several times with an 80 %, v/v, ethanol-water mixture. The procedure of evaporation and washing with ethanol-water was repeated to free the solution from contaminants. The final alcohol solution was centrifuged, if cloudy, and the solution investigated by paper chromatography [4]. The so-called Pauly-reagent [5] was used to visualize the bases.

Controls were performed with pure histamine, tyramine and histidine.

Fig. 1 represents a paper chromatogram for samples corresponding to 1.5 ml of rumen contents.

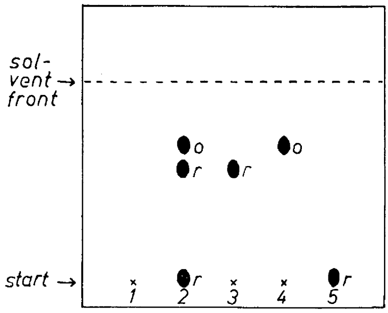

Fig. 1. Paper chromatographic separation of "Pauly-positive" bases. 1, Rumen contents; 2, Rumen contents + histamine, tyramine, and histidine; 3, histamine, sensitivity 0.5 — 1.0×10^{-7} g; 4, tyramine, the same sensitivity; 5, histidine, the same sensitivity; r = red; o = orange.

The method thus affords the possibility of demonstrating "Pauly-positive" bases present in rumen contents without resorting to dialysis [1].

Thanks are due to the Head of the Department, Professor K. Sjöberg, and to Mrs. K. Rönn for her assistance.

1. Dain, J. A., Neal, A. L. and Dougherthy, R. W. *J. Animal. Sci.* **14** (1955) 930.
2. Annison, E. F. and Lewis, D. *Metabolism in the rumen.* Methuens monographs on biochemical subjects. London 1959.
3. Schwyzer, R. *Acta Chem. Scand.* **6** (1952) 219.
4. Pénau, H., Saïas, E. and Andreetti, C. *Ann.* pharm. franç. **10** (1952) 514.
5. Hais, I. M. and Mazek, K. *Handbuch der Papierchromatographie.* Bd. 1, Jena 1958, p. 743.

Received June 19, 1961.

Selena-hexanoic and Selena-pentanoic Acids

ARNE FREDGA and ARILD LINDGREN

Organic Department, Chemical Institute, University of Uppsala, Sweden

In recent years, organoselenium compounds have attracted attention from biochemical viewpoints [1,2]. Earlier, selenium was regarded primarily as a toxic element; if present in soils, for example, it can be taken up by plants and cereals, thus causing injury to grazing animals. It is now known that it may also have a positive effect and that certain dietary diseases of sheep, cattle and rats may be cured by minute amounts of certain selenium compounds. At different times organoselenium compounds have also been tested for chemotherapeutical effects. Very little is known, however, about the metabolism of selenium and its compounds.

In the course of current investigations in selenium chemistry, we have started a programme to study long-chain fatty acids with a selenium atom incorporated in the chain. The biological and pharmacological properties of the acids are being investigated. In this connection the position of the selenium atom in the chain may be important. Long-chain acids with a heavy hetero-atom may also be used as model substances in X-ray crystallographic investigations. Furthermore, their physico-chemical properties, *e.g.* their behaviour in monolayers, may be of interest.

The acids are easily obtained by reduction of ω-diseleno-di-alkanoic acids to ω-selenol acids (not isolated) and subsequent reaction of these compounds with alkyl bromides:

$$[\text{-Se-(CH}_2)_m\text{-COOH}]_2 \rightarrow \text{HSe-(CH}_2)_m\text{-COOH} \rightarrow$$

$$\xrightarrow{\text{CH}_3\text{-(CH}_2)_n\text{-Br}} \text{CH}_3\text{-(CH}_2)_n\text{-Se-(CH}_2)_m\text{-COOH}$$

In our experiments the reduction has been performed with Rongalite in aqueous ammonia, but other reductants will be tested. As the selenol acid is easily oxidised, the solution must be protected against atmospheric oxygen. The reaction is best performed in an ordinary flask, closed by a cork stopper, and opened only momentarily when the reactant is added. About

90 % of the Rongalite is added in one portion and the rest in small amounts until the yellow colour of the diselenide has completely disappeared, but some care must be taken since the reaction is not quite instantaneous. Often the solution assumes a yellow colour during the reaction owing to slight oxidation by the alkyl bromide. In such cases, the solution is decolourised by a little more Rongalite after which a corresponding quantity of the alkyl bromide is added. This should always be done if the diseleno acid is sparingly soluble and is likely to interfere with the purification of the product.

Table 1. Selena-hexadecanoic acids $C_{15}H_{30}O_2Se$: Se calc. 24.57 %.

Position of Se	m.p.	% Se found
4	62.5 – 63.5°	24.61
5	51 – 52°	24.51
6	45.5 – 47°	24.62
7	46.5 – 47.5°	24.70
9	42 – 43°	24.51
12	43 – 44°	24.61

Table 2. Selena-pentadecanoic acids $C_{14}H_{28}O_2Se$: Se calc. 25.69 %

Position of Se	m.p.	% Se found
3	52.5 – 53.5°	25.50
4	57.5 – 58.5°	25.64
5	40 – 40.5°	25.60
6	44 – 45°	25.61
7	36.5 – 37.5°	25.56
12	42.5 – 43.5°	25.54

The acids are recrystallised from petrol ether or dilute methanol. Owing to the rather high solubility and the low melting-points of the acids, it is appropriate and in some cases even necessary to let the crystallisation take place at 0 – 5°. The acids form glistening flakes or plates, very similar to those formed by ordinary long-chain acids.

A list of the acids prepared so far is given in Tables 1 and 2. The preparation of two of them is described in detail in the experimental part.

Experimental. 4-Selena-hexadecanoic acid. 7.60 g (0.025 mole) of β,β'-diseleno-dipropionic acid[3] were dissolved in 75 ml of 2 N aqueous ammonia and reduced with Rongalite as indicated above. A solution of 12.5 g (0.05 mole) of dodecyl bromide in 200 ml of ethanol was then added, the flask was shaken for 12 h and left to stand for one day. The solution was then poured into twice its volume of water, filtered and acidified with excess of 4 N sulphuric acid. The readily crystallising precipitate was filtered off, dried and recrystallised three times from dilute (80 %) methanol and once from petrol ether. Yield of crude product 7.8 g (48 %), after recrystallisation 6.9 g (43 %). The acid forms glistening leaves with m.p. 62.5 – 63.5°. (Found: Se 24.61; equiv. wt. 320.7, 321.0. Calc. for $C_{15}H_{30}O_2Se$: Se 24.57; equiv. wt 321.4).

A quantity of β,β'-diseleno-dipropionic acid could be regenerated from the acidified solution.

12-Selena-hexadecanoic acid. 10.56 g (0.02 mole) of ω,ω'-diseleno-diundecanoic acid (prepared from commercial ω-bromoundecanoic acid)[4] was dissolved in 150 ml of 2 N ammonia + 100 ml of ethanol; if no ethanol was added, a sparingly soluble ammonium salt separated. The solution was reduced with Rongalite, 5.50 g (0.04 mole) of *n*-butyl bromide, dissolved in 100 ml of ethanol were added, the flask was shaken for 12 h and left to stand over-night. The acid was liberated as described above and recrystallised once from dilute methanol and three times from petrol ether. Yield of crude product 11.2 g (87 %), after recrystallisation 9.1 g (71 %). Glistening leaves or plates with m.p. 43 – 44°. (Found: Se 24.61; equiv. wt. 321.4, 321.8. Calc. for $C_{15}H_{30}O_2Se$: Se 24.57; equiv. wt. 321.4).

A grant from *AB Astra* is gratefully acknowledged.

1. Schwarz, K. and Foltz, C. M. *J. Am. Chem. Soc.* **79** (1957) 3292.
2. Schwarz, K. *Vitalstoffe-Zivilisationskrankheiten* **4** (1959) 1.
3. Fredga, A. *Uppsala Univ. Årsskr.* **1935**; 5, p. 106.
4. Fredga, A. and Lindgren, A. *To be published.*

Received May 17, 1961.