## **Short Communications**

## Some Nitrosubstituted Benzylseleno-, Phenylethylseleno-, and Phenylseleno-substituted Alkanoic Acids ARNE FREDGA

Department of Organic Chemistry, Chemical Institute, University of Uppsala, P.O. Box 531, S-751 21 Uppsala 1, Sweden

The title compounds were prepared in order to test their activity in preventing pietary liver necrosis in rats (factor-3-effect). This effect is found in many organoselenium compounds  $^{1-4}$  and the end in view was to study the influence of structural factors, e.g. the distance between the carboxyl group and the selenium atom, and the presence of various substituents in the benzene nucleus. The present paper deals with the synthesis of 36 nitrosubstituted acids (compounds I-III and homologues).

The work on the biological potency was carried out in collaboration with Professor Klaus Schwarz.\* The potency was fairly

good. If the selenium occupied the distal end of an unbranched acid, an alternating effect with the chain length could be observed, at least in two of the series. These results will be presented and discussed in detail elsewhere.

The syntheses were carried out following a general procedure described in detail in previous papers.<sup>5,6</sup> A diselenodicarboxylic acid was dissolved in excess of aqueous ammonia, reduced to selenol-carboxylic acid with rongalite and reacted with the appropriate halogen compound (4-nitrobenzyl bromide, 4-nitrophenylethyl bromide or 1-chloro-2,4-dinitrobenzene). The products were recrystallised 2-4 times, generally from two different solvents (dilute formic acid, carbon tetrachloride, benzene, pure or dilute methanol). The acids of type I and II give pale yellow solutions; in the crystalline state they are more or less yellowish, in some cases practically colourless. All acids of type III show an intense bright yellow colour.

The results are summarised in Tables 1-3. Most of the analyses were carried out by the Analytical Department of the institute. For some of the acids only the content of selenium was determined. The 2,4-dinitrophenylseleno-acetic acid, described earlier by Behaghel and Rollmann, is not included in the table.

Acknowledgements. The author is greatly indebted to Mr. R. Öhberg for preparing starting materials. Grants from the Royal Swedish Academy of Sciences, the Swedish Natural Science Research Council, the National Institutes of Health, U.S.A. (U.S. Public Health Service Grant No. AM 03417), and AB Astra are gratefully acknowledged.

- Schwarz, K. and Foltz, C. M. J. Am. Chem. Soc. 79 (1957) 3292.
- Schwarz, K. et al. Federation Proc. 20 (1961) 655.
- 3. Schwarz, K. Federation Proc. 20 (1961) 666.
- Schwarz, K. and Fredga, A. J. Biol. Chem. 244 (1969) 2103.

<sup>\*</sup> Laboratory of Experimental Metabolic Diseases, Veterans Administration Hospital, Long Beach, California, and Department of Biological Chemistry, School of Medicine, University of California in Los Angeles.

Table 1. 4-Nitrobenzylseleno-alkanoic acids.

		Calculated			Found			
Acid	m.p. °C	$\mathbf{C}$	$\mathbf{H}$	$\mathbf{Se}$	$\mathbf{C}$	$\mathbf{H}$	$\mathbf{Se}$	
Acetic	133 - 134	_		28.80	_	_	28.70	
2-Propionic	103 - 104	41.68	3.85	27.40	41.70	3.79	27.33	
3-Propionic	102 - 103	41.68	3.85	27.40	41.61	3.83	27.31	
2-Butyric	81.5 - 83			26.13	_		26.06	
3-Butyric	78.5 - 79.5	43.72	4.34	26.13	43.85	4.31	26.04	
4-Butyric	76 - 77	_	_	26.13	-		26.07	
2-Isobutyric	139 - 140	_	_	26.13			26.00	
3-Isobutyric	71 - 72	43.72	4.34	26.13	43.57	4.33	26.02	
4-Valeric	67 - 68		_	24.97			24.87	
5-Valeric	77 - 78.5	45.58	4.78	24.97	45.48	4.77	24.86	
6-Caproic	68 - 69	_	_	23.91	_	_	23.81	
7-Oenanthic	80 - 81.5	48.84	5.56	22.94	48.79	5.58	22.84	
8-Caprylic	65.5 - 64	50.28	5.91	22.04	50.24	6.10	21.92	
9-Pelargonic	78 - 80	_	-	21.21		_	21.12	
10-Capric	73.5 - 75		_	20.44	_		20.62	
11-Undecanoic	93 - 93.5	53.99	6.80	19.72	53.91	6.74	19.72	

Table 2. 4-Nitrophenylethylseleno-alkanoic acids.

Acid		Calculated			Found		
	m.p. °C	$\mathbf{C}$	$\mathbf{H}$	$\mathbf{Se}$	$\mathbf{C}$	H	$\mathbf{Se}$
Acetic	101.5 - 103	41.68	3.85	27.40	41.67	3.79	27.27
3-Propionic	76 - 77.5	_		26.13	_	·	26.01
4-Butyric	101.5 - 102.5	_	_	24.97	_	_	25.05
5-Valeric	56.5 - 57.5	47.28	5.19	23.91	47.16	5.17	23.79
6-Caproic	71 - 72	48.84	5.56	22.94	48.78	5.55	22.83

Table 3. 2,4-Dinitrophenylseleno-alkanoic acids.

Acid		Calculated			Found		
	m.p. °C	$\mathbf{C}$	$\mathbf{H}$	$\mathbf{Se}$	$\mathbf{C}$	$\mathbf{H}$	$\mathbf{Se}$
2-Propionic	164 - 165	33.87	2.53	24.74	33.89	2.53	24.56
3-Propionic	155 - 157	33.87	2.53	24.74	33.94	2.59	24.61
2-Butyric	144 - 145		_	23.70			23.63
3-Butyric	157 - 158	36.05	3.03	23.70	36.15	3.02	23.63
4-Butyric	137.5 - 138.5			23.70	_		23.67
2-Isobutyric	189 (dec.)	36.05	3.03	23.70	36.11	3.04	23.34
3-Isobutyric	157 - 158	-	_	23.70	_		23.47
4-Valeric	131 - 132	38.05	3.48	22.74	38.21	3.50	22.59
5-Valeric	164 - 165			22.74		-	22.73
6-Caproic	118.5 - 119.5	39.90	3.91	21.86	39.97	3.97	21.92
7-Oenanthic	150 - 151	_	_	21.04	_		21.03
8-Caprylic	115 - 116.5	43.19	4.66	20.28	43.16	4.70	20.22
9-Pelargonic	140 - 140.5	_	_	19.60	_		19.40
10-Capric	119 - 120	46.04	5.31	18.92	46.01	5.46	18.48
11-Undecanoic	137.5 - 138.5	47.32	5.61	18.31	47.36	5.54	18.29

<sup>5.</sup> Fredga, A. and Lindgren, A. Acta Chem. Scand. 15 (1961) 938.

Received September 3, 1971.

Fredga, A. Acta Chem. Scand. 24 (1970) 1117.

Behaghel, O. and Rollmann, M. Ber. 62 (1929) 2696.