was allowed to stand at room temperature with stirring for 1 h. After evaporation a residue was obtained, which was found to contain sodium bromide and an organic product. It was not possible to separate the components because of low solubility in organic solvents. The infrared spectrum recorded for the crude products was found to contain the same absorption peaks as shown in Fig. 1.

d. Preparation by oxidation of 3,3′-seleno-dipropionic acid (II) in acetic acid. A solution of 5.6 g (25 mmol) of analytically pure 3,3′-seleno-dipropionic acid [20] in 75 ml of acetic acid was cooled on ice and 2.5 g (25 mmol) of 35 % hydrogen peroxide was added dropwise with stirring and cooling. Stirring and cooling was continued for 1 h and the precipitate formed was filtered off and dried in a vacuum desiccator over sodium hydroxide. Yield: 4.5 g (80 %), m.p. 160−161°. (Found: C 32.36; H 3.65; Se 35.08; equiv. wt. by iodometric titration: 222.8. $C_6H_8O_4Se$ requires: C 32.31; H 3.59; Se 35.41; equiv. wt. 223.1.)

e. Preparation by oxidation of 3,3′-seleno-dipropionic acid (II) in acetone. A solution of 3.36 g (15 mmol) of analytically pure 3,3′-seleno-dipropionic acid [20] in 75 ml of acetone was cooled on ice and 1.65 g (15 mmol) of 30 % hydrogen peroxide was added dropwise with stirring and cooling. After completion of the addition, the reaction mixture was allowed to stand with stirring and cooling for 1 h. The precipitate was filtered off

and dried in a vacuum desiccator over sulphuric acid. Yield: 3.25 g (97 %), m.p. 160—161°. (Found: C 32.30; H 3.65; Se 35.00. $C_6H_8O_4Se$ requires: C 32.31; H 3.59; Se 35.41.)

f. Formation by oxidation of 3,3'-seleno-dipropionic acid (II) by nitrogen tetroxide. A suspension of 1.12 g (5 mmol) of 3,3'-seleno-dipropionic acid [20] in dry ether was cooled to −15°. An excess of nitrogen tetroxide [21] was added with stirring to the cold suspension and the reaction mixture was allowed to stand with stirring and cooling for half an hour. The reaction mixture was allowed to reach room temperature and the excess nitrogen tetroxide was allowed to evaporate. The precipitate was filtered off and dried. The infrared spectrum of the product was superimposible with that of the analytically pure product.

g. Formation by oxidation of 3,3'-seleno-dipropionic acid (II) by peracetic acid. A suspension of 1.12 g (5 mmol) of 3,3'-seleno-dipropionic acid [20] in 10 ml of acetic acid was cooled in an ice bath and 3.4 ml (5 mmol) of a solution of 12 % peracetic acid in acetic acid [22] was added dropwise with cooling and stirring. After standing for 2 h, the precipitate was filtered off and dried in a vacuum desiccator over sodium hydroxide. Yield: 0.8 g (71 %), m.p. 160—161°.

3,3'-Seleno-dipropionic anhydride (XII). A mixture of 6.3 g (28 mmol) of 3,3'-seleno-dipropionic acid [20] and 30 g of acetic anhydride was heated under reflux for 2 h. Most of the acetic anhydride was removed by distillation and the residue evaporated to dryness by placing in a vacuum desiccator over potassium hydroxide. Traces of acetic anhydride usually remain even after a long period of time in the desiccator. Yield of crude material: 5.7 g (100 %), m.p. 79—82°. Recrystallisation from chloroform-petroleum ether gave a yield of 4.0 g (69 %), m.p. 95.5—98°. The infrared spectrum recorded for the crude product gave absorption peaks at 1800 and 1740 cm^{-1}, characteristic for an anhydride, while the infrared spectrum recorded for the recrystallised material gave an additional peak at 1710 cm^{-1}, characteristic for the carboxylic acid II. This latter absorption peak became more prominent on further recrystallisation. Similarly, the broad absorption band at 1060—1040 cm^{-1}, characteristic for anhydrides diminishes in intensity on recrystallisation.

4,4'-Seleninyl-dibutyric acid (VIII). A solution of 1.27 g (5 mmol) of 4,4'-seleno-dibutyric acid [23] in 15 ml of acetone was cooled on ice and 0.55 g (5 mmol) of 30 % hydrogen peroxide was added dropwise with stirring. The reaction mixture immediately turned cloudy and a smeary precipitate was formed. By scratching a drop of this oil crystals were obtained and the reaction mixture was seeded with these. After some minutes the crystals obtained were filtered off and dried in a vacuum desiccator. Yield 1.2 g (95 %), m.p. 93—94° (d). (Found: C 35.69; H 5.27; Se 29.27; equiv. wt. by protolytic titration 135.6. $C_8H_{14}O_5Se$ requires: C 35.69; H 5.13; Se 29.33; equiv. wt. 134.6.)

5,5'-Seleninyl-divaleric acid (IX). A solution of 1.41 g (5 mmol) of analytically pure 5,5'-seleno-divaleric acid [24] in 15 ml of acetone, was cooled on ice and 0.55 g (5 mmol) of 30 % hydrogen peroxide was added dropwise with stirring. Immediately a crystalline white precipitate was formed. The reaction mixture was allowed to stand in a refrigerator overnight and the product was filtered off and dried in a vacuum desiccator. Yield: 1.4 g (100 %), m.p. 104—106° (d). (Found: C 40.37; H 6.10; Se 26.59; equiv. wt. by protolytic titration 148.6. $C_{10}H_{18}O_5Se$ requires: C 40.41; H 6.12; Se 26.46; equiv. wt. 148.6.)

3,4'-Seleninyl-propionic-butyric acid (X). A solution of 1.2 g (5 mmol) of 3,4'-seleno-propionic-butyric acid [24] in 15 ml of acetone was cooled on ice and 0.55 g (5 mmol) of 30 % hydrogen peroxide was added dropwise with stirring. A white precipitate was formed, which was immediately filtered off and dried in a vacuum desiccator over sulphuric acid. The vacuum desiccator was placed in a refrigerator overnight. Yield: 1.1 g (86 %), m.p. 68—69° (d). (Found: C 32.81; H 4.76; Se 30.97; equiv. wt. by protolytic titration 126.4. $C_7H_{12}O_5Se$ requires: C 32.95; H 4.75; Se 30.95; equiv. wt. 127.6.)

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