9. *The Configuration of Heterocyclic Compounds. Part VI. An Examination of Derivatives of Selenoxanthone and Phenoxselenine.*

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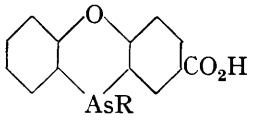
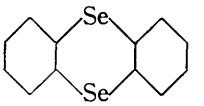
Suitably substituted phenoxarsines are capable of exhibiting optical activity. This is probably due to the fact that the molecule is folded about the oxygen–arsenic axis. The folding has previously been thought to be stabilised as a result of the dissimilarity in size and valency angle of oxygen and arsenic. Phenoxselenines would therefore be expected to have a similar configuration and thus be able, if suitably substituted, to exhibit optical activity. The experiments now described indicate, however, that neither phenoxselenines nor selenoxanthones, which should also be folded, can be obtained in mirror-image forms. The fact that negative evidence is not conclusive is appreciated.

THE optical activity of 10-substituted phenoxarsine-2-carboxylic acids (I) (Lesslie and Turner, J., 1934, 1178; 1935, 1268; 1936, 730) has been explained as being due to a folded configuration of the molecule, stabilised as a result of the particular sizes of the atomic radii and the valency angles of oxygen and arsenic. The non-resolvability of certain derivatives of thianthren, a substance known to have a folded structure (Bergmann and Tschudnowsky, *Ber.*, 1932, **65**, 458; Bennett and Glasstone, J., 1934, 128) and of

similar derivatives of phenoxthionine (Bennett, Lesslie, and Turner, J., 1937, **444**) has been attributed to the identity in size of the sulphur atoms in the one case and the

(I.) 

 (II.)

insufficient dissimilarity in size of the oxygen and sulphur atoms in the other (compare also Keats, J., 1937, 1592).

In phenoxselenine, the factors which at any rate might be regarded as stabilising the folding of the phenoxarsine molecule would appear to be reproduced, since the arsenic and the selenium atom have approximately the same radius; the absence of a substituent in position 10 in phenoxselenines makes them particularly important material for investigation.

The literature contains little information as to the valency angle of selenium. Bergmann, Engel, and Sandor (*Z. physikal. Chem.*, 1930, *B*, **10**, 397) found the dipole moment of diphenyl selenide to be $1{\cdot}38 \times 10^{-18}$ e.s.u., from which it might be inferred, although the difficulties of making correct inferences are well known, that selenium has a preferred valency angle larger than that of sulphur, which is considerably less than 120° (Bennett and Glasstone, *loc. cit.*). The dipole moment of selenanthren (II) (Krafft and Kaschau, *Ber.*, 1896, **29**, 443) has now been found by Le Fèvre and Le Fèvre to be $1{\cdot}43 \times 10^{-18}$ (see Campbell, Le Fèvre, Le Fèvre, and Turner, forthcoming publication), showing that the selenanthren molecule is folded like the thianthren molecule and to a similar extent, and suggesting that the valency angle of selenium is in the neighbourhood of 110°.

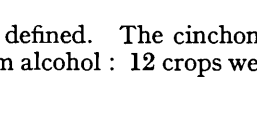
The radii of aromatic carbon, of oxygen, and of selenium being assumed to be respectively 0·70, 0·66, and 1·17 A., the relation between the oxygen angle, θ, the selenium angle, ϕ, and the angle, ψ, of fold about the oxygen–selenium axis may be calculated and is as follows:

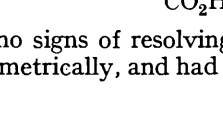
θ	100·0°	110·0°	120·0°	130·0°	136·5°
ϕ	80·5	87·5	94·0	100·0	103·5
ψ	111·0	123·5	137·5	154·5	180·0

The calculation is based on the assumption that, in all possible configurations, the centres of the oxygen and selenium atoms remain in the planes of the two benzene nuclei, and that the oxygen–carbon and selenium–carbon bonds make angles of 120° with the adjacent aromatic nuclear bonds.

In some diaryl ethers the oxygen valency angle reaches as high a value as 128°±4° (Sutton and Hampson, *Trans. Faraday Soc.*, 1935, **31**, 945; cf. Maxwell, Hendricks, and Mosley, *J. Chem. Physics*, 1935, **3**, 669; Pai, *Indian J. Physics*, 1935, **3**, 660; Sutton and Brockway, *J. Amer. Chem. Soc.*, 1935, **57**, 473: these authors find angles somewhat lower). There seems little doubt that the value of θ in the example under review may be taken as something a little greater than 120°, a value it acquires in diphenylene dioxide in which 120° is the maximum possible angle (Bennett and Glasstone, J., 1934, 1179). It appears probable, therefore, that since selenium is a "softer" atom than oxygen, ϕ will give way to θ, so that ψ will be of the order of 140—150°.

We have synthesised *phenoxselenine-2-carboxylic acid* (III) and attempted its resolution. The strychnine, morphine, cinchonine, and quinidine salts of this acid were unsuitable for examination, but the *cinchonidine*, d- and l-*phenylethylamine*, and *brucine*

(III.) 

 (IV).

salts were well defined. The cinchonidine salt showed no signs of resolving when it was crystallised from alcohol: 12 crops were examined polarimetrically, and had $[\alpha]_{5791}^{20°}$ — **64·1°**

to — 66·5°, $[\alpha]^{20°}_{5461}$ — 72·6° to — 76·0°, in chloroform (*c*, *ca.* 1·3). The *d*- and the *l*-α-phenylethylamine salt were fractionally crystallised from alcohol; 7 crops of the salt of the *l*-base and four of that of the *d*-base had no appreciable numerical difference in specific rotation. The brucine salt was fractionally crystallised a very large number of times and the specific rotations of 13 crops were determined: the values of $[\alpha]^{20°}_{5791}$ varied from — 10·3° to — 6·2°, and of $[\alpha]^{20°}_{5461}$ from — 12·8° to — 7·4° (acetone solution), but owing to the smallness of the observed angle (0·3—0·4°) the experimental error was considerable, and the free acids liberated from the salts were invariably inactive. Moreover, none of the solutions of the salts exhibited mutarotation and no asymmetric induction effects could be detected. The inactivity of the acids liberated from different crops cannot therefore be ascribed to swift racemisation.

6: 8-*Dichlorophenoxselenine-2-carboxylic acid* has also been synthesised, but it proved unsuitable for resolution experiments. The acid formed very unstable salts with strychnine, brucine, quinine, cinchonine, and cinchonidine, and even with nor-*d*-ψ-ephedrine. The d-α-*phenylethylamine* salt was stable, but showed no signs of resolving when it was repeatedly crystallised.

Attempts were made to prepare a nitro-derivative of phenoxselenine-2-carboxylic acid, but conditions for effecting satisfactory nitration could not be found. A synthesis of a dimethyl derivative of the acid failed at an intermediate stage.

Selenoxanthone (aliphatic carbon radius 0·77 A.) would be expected to have a folded configuration, as the following table shows:

Carbon angle, θ	100·0°	110·0°	120·0°	130·0°	133·0°
Selenium angle, ϕ	84·5	92·0	98·5	105·5	107·0
Angle of fold, ψ	113·5	126·5	142·0	163·0	180·0

since it is improbable that carbon would tolerate a valency angle exceeding 125°. We have therefore attempted to resolve selenoxanthone-1-carboxylic acid (IV), prepared by Lesser's method (*Ber.*, 1914, **47**, 2515). The brucine, nor-*d*-ψ-ephedrine, *l*-α-phenylethylamine, and *strychnine* salts were prepared. The last was fractionally crystallised from acetone. In one set of experiments twenty, and in another sixteen, crops were examined polarimetrically; no evidence of resolution was obtained, and the investigation was complicated by the tendency for free strychnine to separate. Decomposition of the various crops gave optically inactive acids.

Although negative evidence is never satisfactory, our examination of the salts of phenoxselenine-2-carboxylic acid was so prolonged that we think it extremely improbable that this acid can be resolved. Until further examples of optical activity due to folding are discovered, no conclusions can be drawn as to the effect of the degree of folding on the dissimilarity in diastereoisomeric pairs of salts, but it is possible that when ψ approaches 180°, even when the molecule is rigidly folded, resolution fails because the diastereoisomerides differ insufficiently in solubility. Alternatively, of course, a non-resolution may be due to the flexibility of the folded molecule.

Comparison of the (assumed) optical instability of the phenoxselenines with the (known) optical stability of the phenoxarsines suggests that one reason for the difference is that in the former the selenium atom has two pairs of unshared electrons as against an attached group and one pair of unshared electrons in the case of the arsenic atom. The increased moment of inertia due to the attached group must make a definite contribution to the stability of the configuration of the arsenic atom and therefore indirectly to that of the whole molecule.

Since no selenoxide has yet been resolved, although on theoretical grounds selenoxides should be capable of exhibiting optical activity, we have attempted the resolution of 2-*carboxyphenoxselenine* 10-*oxide* (VII). Gaythwaite, Kenyon, and Phillips (J., 1928, 2280) found that 4-carboxydiphenyl and carboxyphenyl methyl selenoxides underwent partial reduction to selenides during the formation of certain alkaloidal salts, and we obtained a similar result in attempting to resolve the *l*-α-phenylethylamine, strychnine, and brucine salts of 2-carboxyphenoxselenine 10-oxide. The *nor*-d-ψ-*ephedrine* salt of this acid crystallised satisfactorily from water, but its specific rotation was unaffected by

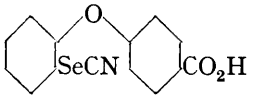
repeated crystallisation, $[\alpha]_{5791}^{20°}$ varying only from + 16·7° to + 17·4°, a variation not exceeding the unavoidable experimental error.

At the outset of this investigation four years ago, the only known phenoxselenine was the parent substance, obtained by Drew (J., 1928, 511) by heating phenoxtellurine with selenium, and various possible routes to this series had therefore to be explored.

Although sulphur reacts with diphenyl ether in presence of aluminium chloride, selenium could not be caused to do so, probably owing in part to the insolubility of selenium in the ether.

As is known, sulphones react with selenium at high temperatures to give selenides, and even thianthren 5 : 5 : 10 : 10-tetraoxide is slowly converted into selenanthren when it is boiled in presence of selenium (Krafft and Kaschau, *loc. cit.*). Yet phenoxthionine 10 : 10-dioxide could not be made to react with selenium and give phenoxselenine.

A new synthesis of phenoxselenines has therefore been worked out, in particular one leading to carboxylic acids. Preliminary experiments showed that the amino-group in 2-aminophenyl *p*-tolyl ether could be replaced by the selenocyanate group (Bauer, *Ber.*,



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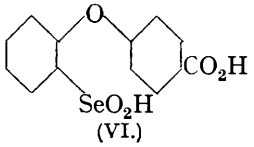

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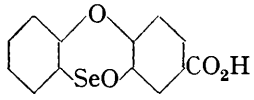
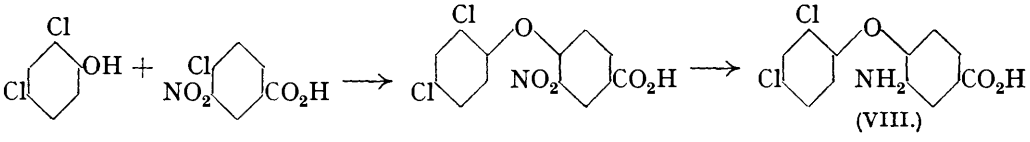


(VII.)

1913, **46**, 92), but it was found impractible to oxidise the selenocyano-derivative satisfactorily. The amino-ether was therefore acetylated and oxidised, and the product hydrolysed. The resulting 4'-*carboxy*-2-*selenocyanodiphenyl ether* (V) was then oxidised with diluted nitric acid (Challenger and Peters, J., 1928, 1366) to 4'-*carboxydiphenyl ether* 2-*seleninic acid* (VI). Ring-closure of this acid to 2-*carboxyphenoxselenine* 10-*oxide* (VII) could not be effected by using concentrated sulphuric acid at 100°, but with 85% acid at 40° it took place readily, and reduction of the product with potassium anhydrosulphite gave phenoxselenine-2-carboxylic acid (III). Decarboxylation of this acid gave phenoxselenine. The selenoxide acid, which is most readily obtained by first isolating phenoxseleninecarboxylic acid and then oxidising it with hydrogen peroxide (Drew, *loc. cit.*), loses oxygen at its melting point, giving the parent acid.

The synthesis employed for 6 : 8-dichlorophenoxselenine-2-carboxylic acid was similar in the last stages to that of the parent acid, but the *amino*-compound (VIII) was obtained according to the scheme :



(VIII.)

Experimental.

2-*Selenocyano*-4'-*methyldiphenyl Ether*.—2-Amino-4'-methyldiphenyl ether (59 g.; 1 mol.) was diazotised, and the filtered solution then treated with sodium acetate until it was no longer acid to Congo-red. The solution was added slowly (15 mins.) to 110 c.c. of a 50% solution of potassium selenocyanate (1·5 mol.). The commercial selenocyanate was used, or a solution was prepared by a simplification of the method of Muthmann and Schröder (*Ber.*, 1900, **33**, 1765) without isolating the solid. A reaction ensued at once and was allowed to become complete at the ordinary temperature. The dark red oil which separated was extracted with chloroform, the extract dried over calcium chloride, and the solvent removed. Distillation gave only 4 g. of 2-selenocyano-4'-methyldiphenyl ether, b. p. 224—227°/18 mm., which later solidified and then separated from alcohol in crystals, m. p. 46°. These became pink when left in air. Several attempts to oxidise the crude selenocyano-compound with various concentrations of nitric acid led to inseparable mixtures.

2-*Acetamido*-4'-*methyldiphenyl Ether*.—Crude 2-amino-4'-methyldiphenyl ether, obtained as an oil by reduction of the corresponding nitro-compound with iron and acidified water, was poured into a solution of twice the calculated quantity of acetic anhydride in water. The

mixture was warmed gently until crystals of the *acetyl* compound separated, and was then poured into much water, and the precipitate filtered off, dried, and crystallised from light petroleum (b.p. 80—100°), from which it separated in needles or prisms, m. p. 92° (Found: N, 6·0. $C_{15}H_{15}O_2N$ requires N, 5·8%).

2-*Acetamido*-4'-*carboxydiphenyl Ether*.—A suspension of 2-acetamido-4'-methyldiphenyl ether (24 g., 1 mol.) in a solution of magnesium sulphate heptahydrate (50 g., 2 mols.) in 1500 c.c. of water was treated (with mechanical stirring) at 85—90° with potassium permanganate (64 g., 2 mols.), added in small quantities during 2 hours. The reaction mixture was cooled and decolorised with sulphur dioxide, the precipitate formed being filtered off and dissolved in sodium carbonate. After filtration from a small amount of alkali-insoluble material, the solution was acidified with concentrated hydrochloric acid. Yield, 22·5 g. (83%). The *acetamido-acid* so obtained formed short rods, m. p. 211°, from alcohol (Found: N, 5·1. $C_{15}H_{13}O_4N$ requires N, 5·2%).

2-*Amino*-4'-*carboxydiphenyl Ether*.—A suspension of 5 g. of the acetamido-acid in 60 c.c. of 20% hydrochloric acid was boiled for ¾ hour. The original heavy powder was gradually replaced by a matte of feathery needles of the hydrochloride, from which the base was liberated by means of concentrated sodium acetate solution. The 2-*amino*-4'-*carboxydiphenyl ether* crystallised from alcohol in square or rectangular prisms, m. p. 137° (Found: N, 6·1. $C_{13}H_{11}O_3N$ requires N, 6·1%). Mayer and Krieger (*Ber.*, 1922, **55**, 1663) state that the acid melts at 120—121°, but give no analysis.

2-*Selenocyano*-4'-*carboxydiphenyl Ether*.—The amino-acid hydrochloride (26 g.) was diazotised, and the solution rendered non-acid to Congo-red by addition of sodium acetate. It was then added gradually to 40 c.c. of 50% potassium selenocyanate solution, kept at 0°. Evolution of nitrogen occurred, and was complete after ¾ hour at the ordinary temperature, followed by a short heating at 100°. The cooled mixture was filtered, and the red solid obtained extracted several times with sodium bicarbonate. The first extraction gave dark-coloured acids on acidification, but the later ones gave rise to pale yellowish-brown acids. The 2-*selenocyano*-4'-*carboxydiphenyl ether* proved difficult to crystallise, but from light petroleum (b. p. 100—120°) pale brownish needles, m. p. 178°, were obtained (Found: C, 53·4; H, 2·9. $C_{14}H_9O_3NSe$ requires C, 52·8; H, 2·85%). The yield of crude acid was 80%.

4'-*Carboxydiphenyl Ether* 2-*Seleninic Acid*.—A solution of the selenocyano-acid (3 g.) in 90 c.c. of 33% nitric acid solution was boiled for a few minutes and then cooled. Some tar and selenium separated and were removed. On addition of an equal volume of water, the *carboxyseleninic acid* was deposited on standing. After being twice crystallised from glacial acetic acid, it had m. p. 212° (decomp.) (yield, 35%) (Found: C, 47·9; H, 3·35. $C_{13}H_{10}O_5Se$ requires C, 47·95; H, 3·1%). From nitric acid (*d* 1·4) the seleninic acid crystallised as a nitrate, decomposing at 120—130°.

Phenoxselenine-2-*carboxylic Acid*.—A large number of experiments were performed before conditions were found for effecting ring-closure of the carboxyseleninic acid. With concentrated sulphuric acid, deep blue products were formed owing no doubt to selenylium salt formation such as Drew observed (J., 1928, 511). The following method gave an 80% yield of the desired phenoxselenine oxide acid; 5 g. of carboxyseleninic acid were gradually added to 36 c.c. of 85% sulphuric acid at 0°. The dark green solution obtained was heated at 40—45° for 40 minutes and then poured on ice. The precipitate was contaminated with small quantities of the above-mentioned blue compounds, but these were removed on thorough washing with water. The crude 2-carboxyphenoxselenine 10-oxide so obtained was ground with one part of potassium metabisulphite and a little water. After an hour, the mixture was filtered and the *phenoxselenine*-2-*carboxylic acid* crystallised from alcohol or benzene. It formed pale yellow needles, m. p. 251° (Found: C, 53·4; H, 2·9. $C_{13}H_8O_3Se$ requires C, 53·6; H, 2·8%). The sodium salt of the acid is sparingly soluble in cold, but readily soluble in hot, water. When bromine is added to a solution of the acid in glacial acetic acid, orange-red plates of the unstable *dibromide*, m. p. 214° (decomp.), are precipitated (Found: Br, 33·7. $C_{13}H_8O_3Br_2Se$ requires Br, 35·4%). Cold water at once converts the dibromide into the selenoxide acid. When the carboxyphenoxyseleninic acid was added to concentrated sulphuric acid at 0°, a red solution, becoming olive-green, was obtained. Heating this solution at 100° for 20 minutes caused the separation of a blue-black precipitate, and treatment with water, followed by crystallisation from glacial acetic acid or benzene, gave a small yield of the phenoxseleninecarboxylic acid (Found: C, 53·3; H, 3·0%) and none of the selenoxide acid. The carboxyphenoxyseleninic acid was unaffected by heating with 75% sulphuric acid at 100° for 15 minutes.

Decarboxylation of Phenoxselenine-2-carboxylic Acid.—A solution of 1 g. of this acid in 30 c.c. of quinoline, to which a little copper bronze had been added, was boiled for ¾ hour. The mixture was poured into dilute hydrochloric acid, and the precipitate collected and warmed with dilute aqueous sodium hydroxide solution. The undissolved solid was crystallised from alcohol, phenoxselenine being obtained, m. p. 87° alone or when mixed with a specimen kindly supplied by Dr. H. D. K. Drew.

Experiments on the Resolution of Phenoxselenine-2-carboxylic Acid.—(a) *With cinchonidine.* The *cinchonidine* salt crystallised readily as prisms m. p. 211° when the base was added to an equivalent amount of the acid in hot alcohol (Found : C, 66·3; H, 5·3. $C_{32}H_{30}O_4N_2Se$ requires C, 65·6; H, 5·2%); it was crystallised repeatedly from this solvent, but all the crops had the same specific rotation within the limits of experimental error (see p. 30).

(b) *With* d- *and* l-α-*phenylethylamine.* Slightly more than the calculated equivalent of base was added to a hot ethyl-alcoholic solution of the acid. Prisms separated, m. p. 207°. The salt was insoluble in acetone and in chloroform, slightly soluble in hot water, and soluble in absolute methyl alcohol. It was crystallised repeatedly from alcohol, but showed no appreciable change in specific rotation. The *l*-base *salt* (Found : C, 60·7; H, 4·7. $C_{21}H_{19}O_3NSe$ requires C, 61·15; H, 4·7%) had $[\alpha]^{20°}_{5791}$ − 3·5°, $[\alpha]^{20°}_{5461}$ − 3·8°; the *d*-base salt had $[\alpha]^{20°}_{5791}$ + 3·7°, $[\alpha]^{20°}_{5461}$ + 4·2°, in methyl alcohol (*c* about 2).

(c) *With brucine.* A hot ethyl-alcoholic solution of 14·55 g. of acid was treated with 1 equiv. (21·5 g.) of brucine dihydrate. On cooling, 27 g. of needles separated; $[\alpha]^{20°}_{5791}$ − 9·7°, $[\alpha]^{20°}_{5461}$ − 11·9° (*c* = 2·012, in acetone). This salt was repeatedly crystallised from ethyl alcohol, and the crops had the rotations given on p. 31, but the acids liberated from different specimens of salt were all inactive. The specific rotation of the brucine salt varies considerably with concentration, $[\alpha]^{20°}_{5791}$ being − 8·5° and − 5·9° for *c* = 1·7 and 2·2 respectively. The brucine salt separates in prisms from alcoholic solution (under ordinary conditions of crystallisation) as a *trihydrate* (Found : C, 58·1; H, 5·5; H_2O, 7·0. $C_{36}H_{34}O_7N_2Se,3H_2O$ requires C, 58·4; H, 5·5, H_2O, 7·3%). From absolute alcohol only a gum separates.

*Experiments on the Resolution of Selenoxanthone-*l*-carboxylic Acid.*—The acid was prepared by Lesser's method (*loc. cit.*) (Found : C, 55·25; H, 2·8. Calc. : C, 55·4; H, 2·7%).

The *l*-α-phenylethylamine salt was obtained by boiling a suspension of 42·4 g. of the acid in 3 l. of alcohol containing 16·9 g. of *l*-α-phenylethylamine. On cooling the filtered solution, 55 g. of yellow prisms separated. The salt was almost insoluble in benzene, chloroform, and ethyl acetate, and although moderately soluble in hot was virtually insoluble in cold alcohol. Fractional crystallisation from ethylene glycol was practicable, but crops which separated were dark and were crystallised from alcohol before being examined polarimetrically: α_{5791} = − 0·01° and − 0·08° (*c* = 1·5; *l* = 2; in ethylene glycol) for all the crops. The *strychnine* salt, prepared similarly, could only be crystallised from acetone. It was microcrystalline, and after being dried to constant weight at 100° and then in a high vacuum had m. p. 240—243° (Found : Se, 12·25. $C_{35}H_{30}O_5N_2Se$ requires Se, 12·4%). Two separate sets of fractional crystallisations were carried out, and although 36 crops were examined polarimetrically, no evidence for resolution was obtained. Free strychnine sometimes separated with the salt, which has $[\alpha]^{20°}_{5461}$ + 3·5° (in chloroform). Samples of acid liberated from crops having rotations somewhat different from this figure were inactive.

2′ : 4′-*Dichloro-2-nitro-4-carboxydiphenyl Ether.*—Potassium hydroxide (60 g.) was melted in presence of 5 drops of water, and 50 g. of 2 : 4-dichlorophenol added. To the clear melt 80 g. of 4-chloro-3-nitrobenzoic acid were added, and the whole boiled for 1·5 hours at 175—180°. The mixture was treated with water, and then saturated with carbon dioxide. The phenol which separated was removed, and that remaining in solution was extracted with ether. Acidification of the aqueous layer precipitated the *acid*, which was microcrystalline from alcohol and had m. p. 207—209° (yield, 54%) (Found : Cl, 21·7. $C_{13}H_7O_5NCl_2$ requires Cl, 21·6%).

2′ : 4′-*Dichloro-2-amino-4-carboxydiphenyl Ether.*—The nitro-acid (26 g.) was dissolved in a mixture of 120 c.c. of ammonia (*d* 0·880) and 240 c.c. of water. A concentrated solution of 224 g. of ferrous sulphate crystals was added, and the mixture boiled for 10 minutes. The black precipitate was extracted with boiling dilute sodium hydroxide. The filtered extract, when slightly acidified and treated with sodium acetate, gave the *amino-acid*, which separated from alcohol in blunt prisms, m. p. 199° (yield, 80—90%) (Found : Cl, 23·6. $C_{13}H_9O_3NCl_2$ requires Cl, 23·8%). The acid was alternatively obtained by catalytic reduction in alcoholic solution in presence of platinum. The product was more easily worked up, but the yield was less satisfactory. The *acetyl* derivative of the acid formed long prisms, m. p. 232°, from alcohol (Found : Cl, 20·7. $C_{15}H_{11}O_4NCl_2$ requires Cl, 20·85%).

2′ : 4′-*Dichloro*-2-*selenocyano*-4-*carboxydiphenyl Ether*.—The amino-acid was diazotised in hydrochloric acid, and the solution added to a 50% solution of potassium selenocyanate at 0°. The whole was kept at 40° for 2 hours (or cold overnight), and then heated at 100° until nitrogen was no longer evolved. The brown precipitate was extracted twice with cold sodium bicarbonate solution, and then with the warm reagent. Acidification of the cold extracts gave tars, but that of the warm extracts afforded the *selenocyano*-compound. This crystallised from alcohol in brown plates, m. p. 247—248° (decomp.) (Found : Cl, 18·4. $C_{14}H_7O_3NCl_2Se$ requires Cl, 18·3%).

2′ : 4′-*Dichloro*-4-*carboxydiphenyl Ether* 2-*Seleninic Acid*.—A mixture of 9 g. of the selenocyano-ether and 330 c.c. of 52% nitric acid was boiled for 40 minutes under reflux, and then cooled and filtered from tar. On addition of the solution to 2 vols. of water, the *seleninic acid* was precipitated. It crystallised from aqueous alcohol in slender needles, softening about 176° and gradually decomposing when heated above this temperature (Found : Cl, 17·8. $C_{13}H_8O_5Cl_2Se$ requires Cl, 18·0%) (yield, 50%). The acid dissolves in concentrated sulphuric acid to a deep blue solution, whereas the chlorine-free acid gives a purple colour under similar conditions.

6 : 8-*Dichlorophenoxselenine*-2-*carboxylic Acid*.—Ring-closure of the seleninic acid could not be effected with 85% sulphuric acid at 40° as in the preparation of the parent acid, but took place to the extent of 90% under the following conditions. The seleninic acid (5 g.) was gradually added to 50 c.c. of concentrated sulphuric acid at 0°. The blue mixture was allowed to acquire room temperature during ½ hour, and then became dark red. On pouring the solution on ice, a white or pale green solid separated, which was treated with a cold saturated solution of potassium anhydrosulphite for ½ hour. The *acid* so obtained crystallised from a large bulk of glacial acetic acid or from dioxan in slender needles, m. p. 309° (Found : Cl, 20·0. $C_{13}H_6O_3Cl_2Se$ requires Cl, 19·9%). The sodium and ammonium salts were soluble in hot water, the solutions becoming gels when cooled.

The d-α-*phenylethylamine salt* was obtained by dissolving the acid in a boiling alcoholic solution of the base. It forms prisms, softening at 186° and melting indefinitely at 250—265° (Found : Cl, 14·6. $C_{21}H_{17}O_3Cl_2NSe$ requires Cl, 14·7%). Fractional crystallisation of the salt from alcohol gave a number of crops having $[\alpha]_{5791}^{20°}$ + 4·2° in alcohol. Samples of acid liberated from the salts were inactive.

5 : 5′-*Dicarboxy*-2 : 2′-*di*-(2′ : 4′-*dichlorophenoxy*)*diphenyl diselenide* was prepared either (*a*) by boiling a solution of the selenocyano-acid in dilute sodium hydroxide for 10 minutes, or (*b*) by reducing the seleninic acid with potassium anhydrosulphite. It crystallises with 2 molecules of solvent from glacial acetic acid in pale yellow needles, m. p. 278° (decomp.) (Found : Cl, 16·9. $C_{26}H_{14}O_6Cl_4Se_2,2C_2H_4O_2$ requires Cl, 16·9%). The unsolvated *acid* was obtained by precipitating an alkaline solution with dilute hydrochloric acid, followed by vacuum drying (Found : Cl, 19·7. $C_{26}H_{14}O_6Cl_4Se_2$ requires Cl, 19·6%).

Nitration of o-*Nitrophenyl* p-*Tolyl Ether*.—The ether (5 g.) was added to a mixture of 50 g. of nitric acid (*d* 1·5) and 50 g. of glacial acetic acid. The warm mixture was heated to 100°, and at once poured into water. Crystallisation of the precipitate from alcohol gave 2 : 2′-dinitro-4-methyldiphenyl ether, m. p. 106°. Since Cook (*Amer. Chem. J.*, 1901, **25**, 64) gave the m. p. as 100°, and did not prove the constitution, we heated the dinitro-compound with piperidine and isolated *o*-nitrophenylpiperidine and 3-nitro-*p*-cresol, thereby establishing the position of the second nitro-group.

Preparation of 4-*Chloro*-3-*nitrobenzoic Acid*.—The following modification of the method described by Hübner (*Z. Chem.*, 1866, 615) proved excellent : 20 g. of *p*-chlorobenzoic acid were added gradually to 140 c.c. of nitric acid (*d* 1·5), the temperature being kept below 30°. The solution was heated to 55—60° for 10 minutes, and poured into water. The acid, after crystallisation from aqueous alcohol, was pure, m. p. 184°. Yield 96%.

2-*Nitro*-4-*carboxy*-3′ : 5′-*dimethyldiphenyl Ether*.—Potassium hydroxide (15 g.) was melted in presence of 3 drops of water and 37 g. of *m*-xylenol were added. To the clear melt, 20 g. of 4-chloro-3-nitrobenzoic acid were added, and the mixture was heated at 170—180° for 1¼ hours. The cooled product was treated with 500 c.c. of water, and then saturated with carbon dioxide. The xylenol which separated was removed, and that remaining in solution was extracted with ether. The aqueous solution was acidified, and the precipitated *acid* crystallised from alcohol. It forms short rods, m. p. 179—181° (yield, 20 g.) (Found : N, 4·6. $C_{15}H_{13}O_5N$ requires N, 4·9%).

2-*Amino*-4-*carboxy*-3′ : 5′-*dimethyldiphenyl Ether*.—The nitro-acid (36 g.) was dissolved in 200 c.c. of ammonia (*d* 0·88) diluted with 200 c.c. of water. To this hot solution was added a

solution of 300 g. of ferrous sulphate crystals in 300 c.c. of acidified water. After ½ hour, the precipitate was filtered off, and the filtrate acidified. A small amount of amino-acid was then precipitated, the rest being obtained by extracting the iron precipitate with boiling dilute sodium hydroxide and acidifying the extract with hydrochloric acid. The impure hydrochloride so obtained was dissolved in water, and sodium acetate added until the solution was alkaline to Congo-red. The *amino-acid* crystallised from alcohol in short rods, m. p. 173° (Found: N, 5·5. $C_{15}H_{15}O_3N$ requires N, 5·5%) (yield, almost theoretical). The *acetyl* derivative, obtained by adding acetic anhydride to a solution of the 2-amino-compound in glacial acetic acid, separates from alcohol in slender needles, m. p. 219° (Found: N, 4·7. $C_{17}H_{17}O_4N$ requires N, 4·7%).

2-*Selenocyano*-4-*carboxy*-3′ : 5′-*dimethyldiphenyl Ether*.—A solution of the amino-acid (10 g.) in one of 2 g. of sodium hydroxide in 30 c.c. of water was treated with 4 g. of sodium nitrite. The mixture was gradually added to 40 c.c. of concentrated hydrochloric acid and 40 c.c. of water, kept in a freezing mixture. Diazonium salt crystallised out during the process, and when this was complete, sodium acetate crystals were added until the solution was no longer acid to Congo-red, whereupon the diazo-salts dissolved. The filtered solution was added to 30 g. of potassium selenocyanate in 30 c.c. of water. Nitrogen was evolved, and a brown-red solid separated. The mixture was heated at 100° until nitrogen evolution ceased, and the solid, now light brown, was filtered off. The *selenocyano*-compound crystallised from alcohol in very pale brown diamond-shaped plates, m. p. 233° (decomp.) (Found: C, 55·5; H, 4·1. $C_{16}H_{13}O_3NSe$ requires C, 55·2, H, 3·8%).

5 : 5′-*Dicarboxy*-2 : 2′-*di*-(4′-m-*xylenoxy*)*diphenyl Diselenide*.—A solution of the selenocyano-acid in dilute sodium hydroxide was boiled for ½ hour. Acidification of the cooled solution precipitated a very hydrated acid, which was dried at 100° and crystallised from glacial acetic acid. The *diselenide-acid* (with 1 mol. of solvent) formed pale yellow plates, m. p. 239—243° (Found: C, 54·9; H, 4·5; $CH_3{\cdot}CO_2H$, 8·55. $C_{30}H_{26}O_6Se_2,C_2H_4O_2$ requires C, 54·8; H, 4·2; $C_2H_4O_2$, 8·6%). The acid forms a highly crystalline nitrate in presence of nitric acid (*d* 1·4).

2-*Carboxyphenoxselenine* 10-*Oxide*.—A solution of 1·8 g. of phenoxselenine-2-carboxylic acid in the least amount of hot glacial acetic acid was treated with 20 c.c. of hydrogen peroxide solution (" 20-vol."). Immediate oxidation occurred and, on cooling, a microcrystalline solid separated, more being obtained by diluting the mother-liquor. The *oxide-acid* crystallised from aqueous acetic acid in needles, and melted at 217—218° to give oxygen and phenoxselenine-2-carboxylic acid. Crystallisation from glacial acetic acid gave a bright yellow compound which was apparently the diacetate, since water converted it into the oxide-acid. The latter is sparingly soluble in water and does not appear to form a dihydroxide, thereby differing from phenoxselenine 10-oxide (Drew, J., 1928, 522). The oxide-acid is sparingly soluble in methyl and ethyl alcohols and soluble in acetic acid (Found: C, 50·5; H, 2·6. $C_{13}H_8O_4Se$ requires C, 50·8; H, 2·6%).

Attempts to Resolve 2-*Carboxyphenoxselenine* 10-*Oxide*.—The *l*-α-phenylethylamine salt could not be prepared in a pure state. On attempting to form the strychnine and brucine salts in absolute-alcoholic solution, mixtures of the oxide-acid and phenoxseleninecarboxylic acid were obtained. The *nor*-d-*ψ-ephedrine salt* was, however, formed by dissolving 3·3 g. of base in 300 c.c. of hot water, adding 6·67 g. of oxide-acid and boiling until all had dissolved. On cooling slightly, iridescent prisms separated, and at the ordinary temperature cubic crystals. Both forms had m. p. 180° (softening at 175°) and the same specific rotation (Found: C, 57·8; H, 4·4. $C_{22}H_{21}O_5NSe$ requires C, 57·6; H, 3·7%). The salt was insoluble in methyl and ethyl alcohols but dissolved in the aqueous alcohols. It was insoluble in acetone, benzene, and chloroform. Repeated crystallisation from water caused no significant change in specific rotation: $[\alpha]_{5791}^{20°}$ + 16·7° to + 17·4°, $[\alpha]_{5461}^{20°}$ + 18·7° to + 19·7° in aqueous methyl alcohol (50%).

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