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The Configuration of Organic Selenoxides: Mixed Crystals of Selenoxides with Sulfoxides

BY HEINRICH RHEINBOLDT AND ERNESTO GIESBRECHT

Dissymmetrically substituted sulfoxides can be resolved into optically active forms.[1] For this reason a tetrahedral configuration was attributed to sulfoxides, with the sulfur atom at the center of the tetrahedron, in three vertices of which are located the oxygen atom and the two organic radicals, and in the fourth vertex an unshared pair of electrons. This view was recently strengthened by the observation of isomorphism of sulfoxides with sulfones.[2]

Although dissymmetric selenoxides should, by analogy with the corresponding sulfoxides, be resolvable into optically active forms, no such resolution has yet been achieved.[3] Hence the admission by some authors "that the linkage between selenium and oxygen may not be an unsymmetrical semipolar double bond,"[4] contrary to the nature of the corresponding bond in the sulfoxides. Others, being more cautious, think that "it is to be expected that the resolution of this type of selenium derivative should be possible if the right conditions were obtained."[5]

According to our actual knowledge analogous organic compounds of sulfur and selenium are, in general, isomorphous.[6] Thus, **dibenzyl sulfide** and **selenide** (Fig. 1) and, according to P. Pascal,[6a] **diphenyl sulfide** and **selenide** form continuous series of mixed crystals of type III of the Bakhuis–Roozeboom classification.

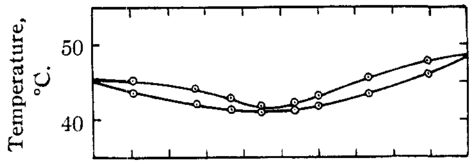

Fig. 1.—Binary system of dibenzyl sulfide and selenide.

As a contribution in the problem of the configuration of organic selenoxides, solid–liquid phase diagrams have been studied for the binary systems of **dibenzyl selenoxide** with **dibenzyl sulfoxide** and of **diphenyl selenoxide** with **diphenyl sulfoxide.** In both cases there has been observed the formation of continuous series of mixed crystals of type I (Fig. 2). This fact shows a similarity in the configuration of these compounds so that a tetrahedral configuration has also to be attributed to the selenoxides.

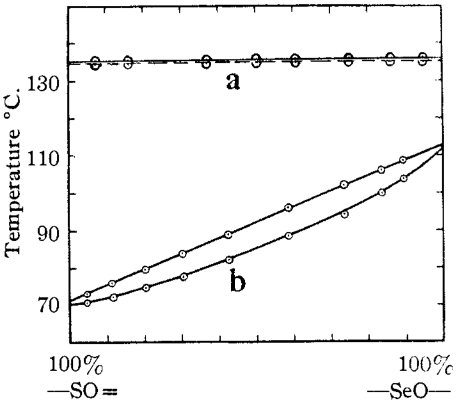

Fig. 2.—Binary systems of (a) dibenzyl sulfoxide and selenoxide; (b) diphenyl sulfoxide and selenoxide.

Symmetrically substituted selenoxides and selenones give a continuous series of mixed crystals in analogy with the corresponding sulfoxides and sulfones.[2] This was proved by the study of the binary system: **diphenyl selenoxide** and **selenone** which gives, as in the corresponding

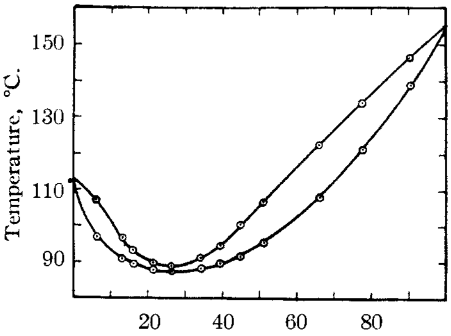

Fig. 3.—Binary system of diphenyl selenoxide and selenone.

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(1) Ph. W. B. Harrison, J. Kenyon and H. Phillips, *J. Chem. Soc.*, 2079 (1926); J. Holloway, J. Kenyon and H. Phillips, *ibid.*, 3000 (1928); W. Piechulek and J. Suszko, *Roczniki Chem.*, **13**, 520 (1933) [*C. A.*, **28**, 1699 (1934)]; *Bull. int. Acad. polon. Sci. Lettres, Ser. A.*, 455 (1934) [*Chem. Zentr.*, **106**, I, 3660 (1935)]; *Roczniki Chem.*, **15**, 221 (1935); F. Gajowczyk and J. Suszko, *Ber.*, **68**, 1005 (1935).

(2) H. Rheinboldt and E. Giesbrecht, THIS JOURNAL, **68**, 973 (1946).

(3) W. R. Gaythwaite, J. Kenyon and H. Phillips, *J. Chem. Soc.*, 2280, 2287 (1928); O. K. Edwards, Gaythwaite, Kenyon and Phillips, *ibid.*, 2293 (1928); F. G. Holliman and F. G. Mann, *ibid.*, 38 (1945).

(4) E. P. Painter, *Chem. Rev.*, **28**, 200 (1941).

(5) R. L. Shriner and R. Adams, in H. Gilman, "Organic Chemistry," 2nd ed., Vol. I, p. 423, J. Wiley and Sons, New York, 1943.

(6) (a) P. Pascal, *Bull. soc. chim.*, [4] **11**, 1030 (1912); (b) N. M. Cullinane and A. J. Plummer, *J. Chem. Soc.*, 63 (1938); (c) H. Rheinboldt, *et al.*, unpublished work, including a large number of binary systems of thiocyanates and selenocyanates, sulfides and selenides, disulfides and diselenides, thioesters and selenoesters, thioamides and selenoamides

sulfoxide and sulfone, a mixed crystal series of type III (Fig. 3).

Dibenzyl selenide and **selenoxide** do not form mixed crystals, the phase diagram showing a simple eutectic system as in the corresponding case of sulfide and sulfoxide.[2]

Experimental

The solid–liquid phase diagrams of the binary systems were studied with our "thaw-melting method" as described in a previous paper.[2] In the tables "Th. p." means thawing point. All the percentages indicated are by weight.

Binary Systems

I. Dibenzyl Sulfide and Dibenzyl Selenide

TABLE I

Sulfide, %	Th. p., °C.	M. p., °C.	Sulfide, %	Th. p., °C.	M. p., °C.
0.0	44.7	45.5	53.6	41.2	42.5
10.3	43.5	45.4	59.9	41.6	43.1
27.1	42.1	44.2	73.9	43.4	45.6
36.7	41.5	42.8	89.3	46.0	47.5
44.7	41.0	42.0	100.0	48.4	49.0

Continuous series of mixed crystals of type III; minimum at 48% of the sulfide and 41.5°.

II. Dibenzyl Sulfoxide and Dibenzyl Selenoxide

Dibenzyl sulfoxide was prepared according to R. Knoll,[7] by oxidation of the sulfide with chromium trioxide in acetic acid. The raw product (yield 96%, m. p. *ca.* 130°) recrystallized from ethanol in presence of active charcoal gave tiny, bright crystals with melting point 135°.

Dibenzyl selenoxide was obtained by hydrolysis of dibenzylselenium dibromide with 15% solution of potassium hydroxide. The raw product dried under vacuum over calcium chloride (yield 99%, m. p. 126–130°) was repeatedly recrystallized from dry benzene, as small colorless plates of melting point 136.0° in agreement with the literature.[8] On continued heating the substance decomposes with separation, far above the melting point, of selenium with formation of benzaldehyde. For this reason the mixtures of the components were prepared by trituration.

TABLE II

Selenoxide, %	Th. p., °C.	M. p., °C.	Selenoxide, %	Th. p., °C.	M. p., °C.
0.0	134.1	135.0	60.4	134.4	135.6
6.9	134.1	135.0	74.5	134.6	135.7
15.4	134.2	135.1	86.0	134.7	135.8
36.6	134.2	135.3	94.5	134.9	135.9
48.9	134.3	135.4	100.0	135.0	136.0

Continuous series of mixed crystals of type I.

III. Diphenyl Sulfoxide and Diphenyl Selenoxide

Diphenyl sulfoxide was prepared by the reaction of benzene with thionyl chloride in contact with aluminum chloride[9] and recrystallized from ethanol; melting point 71.0°.

Diphenyl selenoxide was prepared according to Krafft and Vorster[10] by hydrolysis of diphenyl selenium dibromide with 15% sodium hydroxide solution. The product, a yellowish powder, dried under vacuum over calcium chloride (yield, 82%), was repeatedly recrystallized from dry benzene with active charcoal and finally dried at 100° and 2 mm. to a white powder with melting point 112.8°. Reported melting points are 106–108°,[11] 112°[12] and 113–114°.[10,13,14] Treated in this way the substance is not hygroscopic, contrary to what was reported by Krafft and Vorster.[10]

TABLE III

Selenoxide, %	Th. p., °C.	M. p., °C.	Selenoxide, %	Th. p., °C.	M. p., °C.
0.0	70.1	71.0	58.6	88.5	96.2
4.8	70.7	73.1	73.3	94.8	102.1
11.4	72.3	75.8	83.6	100.0	106.5
20.1	74.8	79.6	89.8	103.8	108.7
30.9	77.4	84.1	100.0	111.7	112.8
42.4	82.2	89.0			

Continuous series of mixed crystals of type I.

IV. Diphenyl Selenoxide and Diphenyl Selenone

Diphenyl selenone was obtained by oxidation of an aqueous suspension of the selenoxide with potassium permanganate at *ca.* 90°. The raw product, washed with 30% cold alcohol (yield 81%, m. p. *ca.* 150°) was many times recrystallized from a small amount of ethanol (1 g. from 1.5 cc.) and gave large brilliant and lamellar crystals which were dried at 135° and 2 mm., and had the melting point 154.9°. Reported melting points are 154–154.5°,[15] 154–155°[16] and 155°.[17]

TABLE IV

Selenone, %	Th. p., °C.	M. p., °C.	Selenone, %	Th. p., °C.	M. p., °C.
0.0	111.7	112.8	39.7	89.5	94.6
6.2	96.5	107.2	45.0	91.6	100.2
13.1	90.9	96.4	51.1	95.2	106.4
16.1	89.1	93.3	66.1	108.1	122.7
21.5	87.6	89.5	77.8	121.2	134.0
26.6	87.2	89.0	90.5	139.1	146.8
34.6	88.1	91.2	100.0	153.8	154.9

Continuous series of mixed crystals of type III; minimum at 25% of selenone and 88°.

V. Dibenzyl Selenide and Dibenzyl Selenoxide

TABLE V

Selenoxide, %	Th. p., °C.	M. p., °C.	Selenoxide, %	Th. p., °C.	M. p., °C.
0.0	44.7	45.5	61.4	41.8	104.0
4.6	41.8	42.8	73.1	41.9	114.0
10.0	41.8	48.7	86.4	41.8	125.8
21.1	41.8	64.2	94.6	41.8	132.2
34.3	42.0	78.3	100.0	135.0	136.0
48.2	42.0	92.2			

All mixtures were prepared by close trituration of the components: simple eutectic system with eutectic point at 5.5% of selenoxide and 41.8°.

Summary

1. Dibenzyl and diphenyl selenoxide form continuous mixed crystal series of the ascendant type (type I) with the corresponding sulfoxides as

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[7] R. Knoll, *J. prakt. Chem.*, [2] **113**, 45 (1926).

[8] W. Strecker and A. Willing, *Ber.*, **48**, 204 (1915).

[9] Ch. E. Colby and C. S. McLoughlin, *ibid.*, **20**, 197 (1887).

[10] F. Krafft and W. Vorster, *ibid.*, **26**, 2820 (1893).

[11] D. G. Foster and St. F. Brown, THIS JOURNAL, **50**, 1184 (1928).

[12] R. E. Lyons and W. E. Bradt, *Ber.*, **60**, 62 (1927).

[13] W. Strecker and A. Willing, *ibid.*, **48**, 205 (1915).

[14] Ch. Courtot and A. Motamedi, *Compt. rend.*, **199**, 531 (1934).

[15] B. A. Arbusow, *Chem. Zentr.*, **108**, I, 4943 (1937).

[16] B. A. Arbusow, *J. prakt. Chem.*, [2] **131**, 370 and 371 (1931).

[17] F. Krafft and R. E. Lyons, *Ber.*, **29**, 425 (1896).

shown by the solid–liquid phase diagrams of the binary system.

2. Diphenyl selenoxide and selenone give a continuous series of mixed crystals of the type with minimum (type III).

3. Dibenzyl selenide forms with the corresponding selenoxide a simple eutectic system. Dibenzyl sulfide and selenide form a continuous series of mixed crystals with minimum.

These results prove that selenoxides have the same steric configuration as the corresponding sulfoxides, having therefore a tetrahedral configuration, the same as attributed to the sulfoxides.

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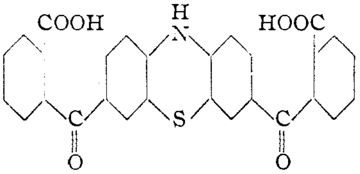
Some Phenothiazine Derivatives. The Course of the Friedel–Crafts Reaction

BY RICHARD BALTZLY, MORTON HARFENIST AND FREDERICK J. WEBB

In the course of synthetic experiments with phenothiazines, in which the primary object was to prepare water-soluble, N-unsubstituted derivatives, recourse was had to the Friedel–Crafts reaction. The only reference on this subject is a paper by Scholl and Seer[1] who employed phthalic anhydride and reported rather poor yields of a dipthaloyl derivative for which they proposed the formula (I). The substance was cyclized by sulfuric acid to a bis-quinone which Scholl and Seer regarded as linear.



(I)

It seemed probable to us that under Friedel–Crafts conditions orientation would be due mainly to the sulfur rather than the nitrogen, since the latter should either be acylated rapidly or maintained in the cationic state. This supposition has proved to be correct, both as to the priority of N-acylation and the dominant orientation by sulfur. In most cases we found it best to operate with N-acetylphenothiazine (thereby avoiding any doubt as to N-acylation) but it was found that phenothiazine itself underwent substitution by acetyl chloride and succinic anhydride in the same position as the N-acetyl compound although with considerably worse yield. These differences may well have been due to fortuitous influences of solubility since in all these reactions the reaction-complex, which usually forms a second layer, came out as a thick gum and largely frustrated attempts at stirring.

When N-acetylphenothiazine reacted with acetyl chloride and aluminum chloride an N,x-diacetylphenothiazine was obtained in fair yield. With succinic anhydride the primary product was undoubtedly an N-acetyl-x-succinyl derivative but in the isolation the acetyl group was intentionally hydrolyzed and the x-succinylphenothiazine was obtained. The position of the acyl groups was in doubt, but it is reasonable to assume that in both compounds the same position had been substituted. In the acetylation product it has been possible to locate the acetyl group in position 2, and the transformations shown in Chart I are formulated on that basis.

The N,2-diacetylphenothiazine (II) was degraded by the haloform reaction to the carboxylic acid (IV). Treatment of IV either with boiling hydriodic acid[2] or with Raney nickel[3] removed the sulfur with the formation of a diphenylamine carboxylic acid melting at 142–143°. Gilman, Van Ess and Shirley[2] had prepared diphenylamine-3-carboxylic acid for which they reported the m. p. as 140°. A sample of our acid was sent to Professor Gilman who found the preparations to be identical (mm. p.). It was thus apparent that the acetyl group had entered at either position 2 or position 4 and in either case had been oriented by the sulfur.

Gilman, Van Ess and Shirley[2] had obtained, by metalation of N-ethylphenothiazine with lithium, an N-ethylphenothiazine carboxylic acid in which the carboxyl group occupied one of the positions, 2 and 4. The melting point of this acid was given as 178–179°, that of its methyl ester as 111–112°. Our acid, IV, was converted to an N-ethyl acid (V), m. p. 184–185°, giving a methyl ester that melted at 84.5–85.5°. Direct comparison with a sample generously furnished by Professor Gilman showed that the acids (and their esters) were different. Thus the two series of phenothiazine derivatives capable of being degraded to diphenylamine-3-carboxylic acid are represented by Gilman's acid and by ours, and the unambiguous orientation of one must also determine the structure of the other.

On the basis of his extensive experience with metalation reactions, Gilman considered that N-ethylphenothiazine would be most likely to metalate *ortho* to the sulfur and provisionally assigned to his acid the structure VIII. In agreement with this, we felt that the Friedel–Crafts reaction, which has a marked tendency to *para* sub-

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[1] Scholl and Seer, *Ber.*, **44**, 1243 (1911).

[2] Gilman, Van Ess and Shirley, THIS JOURNAL, **66**, 1214 (1944).

[3] Roblin, Lampen, English, Cole and Vaughan, *ibid.*, **67**, 290 (1945).