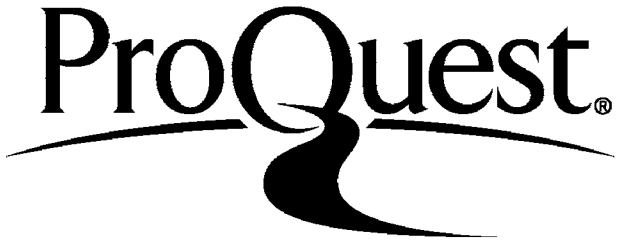
The CONFIGURATION of HETEROCYCLIC COMPOUNDS.

THESIS submitted by
MARY C. THOMPSON.
July, 1937.

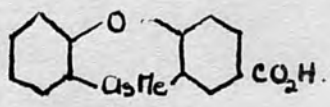


ABSTRACT

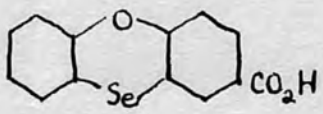
of THESIS entitled

THE CONFIGURATION of HETEROCYCLIC COMPOUNDS.

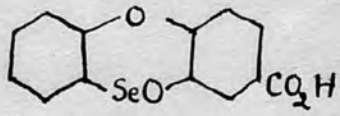
A new cause of molecular dissymmetry was discovered in 1934 by Lesslie and Turner who showed that 10-methylphenoxarsine-2-carboxylic acid (I) could exist in stable dextro and lævo forms.



(I)



(II)



(III)

The dissymmetry was ascribed to the folding of the molecule about the oxygen-arsenic axis, but an alternative explanation was that compound (I) contained the first known example of an asymmetric tervalent arsenic atom. If the cause of the activity in (I) is due to the folding of the molecule, it should be possible to detect similar activity in a number of other types. I have therefore investigated the possibility of obtaining and resolving the phenoxselenine-carboxylicacid (II). The optical properties of the cinchonidine, l- and d-α-phenylethylamine and brucine salts were examined and the latter gave some indication that the acid is a racemate. During crystallisation the specific rotation decreased, and the crop with the lowest rotation, $[\alpha]_{5791}^{20} = -6.6^{\circ}$, when decomposed, gave a free acid

which was dextro-rotatory, $\alpha_{5791} = +0.05^{\circ}$. Since no successful resolution of a selenoxide has been recorded, salts of the selenoxide-carboxylic acid (III) were investigated. Only the nor-d-ψ-ephedrine salt was found to be suitable for the examination of its optical properties and its specific rotation was found to remain constant during repeated fractional crystallisation. Resolution experiments were conducted upon the salts of selenoxanthone-4-carboxylic acid, but this substance does not appear to be a racemate. The nitration of phenoxselenine-2-carboxylic acid was investigated, but I failed to get a single mono-nitrated product. An unsuccessful attempt was made to prepare 1:3-dimethylphenoxselenine-8-carboxylic acid, but 2:4-dichlorphenoxselenine-8-carboxylic acid has been prepared with a view to examining its optical properties.

Mary C. Thompson,

April 1937.

C O N T E N T S .

	Page
Historical and Theoretical Discussion	1
Stereochemistry of Selenium Compounds	25
Experimental Discussion	28
Resolution of α-Phenylethylamine	28
Preparation of Selenoxanthone-4-carboxylic Acid	32
Preparation of Phenoxselenines	34
Experimental	43
Preparation and Resolution of α-Phenylethylamine	43
Preparation of and Resolution experiments on Selenoxanthone-4-carboxylic Acid	49
Preparation of and Resolution Experiments on Phenoxselenine-2-carboxylic Acid	67
Preparation of and Resolution Experiments on Phenoxselenine-10-oxide-2-carboxylic Acid	99
Preparation of Selenanthren	104
Nitration of o-Nitrophenyl p-Tolyl Ether	106
Nitration of Phenoxselenine-2-carboxylic Acid	108
Attempted Preparation of 2:4-Dimethylphenoxselenine-6-carboxylic Acid	110

The CONFIGURATION of HETEROCYCLIC COMPOUNDS.

This preamble endeavours to put forward a hypothesis as to the non-planar nature of certain heterocyclic compounds and describes experiments which have been designed to support it.

Historical and Theoretical Discussion.

Bergmann and Tschudnowsky (Ber., 1932, 65, 457,) measured the dipole moments of benzophenone, p-chloro- and pp'-dichlorobenzophenone, and from the results concluded that the valency angle of the extranuclear carbon atom was the same in all cases and that the C = O bond lies in the same plane as the other two valencies of the same carbon atom. For comparison, the dipole moments of the corresponding sulphur compounds, diphenyl sulphoxide, p-chlorodiphenyl sulphoxide and pp'-dichlorodiphenyl sulphoxide were measured and from the values obtained the authors inferred that the sulphur atom in all cases had

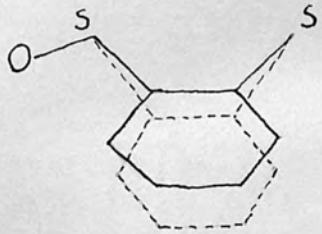
the same valency angle, but that the S- O valency does not lie in the same plane as those between the sulphur atom and the other radicles attached to it. By way of confirmation the two disulphoxides of thianthren previously described by Fries and Vogt (Ber., 1911, 44, 756.) were examined, and it was found that although the cis-form had the expected larger moment ($4.2 \cdot 10^{-18}$ e.s.u.) the trans form had the smaller but unmistakeable moment of $1.7 \cdot 10^{-18}$ e.s.u. Theoretically the trans form should have the same moment as the parent substance thianthren. This had always been assumed to have a symmetrical structure and therefore zero dipole moment, but when it was measured in benzene solution the value observed was $1.68 \cdot 10^{-18}$ e.s.u. The authors explained their results by assuming the thianthren molecule was folded about the S - S axis. This work was confirmed by Bennett and Glasstone (J., 1934, 128) who, to eliminate the possibility of Bergmann and Tschudnowsky's results being due to some solvent action of atom polarisation, measured the dipole moment of thianthren in other solvents. They obtained the value $1.54 \cdot 10^{-18}$ e.s.u. in carbon tetrachloride and $1.47 \cdot 10^{-18}$ e.s.u. in carbon disulphide. Using the latter solvent the results of measurements made at two different temperatures indicated that atom polarisation was negligible.

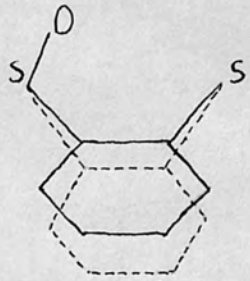
Although the above measurements indicate that thianthren is heteroplanar, no evidence has yet been obtained from the stereochemical standpoint. Baw, Bennett and Dearns (J., 1934, 680.) prepared 2:6-dichlorothianthren disulphoxide, 2:6-dimethylthianthren disulphoxide and the corresponding 2:6-dimethoxy compound and, although they obtained each of these in the α and β forms corresponding with the tetrahedral nature of the sulphur atom, they could obtain none of the additional isomers which are theoretically possible if the molecules are folded. They investigated all the oxidation products of these substituted thianthrens for the possible two monoxides, three dioxides and two trioxides indicated in diagram I, but failed to find any evidence of their existence. The authors concluded that they were not sufficiently stable to be distinguished from the α and β forms. The case was considered analogous to that of the amines $R_1R_2R_3N$ whose non-planar configurations have been demonstrated from dipole moment measurements, yet attempted separation of which into enantiomorphous forms has not yet been successful.

Now since precise X-ray measurements of aromatic compounds (Lonsdale, Trans. Faraday Soc., 1929, 25, 306; Proc. Roy. Soc., 1931, A, 133, 536; Robertson, Proc. Roy. Soc., 1933, A, 141, 79, 594; Pickett, ibid., 142, 333.) indicate

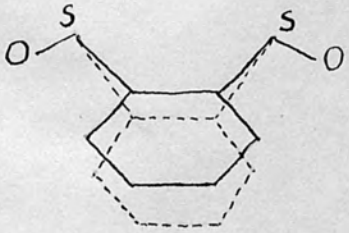
Diagram I.

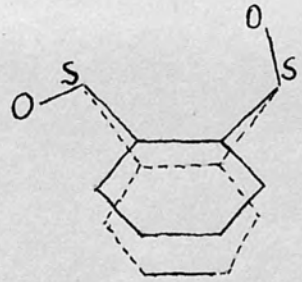
Monoxides

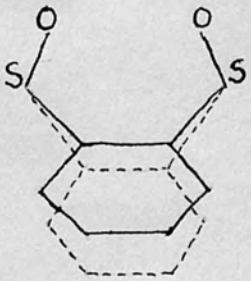




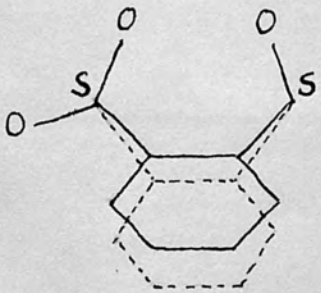
Dioxides

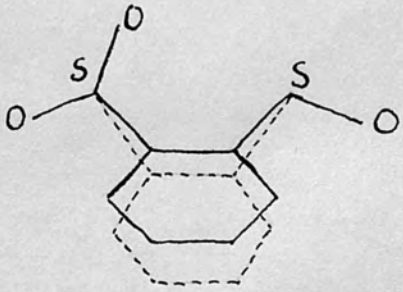




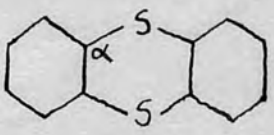


Trioxides





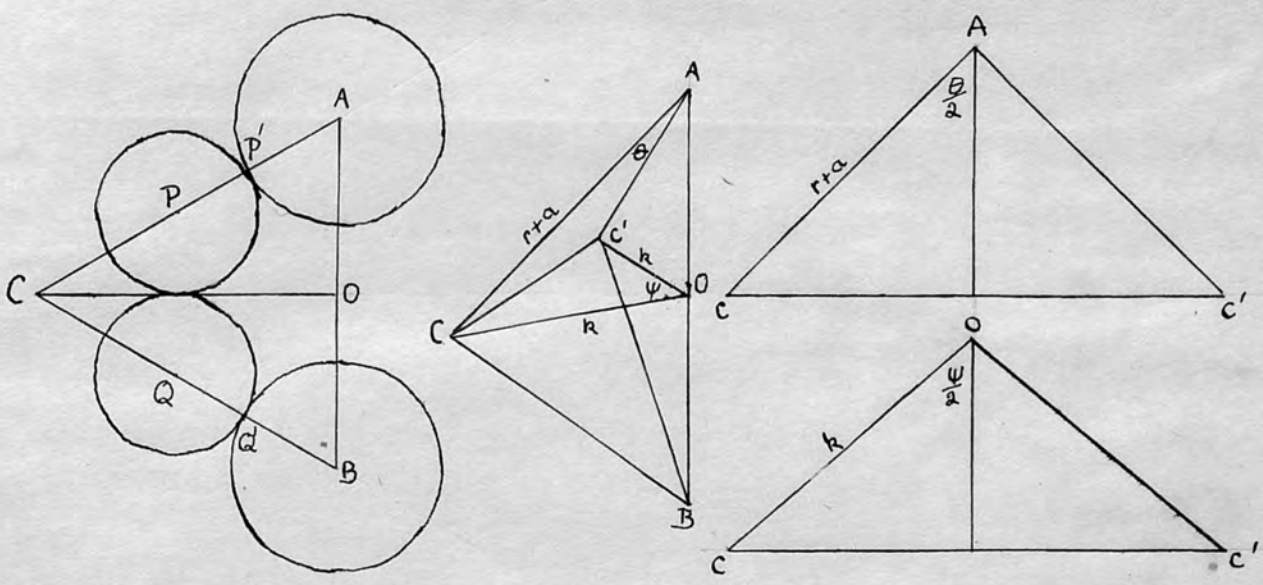
that each benzene nucleus and its directly attached atoms have a strong tendency to remain in a single plane, the most obvious and probable cause of the folding of the thianthren molecule is that the valency angle of sulphur is less than 120°. Widely divergent values for this angle have been recorded; from wave mechanical considerations Pauling (J. Amer. Chem. Soc., 1931, 53, 367.) considered the value should be 90°, from dipole measurements of some thiocyanates Hunter and Partington (J., 1932, 2812.) deduced the value 120°, whilst from those of diphenyl sulphides values of 142° (Bergmann, Engel and Sandor, Z. physikal. Chem., 1930, B, 10, 397.), 146° (Smyth and Walls, J. Amer. Chem. Soc., 1932, 54, 3230.), and 118 ± 8° (Hampson, Sutton and Farmer, Proc. Roy. Soc., 1933, B, 140, 562.) were obtained. Recalculation by Sutton and Farmer (Trans. Faraday Soc.,1935, 31, 945.), making allowance for interaction moments, solvent effects, atom polarisation and errors in observation, produced the value 113 ± 3°, and Maxwell, Mosley and Hendricks (Physical Review, 1936, 50, 41.) found that in sulphur vapour which would contain complex molecules the valency angle is 100°. In view of the facts (a) that the angle α (diagram II) is capable of assuming a value of more than 120° when the benzene



II

ring is attached to another six-membered ring, (Mills and Nixon, J., 1930, 2510.) (b) the measurements of the dipole moments of o-substituted derivatives of benzene indicate a deflection of the ortho substituents away from each other, both of which would increase the likelihood of a stable planar configuration for the thianthren molecule even if the valency angle of sulphur were slightly less than 120°, the value of the angle is probably near the normal tetrahedral angle 109°; and, in fact, from the moment of the bond C_6H_5 - S, estimated from measurements of diphenyl sulphide and applied to that of thianthren, the value of the sulphur valency angle has been calculated to be 110°. (Sutton and Hampson, Trans. Faraday Soc., 1935, 31, 951; Bennett, ibid., 1934, 30, 858.)

Now assuming the angle α remains 120°, i.e. that the direction of the C - S valency is along the line joining the same carbon atom to the centre of the benzene ring, it is possible to calculate the value of the angle of fold, for any value of the sulphur valency angle, which would cause no strain in the thianthren molecule.



C and C' are the centres of the two benzene rings, A and B are the centres of the two sulphur atoms, $\underline{\theta}$ is the sulphur valency angle and ψ is the angle of fold. Then angle ACB is 60°.

Let $\frac{r}{3}$ be the radius of the carbon atom and $\underline{a}$ the radius of the sulphur atom.

Then CP' = CP + PP' = 3 x radius of C atom = $\underline{r}$.

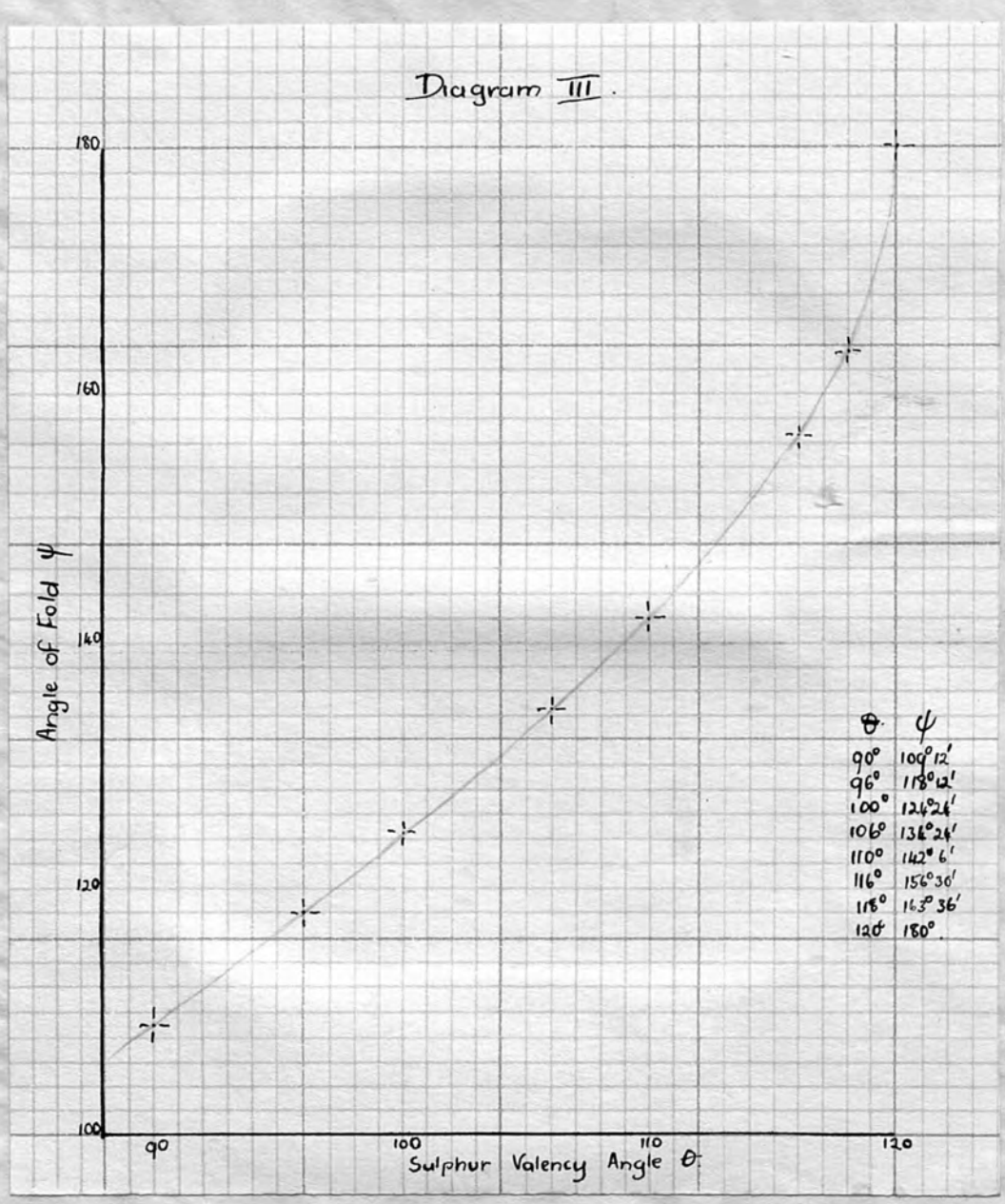
and CA = CP' + P'A = r + a.

$\therefore$ CC' = $2(r + a) \sin \frac{\theta}{2} = 2k \sin \frac{\psi}{2}$

$\therefore$ $\sin \frac{\psi}{2} = \frac{r - a}{k} \sin \frac{\theta}{2}$

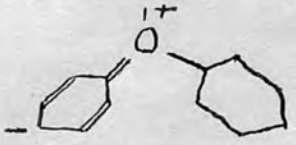
$= \frac{2}{\sqrt{3}} \sin \frac{\psi}{2}$.

Diagram III.



θ	ψ
90°	109° 12′
96°	118° 12′
100°	124° 24′
106°	136° 24′
110°	142° 6′
116°	156° 30′
118°	163° 36′
120	180°.

If the value of ψ obtained from this equation is plotted against θ (diagram III) it may be seen that when θ has its most probable value of 110°, ψ is 142°; but for higher values of θ, ψ increases very quickly, i.e. if the sulphur valency angle is capable of small increases above 110° because of resonance phenomena, kinetic energy or any other cause, there is a reasonable chance of the molecule assuming a planar configuration and "racemisation" occurring, e.g., if the state of the sulphur atom in thianthren is at all comparable to that of the oxygen in diphenyl ether (Glasstone, Ann.Rep., 1935, 133.) where one of the resonance structures is thought to be

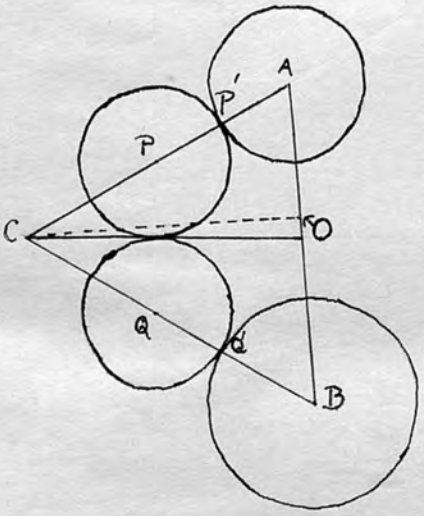


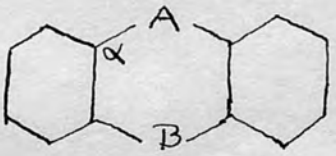
giving oxygen a double and single bond the angle between which is usually 125° 16' in a tetrahedral atom, then the folded thianthren molecule and the oxides which theoretically could be derived from it, would not be sufficiently stable for the maintenance of a separate existence.
Also assuming the sulphur valency angle to be 110° and the angle of fold 142°, the distance between the centres of two carbon atoms to which one sulphur atom is attached is 2.84 A.U. (assuming Pauling's values for the radii of carbon and sulphur atoms, namely 0.695 A.U. and 1.04 A.U.). This is more than sufficient to contain the radii of the

carbon atoms plus envelope of 0.5 A.U. which, according to Sidgwick (Ann. Rep. 1933, 199.), is the minimum distance between two unattached atoms imside which their electrons have a serious repulsive influence on each other. Very little exact knowledge, however, has been obtained on this subject, and it is possible that the mutual repulsion of the carbon atoms of the two benzene rings might have an appreciable influence on the stability of thianthren and its derivatives.

It thus appeared that some stabilising factor must be introduced before the folded structure of such heterocyclic compounds as thianthren could be demonstrated other than by measurement of dipole moments. Now suppose the two sulphur atoms in thianthren were replaced by atoms of unequal size; when the molecule assumed a planar configuration the valency angle of the smaller atom would have to undergo a much larger increase than if there were an atom of equal size in place of the larger atom. So that if one benzene rind contained a substituent making the folded molecule asymmetric, the molecule would undergo a much greater strain in passing from one enantiomorphous form to another when there were two atoms of unequal radius than if there were two equal atoms in the place of the sulphur atoms in thianthren.

Assuming there is no divergence of the angle α (diagram IV) from 120°, and neglecting effects due to the relative proximity of A and B (IV), the relationship between the valency angles of the unlike atoms A and B and the angle of fold ψ which would cause the least strain in the molecule can be calculated in a similar manner as for the thianthren molecule.





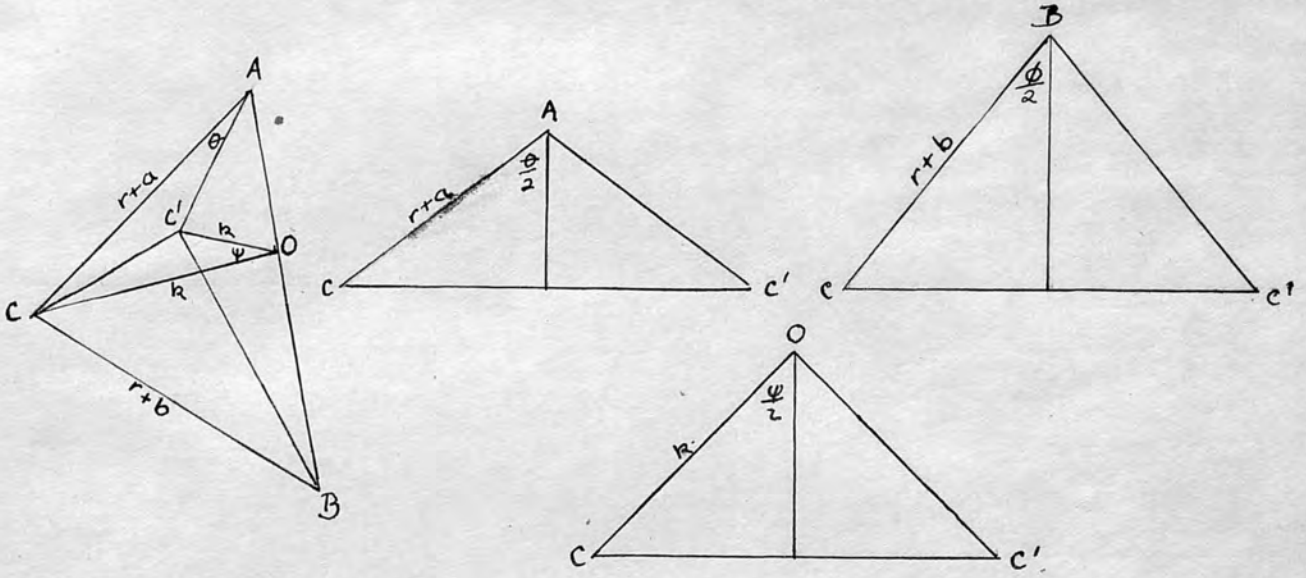
IV

The following expression connecting the valency angles θ and ϕ of A and B has been derived for us by Dr. J. Marshall of Bedford College:-

$$(r + b)^2 \cos\phi - (r + a)^2 \cos\theta = (b-a)(2r + a + b). \quad . \quad . \quad . \quad .1$$

where r = CP' (3 x radius of C atom), a = radius of atom A, valency angle θ, and b = radius of atom B, valency angle ϕ.

The relationship between the angle of fold and the valency angle of A or B may be deduced as follows:-



$$CC' = 2(r+b)\sin\frac{\phi}{2} = (r+a)2\sin\frac{\theta}{2} = 2k\sin\frac{\psi}{2} \quad \ldots\ldots\ldots 2.$$

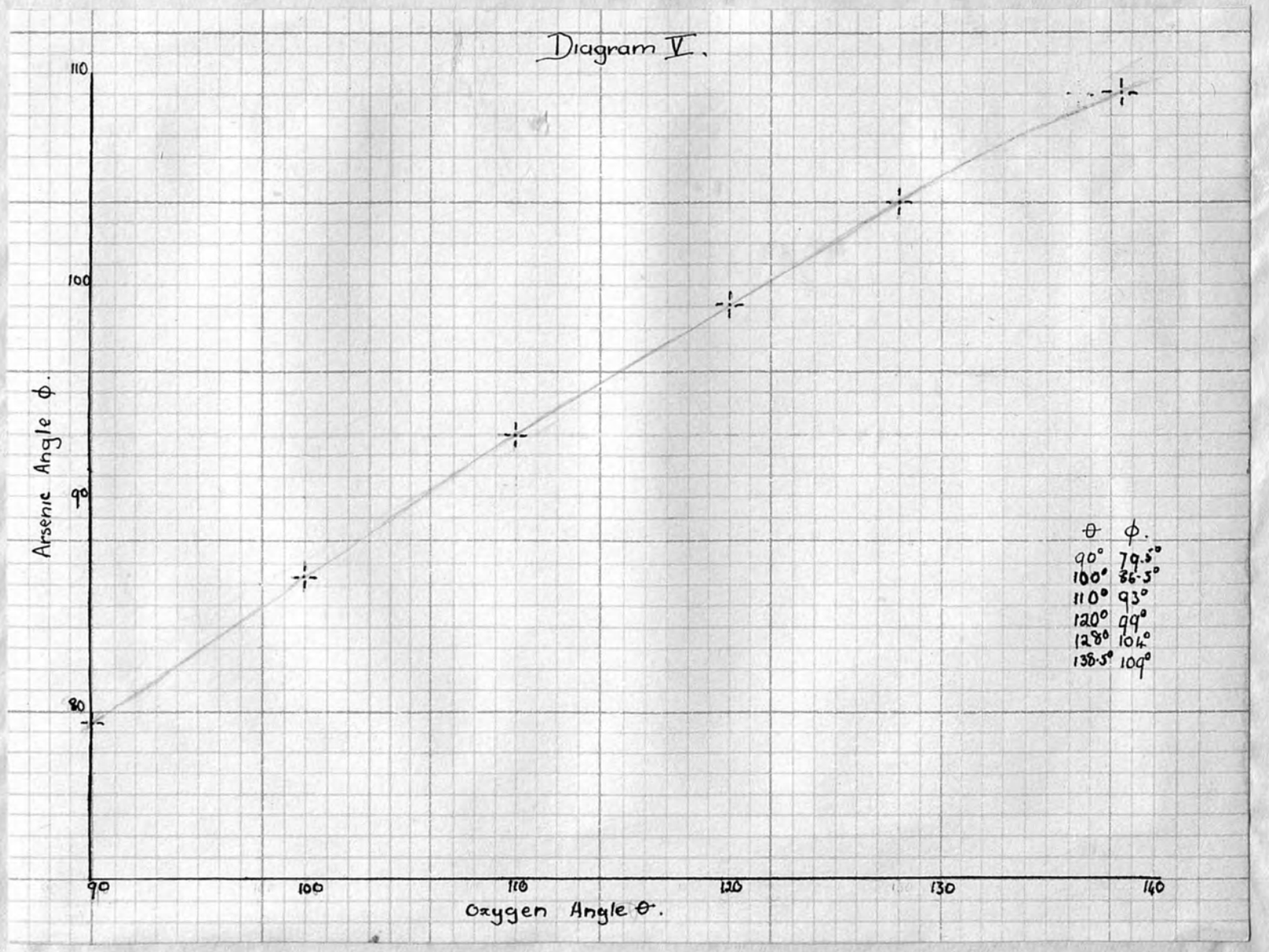
$$AB^2 = (r+a)^2 + (r+b)^2\cos 60^\circ = (r+a)^2 + (r+b)^2 - (r+a)(r+b).$$

$$k.AB = 2(\text{area } ACB) = (r+a)(r+b)\sin 60^\circ.$$

$$\therefore k^2 = \frac{3(r+a)^2(r+b)^2}{4\left[(r+a)^2+(r+b)^2-(r+a)(r+b)\right]}$$

Compounds which have been investigated are phenarsazines and phenoxarsines. Diagram V indicates the relative values of θ and ϕ which might be expected to give a strainless molecule, and the table below indicates the corresponding values of ψ when A is an oxygen atom and B an arsenic atom. (Pauling's values of 0.66 A.U. and 1.21 A.U. of the radii of oxygen and arsenic atoms were used).

Diagram V.



θ	ϕ.
90°	79·5°
100°	86·5°
110°	93°
120°	99°
128°	104°
138·5°	109°

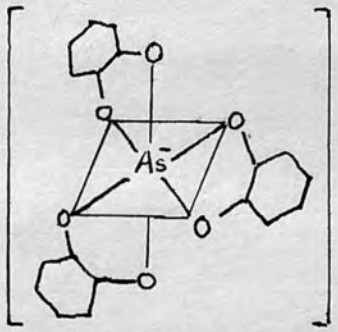
Oxygen Angle Θ	Arsenic Angle ϕ	Ψ
90°	79.5°	98°
110°	93.5°	122°
128°	104°	147.5°
138.5°	109°	180°

As in the case of sulphur, the valency angles given for oxygen vary widely. Sutton and Hampson (Trans.Faraday Soc., 1935, 31,945.) from dipole moments of substitutes diphenyl ethers give the value 128 ± 4°, Maxwell, Hendricks and Mosley (J. Chem. Phys.,1935, 3, 699.) from electron diffraction measurements of pp'-diiododiphenyl ether obtain the value 118 ± 3°. From the Raman Spectrum of diphenyl ether,N.G.Pai (Indian Journal of Physics, 1935, 3, 660.) gets 118°, whilst Sutton and Brockway (J. Amer.Chem. Soc., 1935, 57, 473.) from similar measurements get 111 ± 4°. R. Mecke (Z.Physik., 1933, 81, 313.) from spectroscopic measurements of water obtains the value 105°. Glasstone (Ann. Rep., 1935, 132) explains the fact that the angle is diphenyl ether is greater than in simpler oxygen compounds by assuming that resonance occurs between the normal molecule and the two possible excited states

and, as previously stated, the angle between the double and single bonds of a tetrahedral atom is about 125°.

Furthermore, such resonance would favour a co-planar configuration for the two benzene rings and this would necessitate an angle lying between 123° and 145°, according as one made an allowance of 0 to 0.5 A.U. for the envelope around the hydrogen atoms in the ortho positions to the oxygen atom. Since in substituted phenoxarsines probably the first and certainly the second factor would not operate, it is justifiable to assume that a smaller valency angle than 120°, probably one nearer to the approximately tetrahedral value obtained for the simpler oxygen compounds, obtains. Pauling, from wave mechanical calculations, came to the conclusion that for 2- or 3-covalent atoms the normal valency angle is 90° _, but very little experimental evidence bears out this value.

From the graph (V) and the table given above, if the oxygen angle is assumed to be about 110°, the angle of fold is about 125°, and the arsenic atom for complete accommodation should have a valency angle of 90°. Now, in spite of Pauling's calculations, this is probably low, although the resolution of tripyrocatechyl arsenic acid (VI) (Rosenheim and Plato, Ber., 1925, 58, 2000.) where the arsenic atom has an octahedral structure and therefore a valency angle of 90°, supports it, since, as a general rule, atoms do not appear to change their valency angle when they change their

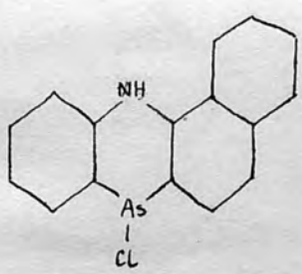
(VI)  H^+, H_2O.

co-valency. But, even if the angle were slightly greater than 90° and the strain on the molecule was relieved by increasing ψ, it is unlikely that the oxygen angle would increase at all readily by 20° to reach a value of 137°, which it would have to do before the molecule could attain a planar configuration. Therefore, it is likely that phenoxarsines have a folded structure and substituted asymmetric derivatives would undergo racemisation less readily than similar derivatives of thianthren. Since the valency angle of nitrogen is found to be 105-110° (Penny and Sutherland, Trans. Faraday Soc., 1934, 30, 898; J. Chem. Physics, 1934, 2, 492.) a non-planar configuration for phenarsazines is even more possible than for phenoxarsines, even though the nitrogen has a slightly larger atomic radius (0.7 A.U.) than oxygen (0.66 A.U.).

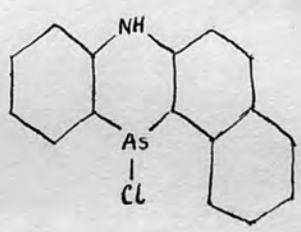
Some substituted phenarsazines were examined polarimetrically by Allen, Wells and Wilson (J. Amer. Chem. Soc., 1934, 56, 223). The compounds produced by the action of silver bromocamphor sulphonate on 7-chloro-7:12-dihydro-γ-benzo-

phenarsazine VII, 7-chloro-7:12-dihydro-α-benzophenarsazine, VIII, and 9-methyl-7-chloro-7:12-dihydro-γ-benzophenarsazine, IX, were described. The bromocamphorsulphonates of VII and VIII were said to exist in two forms, and, in the case of VII, these forms were shown to differ in their specific rotation.

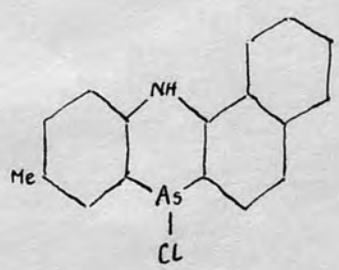
VII



VIII



IX



Now this activity might be due to one of three causes:-

(a) If a tetrahedral structure is assumed for both nitrogen and arsenic, geometrical isomerism is possible, the hydrogen and chlorine atoms being on the same or opposite sides of the molecule. In this case two optically active compounds might be derived from the two possible forms. However, since there is yet no recorded instance of optical activity of compounds containing secondary amine nitrogen, the activity is not likely to be due to this type of isomerism.

(b) The asymmetry may be due to the tetrahedral nature of the arsenic atom alone. If so, the authors of this

paper have recorded the first example of asymmetry due to a tervalent arsenic atom, and this is, in fact, the conclusion at which they arrive, since, they argues, even though there has not been a successful resolution of a tervalent nitrogen compound, a corresponding arsenic compound is likely to be more stable spatially and therefore more capable of resolution.

(c) The substance may exist in stereoisomeric forms due to the folding of the molecule about the As- N axis. From the foregoing considerations this is extremely probable.

This work, however, is not very conclusive; the combined yield of the two isomers was only ten per cent of the theoretical, and it was isolated from substances containing no halogen. The observed rotations were very small and in view of the uncertainty as to the nature of the bond between the arsenic atom and the sulphonic acid group, the value of this work cannot be definitely estimated.

More definite conclusions were reached by Lesslie and Turner in their investigation of phenoxarsines. (J. 1934, 1170; 1935, 1268; 1936, 730.). These authors prepared 10-methyl-, 10-ethyl- and 10-phenyl-phenoxarsine-2-carboxylic acid. The methyl compound was resolved by way of its strychnine salt and free dextro

and laevo acids were obtained $[\alpha]^{20}_{5791}$, + 95.8° and -96.0° (in alcohol) respectively. The pure active acids retained their activity even after heating their alcoholic solutions under pressure at 100° for several hours; a solution of the laevo acid in benzyl alcohol retained 90% of its optical activity after being kept at 200° for two hours; Six hours heating of a solution of the laevo acid in N-sodium hydroxide solution at 100° caused no measurable racemisation. Racemisation did occur when an alcoholic solution of the laevo acid was left standing with methyl or ethyl iodide, the rate of racemisation increasing with increasing concentration of methiodide ions present. The ethyl compound was also separated into its enantiomorphous forms by means of the fractional crystallisation of its strychnine salt and dextro and laevo acids $[\alpha]^{20}_{5791}$, ± 119.0 ± 3° (in alcohol) were obtained. A solution of the dextro acid in N-sodium hydroxide, which originally had α_{5461}, +0.91° ($\underline{l}$ = 2, $\underline{c}$ = 0.275) was heated in a sealed tube at 100°; after four hours α_{5461} was 0.90°, and after nine hours 0.81°. The optical stability af the ions of the acid is therefore of the same order as those of the methyl acid. A solution of the dextro acid in alcoholic methyl iodide lost its activity slowly during two hours and then much more rapidly. The phenyl compound was resolved

by fractional crystallisation of the l-α-phenylethylamine salt and the free optically pure acids had much higher rotations, $[\alpha]^{20}_{5791}$, ± 223° (in alcohol) than either the methyl or ethyl compounds, but their optical stability was similar to that of the latter. An ethyl alcoholic solution of the laevo acid lost none of its activity when it was heated for four hours in a closed tube at 100°. Oxidation of the laevo acid to 10-phenylphenoxarsine-10-oxide-2-carboxylic acid was accompanied by complete loss of activity.

This asymmetry is thought to be due to the folding of the molecule about the oxygen-arsenic axis rather than to the asymmetric tervalent arsenic atom because of the following facts:-

(a) The reason put forward and generally accepted as the cause of the non-resolution of tervalent nitrogen compounds is the vibration of the nitrogen atom at right angles to the plane containing the atoms attached to it, so that the nitrogen might be on either side of the plane and thereby enabling racemisation to take place very easily. Since this phenomenon also may occur in arsines and is in no way prevented in phenoxarsine, if the arsenic had been the only centre of asymmetry in the molecule, resolution would have been effected far less readily, if at all.

(b) The optically active phenoxarsines are far more stable than would be expected if the activity was solely due to a tervalent arsenic atom. Most of the tertiary ammonium salts which have been resolved, e.g. benzyl methyl phenyl allyl ammonium iodide (Pope and Harvey, J, 1901,830), benzyl methyl phenyl ethyl ammonium iodide and the corresponding d-camphorsulphonate (Pope and

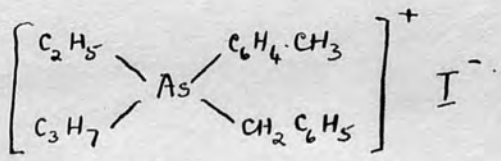
and the one active arsonium compound described, phenyl naphthyl benzyl methyl arsonium iodide (Burrows and Turner, J.1921, 426) lost their activity very easily - the activity of the d-camphorsulphonate mentioned changed to that of the dl-base-d-acid on warming a solution - and it seems probable that in tricovalent compounds where the fourth valency might be considered as the unshared pair of electrons racemisation would be even more rapid.

(c) Had the resolution been due to the asymmetric arsenic atom alone some retention of activity during the addition of methyl or ethyl iodide under such mild conditions (room temperature and in very dilute alcoholic solution) would have occurred. But an explanation of the complete loss of activity is readily forthcoming if the latter is due to the folding of the molecule. For during the addition of an alkyl iodide to an arsine the arsenic atom becomes positively charged, $R_3As + RI = R_4As^+ \} I^-$, and therefore is considerably

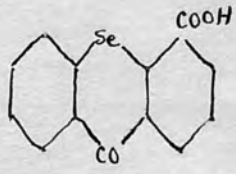
reduced in size. There are no actual data recorded in the literature of the magnitude of this decrease, but, as an example, that of copper, the element in the first group in the same long period as arsenic, may be considered. The atomic radius is 1.29 A.U., that of its ion with unit positive charge is 1.0 A.U.. This represents a decrease of 22.5 per cent. If there was a corresponding decrease in the case of arsenic the positively charged atom would have a radius of 0.9 A.U.. This value is not very much greater than that of oxygen, and therefore the molecule has lost the stabilising factor, discussed in the previous pages, which is considered to contribute much to prevent its racemisation.

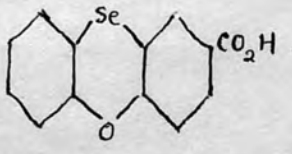
But in spite of the above considerations there still remained the possibility that the optical activity of these phenoxarsines was due to the tetrahedral arsenic atom. For it is not inconceivable that an optically active quaternary arsonium salt, as soon as it is formed, would racemise in the same manner as the corresponding ammonium iodide, namely, by the reversible reaction, $R_4NI \rightleftharpoons R_3N + RI$, taking place, although the speed at which the racemisation takes place and the fact that Lesslie and Turner (J.,1935, 1051.) failed to resolve 2:10-dimethyl- and 10-phenyl-2-methyl phenoxarsonium iodides whilst Kamai (Ber., 1933, 66, 1779.) obtained the dextro form of ethyl n-propyl p-tolyl benzyl arsonium iodide (X)

does not bear out this suggestion.

X. 

It therefore seemed desirable to examine compounds where there could be no ambiguity of this sort. Krishna (J.,1923,156.) obtained the d-camphorsulphonate of 2-aminothianthren, but was unable to resolve it. Bennett, Lesslie and Turner (J., 1937, 444.) examined the α -phenylethylamine salts of a carboxy-thianthren and a carboxy-phenoxthionine and also the brucine salt of 3-nitro-8-methylphenoxthionine-1-carboxylic acid but failed to find any indication of asymmetry. This thesis describes the examination of the selenoxanthone-carboxylic acid XI, and the phenoxselenine carboxylic acid XII in which any activity observed could only be due to the folding of the molecule about the selenium-carbon axis in the one case and the selenium-oxygen axis in the other.

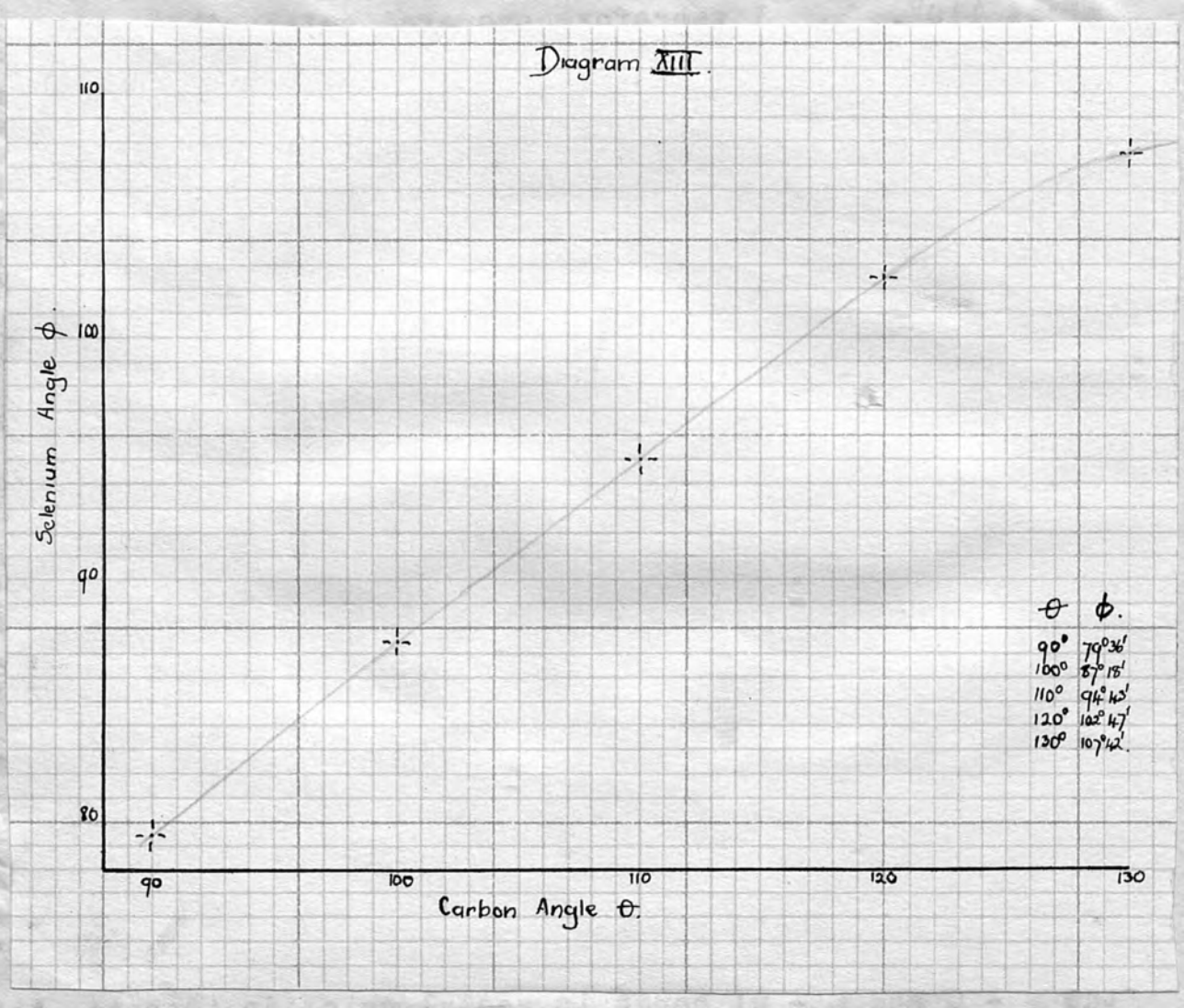
XI 

XII. 

There are very few data concerning the valency angle of selenium. The only evidence obtainable was from (a)the dipole moment of diphenyl selenide ($1.38.10^{-18}$ e.s.u.)

indicating an angle of less than 180° and (b) the resolution by Pope and Neville (J., 1902, 1552.) of phenyl methyl selenetine bromide $\left.\begin{matrix} C_6H_5 \\ CH_3 \end{matrix}\right\rangle Se^{+}.CH_2.COOH \}\ Br^{-}$ indicating a tetrahedral structure for selenium and therefore an angle of about 110°. I therefore prepared selenanthren by the method of Krafft and Kaschau (Ber., 1896, 29, 443.) in order that this fact might be verified by the determination of its dipole moment. The measurement was made by Dr. Le Fèvre of University College, London, and the value $1.43.10^{-18}$ e.s.u. was obtained. Hence in a similar manner to thianthren, seleanthren must be folded about the Se - Se axis and since the carbon valency angle is definitely known to be 109°, there seems every reason to believe that a selenoxanthone molecule would not be planar and a suitable derivative would exhibit optical activity. (Recent work on the angle between the C - Cl valencies in such compounds as carbonyl chloride (Dornte, J. Amer Chem. Soc., 1933, 55, 4126) chloroform and methylene chloride (Sutton and Brockway, J. Amer. Chem. Soc., 1935, 57, 473.) and between the C - C and C - Cl bonds in acetyl chloride (Dornte, ibid.) indicates that the carbon valency angle remains tetrahedral in spite of the close proximity to each other of the chlorine atoms. This fact would prevent facile racemisation of selenoxanthone derivatives).

Diagram XIII.



θ	ϕ.
90°	79°36′
100°	87°15′
110°	94°43′
120°	102°47′
130°	107°42′.

The relationship between the valency angles of carbon and selenium has been calculated in a manner similar to that used for phenoxarsines. The graph (diagram XIII) indicates the relative values of the valency angles and the table below shows the angle of fold calculated from equation (2) using Pauling's values of the atomic dimensions, namely, C, 0.77 A.U. and Se, 1.17 A.U..

Carbon Angle θ	Selenium Angle ϕ	ψ
90°	79.5°	101°
100°	87.5°	113°
110°	94.5°	127°
120°	103°	141.5°
130°	107.5°	162°
133°		180°

This indicates that if the natural valency angle of selenium lies anywhere between 90° and 105° the molecule would almost certainly be non-planar. However, all resolution experiments were completely unsuccessful. The rotation of the strychnine salt only varied because the salt tended to split. As far as could be ascertained the l-α-phenylethylamine salt was homogenous, but its solubility was such that non-resolution by this means would be even less conclusive than most non-resolutions.

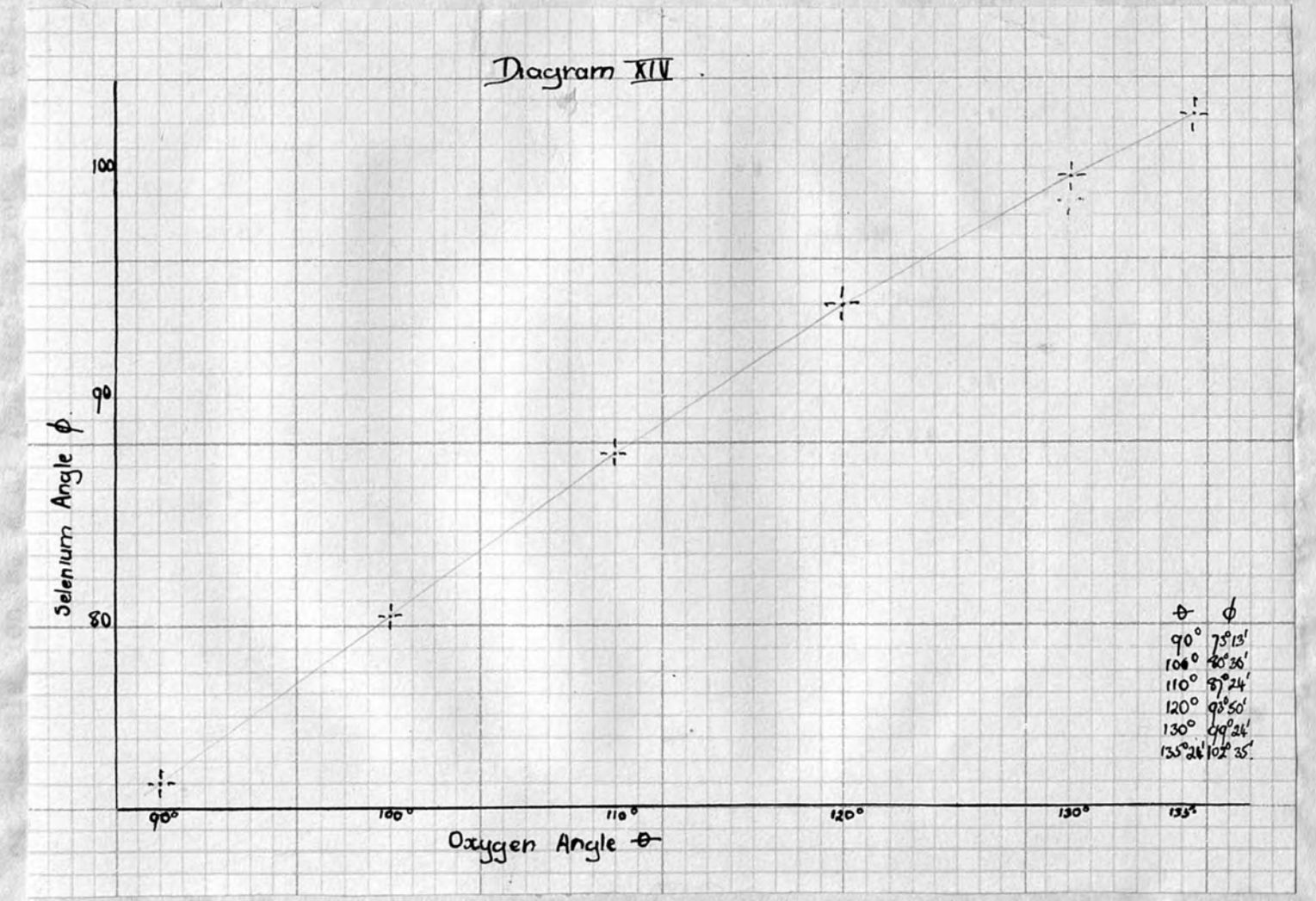


Diagram XIV
100
90
80
Selenium Angle ϕ
90°
100°
110°
120°
130°
135°
Oxygen Angle θ
θ ϕ
90° 75° 13'
100° 85° 36'
110° 87° 24'
120° 93° 50'
130° 99° 24'
135° 24' 102° 35'

In a similar manner phenoxselenine-2-carboxylic acid was examined. This compound might be expected to give more stable non-planar molecules than selenoxanthone derivatives, because the oxygen atom has a smaller radius than carbon and the valency angle might be rather less also. The graph (diagramXIV) and the following table show the same relationships as were calculated for phenoxarsine and selenoxanthone.

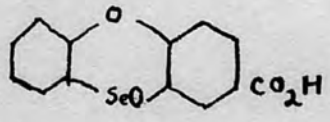
Oxygen Angle θ	Selenium Angle ϕ	ψ
90°	73°	100°
100°	80.5°	112°
110°	87.5°	125°
120°	94°	139°
130°	99.5°	157°
135°	102.5°	180°

These indicate that in a strainless form for a reasonable value for the valency angle of oxygen (100-115°) the selenium angle would have to be small (75-90°), and hence if the strain produced because the selenium valency angle is larger than this was relieved by increasing the angle of fold a greater tendency to racemisation would result. However, the chances of a folded structure for phenoxselenine molecules appeared quite large and salts of phenoxselenine-2-carboxylic acid were prepared and investigated. The cinchonidine, l- and d-α-phenylethyl-

amine salts were fractionally crystallised but no separation into diastereoisomerides could be detected. As crystallisation of the brucine salt proceeded, the rotation appeared to decrease. The crop with the lowest rotation, $[\alpha]^{20}_{5791}$, - 6.6° gave a free acid which was slightly dextro-rotatory, α^{20}_{5791} = + 0.05° (about 0.15 g. in 20 cc. absolute ethyl alcohol, $\underline{l}$ = 2). The rotation of the salt increased and that of the free acid became zero when their solutions were heated. These changes however were only slight and certainly cannot be considered conclusive. It may be that the activity of the free acid is very small.

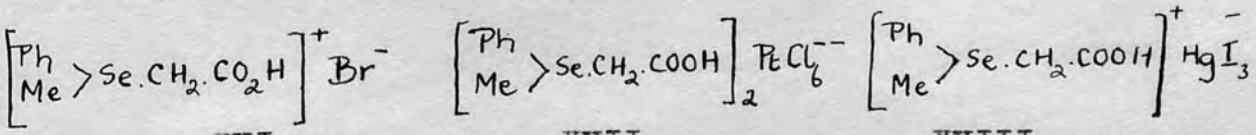
Stereochemistry of Selenium Compounds.

Since there has been no successful resolution of a selenoxide recorded and as phenoxselenine-10-oxide-2-carboxylic acid (XV) was easily obtained from phenoxselenine-2-carboxylic acid, an attempt was made to resolve it. If the hypothesis regarding the non-planar structure of phenoxselenines is valid, it would probably not function in the case of the selenoxides since the positive charge of the selenium would considerably reduce the diameter of that atom.



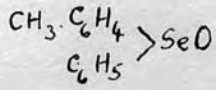
XV

The only optically active compounds recorded where the activity has been ascribed to an asymmetric selenium atom are those obtained by Pope and Neville (J., 1902, 1552) namely, phenyl methyl selenetine bromide, platinichloride and mercuriiodide (XVI, XVII, XVIII).

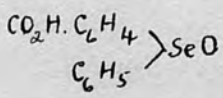


XVI XVII XVIII.

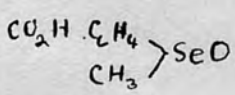
Gaythwaite, Kenyon and Phillips (J., 1928, 2280) attempted to resolve phenyl tolyl selenoxide (XIX), phenyl carboxyphenyl selenoxide (XX) and methyl carboxyphenyl selenoxide (XXI). These authors found that during the formation and crystal-



XIX

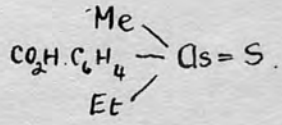


XX



XXI

lisation of the salts of these compounds the selenium tended to lose its oxygen. I obtained similar results in the case of XV. During the formation of the l-α-phenylethylamine, strychnine and brucine salts the selenoxide lost part of its oxygen. The nor-d-ψ-ephedrine salt was stable however, but its rotation remained unaltered during several recrystallisations. In view of the fact the Mills and Raper (J., 1925, 2479.) resolved an arsine sulphide (XXII) where attempts to resolve oxides have failed (Burrows and Turner, J., 1921, 426; Aeschlimann and McClelland, J., 1924, 2025; Aeschlimann, J., 1925, 811), an attempt was made to prepare the sulphide of phenoxselenine-2-carboxylic acid by passing hydrogen sulphide through a suspension of the corresponding oxide in water, in the same manner as Mills and Raper prepared XXII from the corfesponding arsine oxide. Only a mixture of the original oxide and phenoxselenine-2-carboxylic acid was obtained.



XXII.

The failure of the attempted resolutions of selenoxides is ascribed by Gaythwaite, Kenyon and Phillips (J., 1928, 2281.) to the fact that both the lone pairs of electrons in selenides contribute in some way to the formation of the bond between selenium and oxygen when an oxide is formed, and therefore the oxygen is symmetrically situated with regard to the other two radicles attached to the selenium atom. They support their reasoning by the difficulty encountered when attempts are made to oxidise the selenoxides to selenones; in fact, the only selenone described in the literature, diphenyl selenone, (Krafft and Vorster, Ber., 1893, 26, 2813.) has the properties of a peroxide. These theories, however, were rendered invalid when Sugden (J., 1929, 1058) measured the parachor of diphenyl selenoxide, Ph_2SeO, phenyl seleninic acid, $PhSeO_2H$, and selenium oxychloride. The association in the last two compounds was demonstrated by the determination of their molecular weights by the Beckmann Freezing Point method. Sugden found that if this was taken into account, all three compounds had parachors which approximated to the value calculated on the assumption of the presence of a semi-polar double bond. The probability is therefore that experimental conditions have not yet been discovered under which the resolution of selenoxides may be effected.

Experimental Discussion.

Resolution of α-Phenylethylamine.

The base was prepared by the reduction of acetophenone oxime with sodium and ethyl alcohol.

$PhCOCH_3 + NH_2OH \longrightarrow Ph.C(:NOH).CH_3 \longrightarrow Ph.CH(NH_2)CH_3$.

All the methods for resolving α-phenylethylamine consist of two separate experiments - one salt is used for obtaining one enantiomorph and another for isolating the other. Even then, in most cases, only one enantiomorph is obtained optically pure.

The first recorded experiments are those of Loven. (Journ. prakt. Chem., 72, 312). The pure l-base was obtained from the hydrogen d-tartrate and the pure d-base obtained from the impure substances in the mother liquors of the hydrogen tartrate by way of the hydrogen l-malate. Hunter and Kipping (J., 1903, 114.) evidently repeated Loven's method and did not find it altogether satisfactory. They obtained the optically pure l-base by way of the d-bromocamphorsulphonate but failed to purify the d-base. They found that the most sparingly soluble salt had the same molecular rotation as the free acid and inferred that the basic ion has no appreciable optical activity. They confirmed this by

preparing the salts of the dl- and l-base respectively with Reychler's d-camphorsulphonic acid and ascertained that the two substances differed very little in melting point and had practically the same specific rotation.

dl-α-Phenylethylamine-d-camphorsulphonate.

m.p. 141-144°, $[\alpha]_D$, +14.6° $[M]_D$, +51.5°.

l-α-Phenylethylamine-d-camphorsulphonate.

m.p. 149-150°, $[\alpha]_D$, + 14° $[M]_D$, + 50°.

They considered this the reason for the difficulties encountered during the resolution of the base.

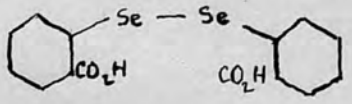
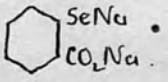
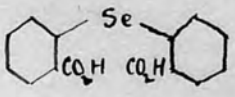
Betti (Gazetta, 1920, 50, 276) attempted a modification of Loven's method. He obtained the pure l-base and the pure d-base by way of the hydrogen tartrate. Aeschlimann (J., 1925, 815.) repeated this work and could not obtain the pure d-base as described by Betti. He therefore combined the impure d-base with malic acid and obtained a hydrogen l-malate, α_D, +0.05° (l=2) in 5% aqueous solution, whereas Loven's method after a greater number of crystallisations only gave a salt, α_D, -0.1°. Ingersoll (J. Amer. Chem. Soc., 1925, 1172.) resolved the base using l-malic and dl-malic acids. The rotation of the pure d-base hydrogen l-malate is given as α_D, -0.15° (4% aqueous solution in 2dm. tube). This author and Little (J. Amer. Chem. Soc., 1934, 2123.) obtained

the pure d-base by digesting its salt with d-66'dinitrodiphenic acid several times with acetone. On hydrolysis the least soluble salt gave the pure d-base. The l-base was obtained pure in a similar manner by way of l-66'-dinitrophenic acid. Ingold and Wilson (J., 1933, 1503.) obtained both enantiomorphs, first the laevo by Kipping and Hunter's method and then the dextro by way of the hydrogen malate. Later Reihlen and Flohr (Ber., 1936, 69, 328.) resolved the base successfully by Loven's method.

For optical experiments on compounds XI and XII an attempt to resolve the base according to Aeschlimann's directions (J., 1925, 815.) was made. The hydrogen tartrate was prepared by heating an alcoholic solution of the correct quantities of acid and base for 24 hours at 60° as directed. On crystallising the solunility of the salt was such that either large quantities of absolute alcohol had to be used or, if a little water was added to increase the solunility, hard crystals first appeared and then a semi-solid jelly-like hydrate was produced quite unsuitable for observing optical rotations. However, if on each crystallisation the mother liquor was decanted as soos as the gel appeared, the rotation decreased until a constant value of $[\alpha]_{5793}$,-13.6°, was obtained. This is not as low as the value recorded by Aeschlimann, ($[\alpha]_{5793}$, -13.0°), but repeated crystallisation failed to shift it. The free base also had a lower rotation

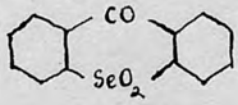
$[\alpha]_{5793}$, -42.73° in benzene than Aeschlimann's specimen ($[\alpha]_{5793}$, -49.6°) but when recombined with the tartaric acid and the salt crystallised, the specific rotation still remained constant. It was therefore considered pure. The mixture of d- and dl-base was then recovered from the residue and the acid salt of l-malic acid prepared. On crystallising anomalous results were obtained; for its rotation was +0.01°(4% aqueous solution, l = 2), yet the free base derived from it was only slightly dextrorotatory. Aeschlimann states that his malate, α_{5793}, +0.05°, (4% aqueous solution, l = 2), only gave impure base, but other authors (Loven, loc. cit., and Ingersoll, loc. cit.,) obtained optically pure base from a malate which had a small negative rotation; and in these laboratories a specimen was obtained which had an unalterable laevo rotation and yet yielded pure laevo base.

Preparation of Selenoxanthone-4-carboxylic Acid.

This compound was prepared by the very tedious process described by Lesser and Weiss (Ber.,1913, 46,2648; 1914, 47, 2515). The diselenide  was first prepared by the action of potassium polyselenides on the diazonium chloride obtained from anthranilic acid. This was then reduced by means of zinc and caustic soda to the sodium derivative of selenosalicylic acid,  . This compound is only obtained in alkaline solution; when solidified it reverts to the diselenide instead of forming selenosalicylic acid. In the presence of copper and under pressure at about 180-190° this sodium derivative reacted with o-iodobenzoic acid to give 22'-dicarboxydiphenyl selenide  . This process is very lengthy since only about 3 g. could be made at one time. Ring closure was effected by heating with sulphuric acid at 40° for six hours.

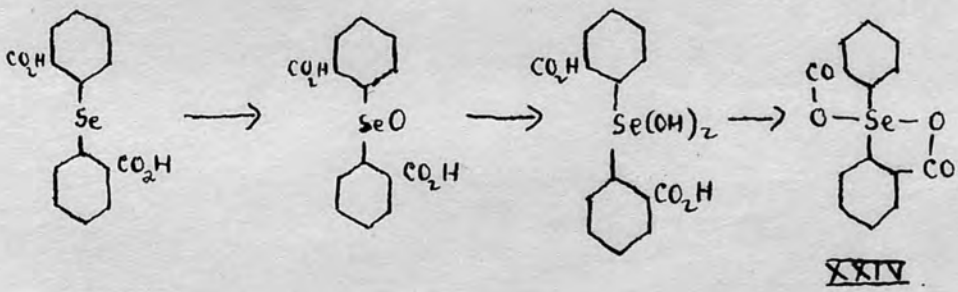
The action of sulphuric acid on selenium compounds has caused much difficulty both in the preparation of this compound and phenoxselenine-2-carboxylic acid. Lesser and Weiss first attempted to prepare XI by treating the diphenylselenide dicarboxylic acid with sulphuric acid at water bath temperature. They obtained two compounds, one of which was

alkali soluble and the other an entirely neutral substance which they considered to be the benzophenoneselenone (seleno-xanthone-10:10-dioxide) XXIII



XXIII

The proportion of this substance formed with the degree and length of time of heating. In their later paper these authors state that, instead of XXIII, this compund is the dilactone, XXIV, formed as the result of the oxidation of the selenium atom thus:-



XXIV

It therefore appears that sulphuric acid has an oxidising action at higher temperature, and at a lower temperature the expected ring closure occurs. I carried out the ring closure at 40° and the whole of the product was soluble in 1% cold caustic soda solution.

Resolution experiments were done on the l-α-phenylethylamine and strychnine salts of the selenoxanthone acid. The l-α-phenylethylamine salt was so insoluble that no con-

clusive results could be obtained. The strychnine salt showed changes in rotation but where negative values were obtained there was always some residue which was insoluble in chloroform. This was found to be the free acid indicating that some decomposition of the salt occurred. The fractional crystallisation was repeated to confirm this, and in the second experiment the negative rotations were less frequent, smaller in value and more or less fortuitous. Measurements of the rotations of different mixtures of acid and base indicated that the partial racemate has a positive rotation. I could obtain no evidence at all that this selenoxanthone existed in enantiomorphous forms. I attempted to reduce the compound to a xanthen using zinc amalgam and hydrochloric acid but was unsuccessful.

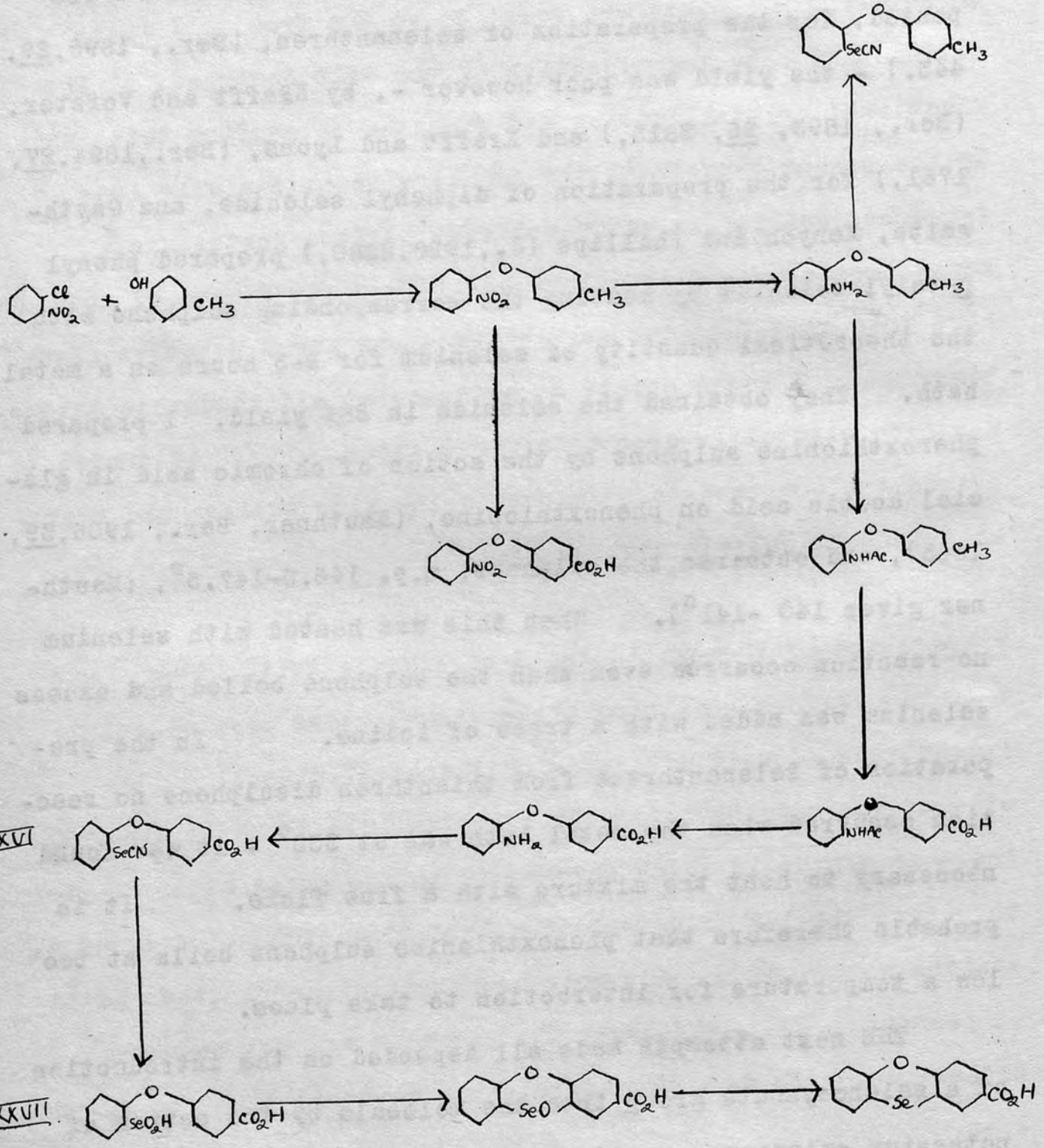
Preparation of Phenoxselenine-2-carboxylic Acid.

Various preliminary experiments were carried out to investigate methods of preparing phenoxselenines. An attempt was made to introduce selenium into diphenyl ether in the same manner in which sulphur is in the preparation of phenoxthionine, namely, using selenium, and aluminium chloride as a condensing agent. But only unchanged diphenyl ether could be recovered. Probably the reaction was not successful because selenium does not dissolve in diphenyl ether as sulphur does.

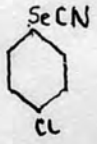
The next reaction tried was the replacement of the $-SO_2$ group in sulphones by selenium. This reaction was used successfully by Krafft and Kaschau, whose work I repeated, for the preparation of selenanthren, (Ber., 1895,29, 443.) - the yield was poor however -, by Krafft and Vorster, (Ber., 1893, 26, 2813,) and Krafft and Lyons, (Ber.,1894,27, 1761,) for the preparation of diphenyl selenide, and Gaythwaite, Kenyon and Phillips (J.,1928,2280,) prepared phenyl p-tolyl selenide by heating the corresponding sulphone with the theoretical quantity of selenium for 2-3 hours on a metal bath. They obtained the selenide in 28% yield. I prepared phenoxthionine sulphone by the action of chromic acid in glacial acetic acid on phenoxthionine, (Mauthner, Ber., 1906,39, 1345), and obtained the sulphone, m.p. 146.5-147.5°, (Mauthner gives 140 -141°). When this was heated with selenium no reaction occurred even when the sulphone boiled and excess selenium was added with a trace of iodine. In the preparation of selenanthrene from thianthren disulphone no reaction occurred when the metal bath was at 350° - it was found necessary to heat the mixture with a free flame. It is probable therefore that phenoxthionine sulphone boils at too low a temperature for interaction to take place.

THE next attempts made all depended on the introduction of a selenocyanate group into the molecule by the action of potassium selenocyanate on a diazonium salt. This has been

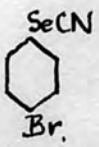
Diagram XXV.


SeCN
CH3
Cl
NO2
OH
CH3
NO2
CH3
NH2
CH3
NO2
CO2H
NHAc.
CH3
XXVI
SeCN
CO2H
NH2
CO2H
NHAc
CO2H
XXVII
SeO2H
CO2H
SeO
CO2H
Se
CO2H

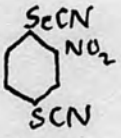
dine successfully by Bauer (Ber., 1913,46,92,) who obtained o- and p-nitrophenylselenocyanate, the former in 100% yield, Pyman (J., 1919, 166) who prepared m-nitrophenylselenocyanate, his product was only prepared in a crude state and none of its properties nor an analysis are given, Challenger and Peters, (J., 1928, 1366) who prepared the compounds 1 - 9 without any difficulty in 60-70% yields and Loevenich, Fremdling and Fohr (Ber., 1929, 62 2856) who obtained β -naphthylselenocyanate in 55% yield.



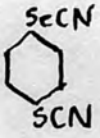
1.



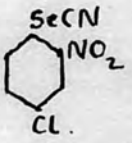
2.



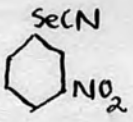
3.



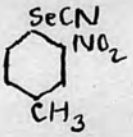
4.



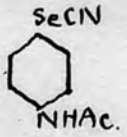
5.



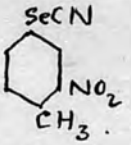
6.



7.



8.



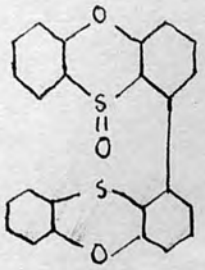
9.

In the preparation of phenoxselenine-2-carboxylic acid several routes were attempted before a suitable one was found. These are indicated in diagram XXV. In the first place 2-aminophenyl p-tolyl ether was prepared according to the method of Lesslie and Turner (J., 1934, 1170) and the base diazotised and treated with potassium selenocyanate, The product was a dark red oil which decomposed when distilled under reduced pressure, and attempts to oxidise the crude product were unsuccessful. It was then decided to put in the carboxyl

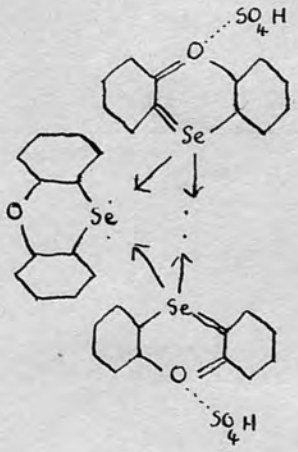
group before the selenocyanate group so that in introducing the latter, the product could be isolated by taking up in dilute alkali. o-Nitrophenyl p-tolyl ether was accordingly oxidised with chromic acid in glacial acetic acid(Cook and Hillyer, Amer. Chem. J., 24, 528). But since the product had to be esterified, reduced, hydrolysed, diazotised, oxidised and a ring closure effected before the final product was reached, it was decided the yield would be insufficient for the compound to be of any use. o-Aminophenyl p-tolyl ether was therefore acetylated and the acetyl derivative oxidised. The oxidation caused some difficulty since the theoretical quantity of permanganate only produced a 2% yield and it was discovered that the permanganate attacked the carboxylic acid produced. Several experiments had to be carried out before conditions were found yielding the maximum quantity of the required carboxylic acid with the minimum of labour. The hydrolysis of the acetyl carboxylic acid was found to proceed withput much difficulty using either concentrated sulphuric acid or 20% hydrochloric acid, and since the hydrochloridecwas required for diazotisation, the latter method was used. The amino-acid produced was obtained by Meyer and Krieger (Ber., 1922, 55, 1663.) by the reduction of the corresponding nitro-compound, but their product had a melting point 12° lower than mine and they give no analysis. The selenocyanate was obtained

mostly just in the crude state and oxidised with 33% nitric acid to the seleninic acid. This reaction has been used chiefly by Challenger and Peters (loc. cit.,) and Loevenich, Fremdling and Fohr (loc. cit.,) the former of whom found that different conditions had to be used according to the ease of nitration of the compounds dealt with. However, in the formation of 4'-carboxydiphenyl ether 2-seleninic acid, XXVII, possible nitration did not interfere although the yellow colour of the solutions seemed to indicate that it took place to a slight extent.

Several experiments also had to be performed before satisfactory conditions for the ring closure were discovered. This was done with concentrated sulphuric acid; if the mixture was heated on a water bath, a dark blue precipitate appeared and the phenoxselenine was only obtained in very poor yield. Lesser and Weiss, in the preparation of seleno-xanthone-4-carboxylic acid, had already discovered that sulphuric caused some oxidation, and Drew (J., 1928, 511,) found that it acts both as an oxidising and reducing agent towards phenoxthio-nine and phenoxselenine and their oxides. He states that the action of sulphuric acid on phenoxthionine produces such compounds as XXVIII, and he actually isolated, by the action of sulphuric acid on phenoxselenine red crystals of a compound to which he gave the formula XXIX.



XXVIII



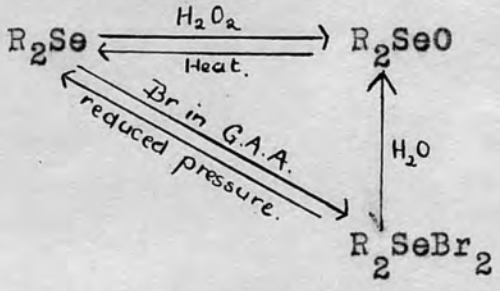
$H_2SO_4 + 2H_2O$

XXIX

In the case of XVII when the sulphuric acid mixture was heated to 100°, a small quantity of phenoxselenine-2-carboxylic acid was isplated without any reduction. But if the reaction was done in ice and the mixture heated to 40° for half an hour, the selenoxide was obtained only slightly contaminated with coloured products and was reduced very easily with potassium metabisulphite to the phenoxselenine. The constitution of XII was proved by decarboxylation by boiling in quinoline with a little copper. The compound obtained had a melting point of 87° either alone or mixed with a specimen of phenoxselenine given to me by Dr. H.D.K.Drew.

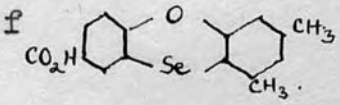
The pure phenoxselenine-10-oxide-2-carboxylic acid was obtained in the same way as Drew (loc. cit.,) prepared the parent substance phenoxselenine oxide, namely by the action of hydrogen peroxide on a solution of the phenoxselenine in

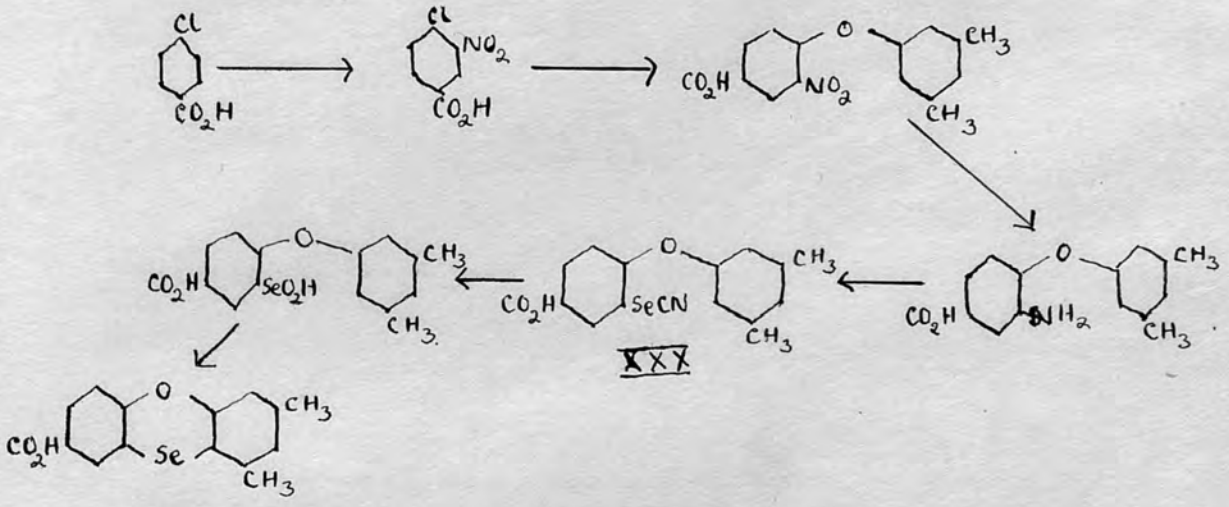
glacial acetic acid. This oxide differed from the parent substance in that it did not appear to form a water soluble hydroxide, but was similar in that it gave off its oxygen at the melting point to give the phenoxselenine, and also was produced when the dibromide, obtained by the action of bromine in acetic acid, was digested with water or caustic soda in the cold. An intensely yellow substance was obtained on attempting to crystallise the oxide from glacial acetic acid. This substance lost its colour on treatment with water and was probably the diacetate.



It thus appears that selenium passes from the divalent to the quadrivalent state very easily and the selenoxides are considerably less stable than the corresponding sulphoxides.

Since the resolution of phenoxselenine-2-carboxylic acid met with so little success attempts were made to nitrate this compound with the idea of accentuating any possible asymmetry by making the groups attached to the asymmetric centre heavier and tightening the nuclear-hetero atom bonds. Nitration under varying conditions however, could only be made to yield a mixture. Nitration is most likely to occur

in the unsubstituted ring but the oxygen and selenium atoms which would have similar orienting effects, being ortho to each other, would act against each other and therefore produce a mixture. To obtain the same effect, the synthesis of  was tried by a method illustrated in the following scheme:-



The selenocyanate XXX was very much more crystalline and more stable than 4'-carboxydiphenyl ether 2-selenocyanate XXVI but in spite of repeated attempts, it could not be oxidised to the corresponding seleninic acid. Nitric acid either had no action or nitration occurred. The action of excess bromine on the selenocyanate followed by hydrolysis was tried, but without success.

$$RSeCN \longrightarrow RSeBr_3 \longrightarrow RSeO_2H.$$

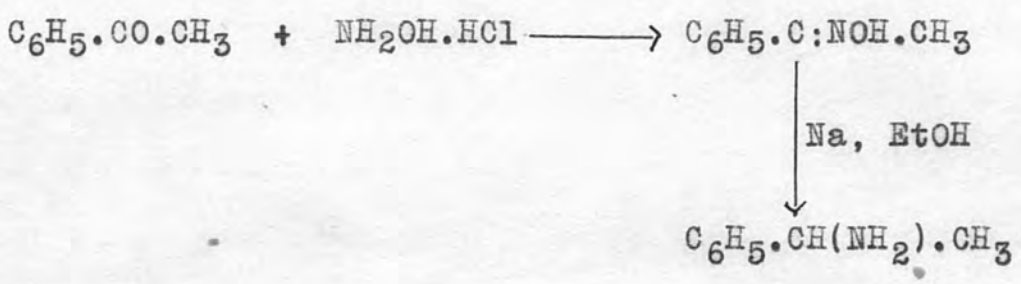
Challenger and Peters (loc. cit.,) investigated the

action of nitric acid on various substituted selenocyanates and the results were as follows:-

Group in p-position to -SeCN group.	Reaction.	
H	Nitration	
Methyl.	Nitration	
NHAc.	Nitration Oxidation	about 50% each.
Halogens	Oxidation	
Thiocyanate	Oxidation.	

It appears probable therefore that substituents which increase the reactivity of the benzene nucleus cause nitration while deactivating groups cause oxidation. In compound XXX therefore it is probable that nitration first ~~appears~~ occurs in the ring containing the two methyl groups. If oxidation does then occur probably a mixture of substances is produced.

SYNTHESIS and RESOLUTION of α -PHENYLETHYLAMINE.



Preparation of Acetophenoneoxime.

174 g. (1.25 mol.) hydroxylamine hydrochloride were dissolved in the least possible quantity of water and added to a slolution of 200 g. caustic soda (2.5 mols.) in two litres of water, the solution being kept cool. 240 g. (1 mol.) acetophenone were added and the mixture shaken until the latter had completely disappeared (20 minutes - ½ hour). The oxime then began to separate out and its precipitation was completed by passing carbon dioxide through the solution. It was filtered off, washed with water, air dried and used without further purification for the reduction.

Preparation of α -Phenylethylamine. Cumming, Hopper and Wheeler, p. 366.

All the aocohol used in this preparation was dried over magnesium turnings. 100 cc. together with 50 g. aceto-

phenoneoxime were placed in a litre flask with a side arm down which sodium could be added. The mixture was boiled under reflux on a water bath. 40-50 g. Sodium were weighed out under benzene and added bit by bit to the oxime solution. When the reaction became sluggish or the solution became too thick with sodium ethoxide another 100 c.c. absolute alcohol were added. The alcohol was kept boiling as long as possible, but towards the end of the reaction it was so saturated with sodium ethoxide that this was impossible on a water bath. The reaction was allowed to continue until the solution did not reduce Fehling's solution. When it was finished the mixture was cooled and 200 c.c. water added to decompose the sodium ethoxide. A thermometer was then placed in the side arm and the mixture distilled on a sand tray until the temperature rose to 83-84°. A further 200 c.c. water were added and the distillation continued until the temperature rose to 96°. In the flask there were then two layers - an upper consisting of the base containing some alcohol and a lower of strong caustic soda. The contents of the flask were cooled and placed in a separating funnel. Some base had passed over into the distillate which was therefore acidified with concentrated hydrchloric acid and evaporated to a small bulk on a water bath and then added to the mixture in the separating funnel where the free base was liberated by the

strong caustic soda present. The lower layer of caustic soda was separated off and washed two or three times with ether. The ethereal solution of the base was dried over potassium carbonate and distilled, ether, alcohol and finally the base coming over. The latter was collected in a flask fitted with a tube containing soda-lime owing to its avidity for carbon dioxide. Carbond dioxide was passed through the ether distillate and by removing the ether under reduced pressure a small quantity of α-phenylethylamine carbamate was obtained.

The yield varied from 31 to 41 g.. From 270 g. acetophenoneoxime 188 g. of the base were obtained (78% yield) and a further 20 g. base carbamate were extracted from the washings, bringing the yield up to 86%.

Resolution of α -Phenylethylamine. Aeschlimann

(J. 1925, 815)

(a) Preparation of α -phenylethylamine hydrogen tartrate. 233 g. (1 mol.) tartaric acid were dissolved in one litre of absolute alcohol at 60°, in a 5-litre flask fitted with a condenser having a stirrer passing down it. 188 g. (1 mol.) α -phenylethylamine in 1,820 cc. absolute alcohol at 60° were added. A salt was immediately precipitated. The mixture was stirred at 60° for 23 hours. It was then filtered while still hot and the bulk of the theoretical quantity of the acid salt thus obtained insteadof the practically pure l-base d-tartrate, as described by Aeschlimann. On crystallisation from water a solid gel was obtained. From 3 litres of absolute alcohol, to which 200 cc. water were added, well defined prisms first appeared and then the gel-like hydrate. On recrystallisation from this same aqueous alcoholic solvent and decanting of the mother liquor as soon as the hydrate began to appear the rotation of the salt decreased as shown in the following table:-

Crystallisation and Specific Rotation of α -Phenylethylamine Hydrogen Tartrate.

	c	α^{20}_{5791}	$[\alpha]^{20}_{5791}$	α^{20}_{5461}	$[\alpha]^{20}_{5461}$	ε
Racemate crystallised from water.	2.7140	+0.88°	+16.2°	+0.99°	+18.2°	1.13
1st crystallisation; allowed to go to completion.	3.9520	+1.26°	+16.0°	+1.41°	+17.8°	1.11
2nd crystallisation; M.L.decanted when hydrate appeared.	3.8540	+1.09°	+14.2°	+1.25°	+16.2°	1.15
3rd crystallisation.	3.9820	+1.07°	+13.4°	+1.19°	+14.9°	1.12
4th crystallisation.	4.0690	+1.11°	+13.6°	+1.265°	+15.5°	1.14

All rotations measured in water, l = 2 dm.

Thus a constant value for the specific rotation of the salt was obtained which, however, was not quite in accordance with Aeschlimann's value ($[\alpha]^{20}_{5791}$, + 13.0°). 70 g. of the salt were therefore decomposed with 50% caustic potash and the base obtained (30 g.) had the following rotation in benzene solution: α^{20}_{5791} -3.65°, i.e. $[\alpha]^{20}_{5791}$, - 42.7°. α^{20}_{5461}, - 4.13°, i.e. $[\alpha]^{20}_{5461}$ - 48.35°. (c = 4.2705, l = 2 dm.). This also was not as low as Aeschlimann's value, but on recombining the base with tartaric acid and allowing 54 g. of the salt to

crystallise from a possible 68 g. the specific rotation of the salt remained constant - α^{20}_{5791}, + 1.08°, i.e. $[\alpha]^{20}_{5791}$, + 13.5°, α^{20}_{5461}, +1.20°, i.e. $[\alpha]^{20}_{5461}$, +15.00°. (c = 3.9890, l = 2 dm.)

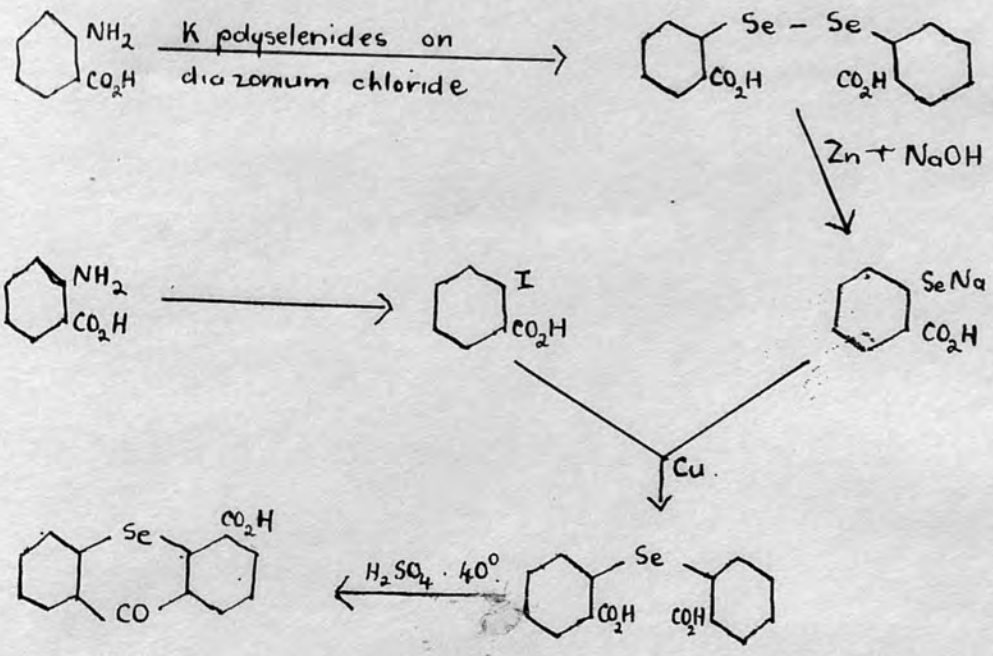
(b) Preparation of d- Phenylethylamine Hydrogen l-Malate.

The impure tartrate was decomposed and the free base converted into the sulphate and enough potassium hydrogen malate added for partial double decomposition. The following quantities were used.

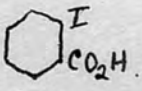
		M.W.	Used.	
d-Phenylethylamine		121 g.	136 g.	400 cc. H_2O
Sulphuric Acid		98 g.	55.1g. 100%	400 cc. H_2O
l-Malic Acid.		134 g.	93 g.	500 cc. H_2O
Caustic Potash.	taken as	75 g.	52 g.	500 cc. H_2O

The solution was inoculated with a crystal of pure d- α -phenylethylamine hydrogen l-malate. 50 g. of the salt were obtained, the rotation, α^{20}_{5791}, of which was + 0.01° in a 5% aqueous solution. This remained constant on crystallisation. The free base obtained from it, however, was only slightly dextrorotatory despite the fact that the rotation of the salt was the same as that obtained by Aeschlimann.

SYNTHESIS of SELENOXANTHONE-4-CARBOXYLIC ACID.



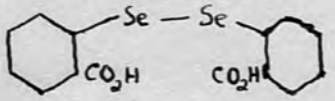
Preparation of o-Iodobenzoic Acid.



The sulphate of anthranilic acid was prepared by heating 28 g. (1 mol.) of anthranilic acid with 25 cc. concentrated sulphuric acid diluted with 200 cc. water until the former had completely dissolved. The solution was stirred and cooled in a freezing mixture and then diazotised in the usual way with 15 g. (1 mol.) sodium nitrite dissolved in 20 cc. water. The filtered diazo solution was then added to a solution of 50 g. potassium iodide (1½ mols.) in 50 cc. dilute sulphuric acid to which a little water was added if the potassium iodide would not dissolve. After allowing the mixture to stand for half an hour

it was slowly heated to the boiling point to complete the evolution of nitrogen. The iodobenzoic acid precipitated was filtered off and recrystallised ~~in~~ from hot water. Yield 30 g.

Preparation of Di-(2-carboxyphenyl-) diselenide. (1) Lesser and Weiss, Ber., 1912, 45, 1835.



Iron selenide was prepared by quickly heating iron filings and precipitated red selenium, thoroughly mixed together in equimolecular proportions, to a dull red heat. Hydrogenselenide, prepared by the action of 60 cc. 24% hydrochloric acid on 24 g. of the iron selenide, after being washed with water, was passed into a concentrated solution of 8 g. of caustic potash and 24 g. of potassium carbonate contained in a two-litre round bottom flask fitted with a dropping funnel, and from which air had already been driven out with nitrogen, a slow stream of which was passed through the apparatus during the whole of the experiment. After the evolution of hydrogen selenide had ceased, the diazonium chloride solution obtained from diazotising 13.7 g. anthranilic acid was slowly added through the dropping funnel, the mixture being well shaken all the time. After allowing to stand for about half an hour the solution was heated

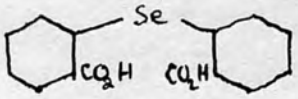
on a water bath until the evolution of nitrogen had ceased, and after filtering from precipitated selenium it was acidified while still hot with dilute hydrochloric acid. Only an acid with an indefinite melting point was obtained, and it was considered that the preparation of iron selenide had not been successful, since a large quanity of free selenium remained in the flask in which the former had been prepared.

(2) Method of A.Schoeller, Ber., 52, 1919, 1518.

16 g. of black powdered selenium and 24 g. powdered caustic potash were ground together and heated to 140° in a metal bath. The melt obtained was poured into 200-300 cc. ice. 13.7 g. anthranilic acid were diazotised in the usual way and the filtered diazonium chloride solution added slowly with shaking to the potassium polyselenides cooled in ice. There was an immediate evolution of nitrogen and the orange coloured solution was boiled to bring this to completion and to coagulate the free selenium present. After the latter had been filtered off the solution was acidified. The precipitated acids, which were either colourless or pink according to the quantity of free selenium present, were crystallised from glacial acetic acid when the diselenide first came out and any monoselenide present remained in solution.

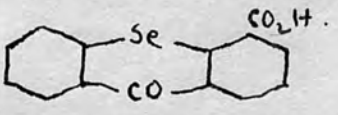
The acid was obtained in colourless crystals, m.p. 296-297° (decomp.). Yield 50%. From the mother liquor only impure monoselenide was obtained and it was not considered worth isolating this.

Preparation of Di-(2-carboxyphenyl-) selenide. Lesser, Ber., 1914, 47, 2514.



16 g. di-(2-carboxyphenyl-) diselenide and 12 g. caustic soda were dissolved in 150-200 cc. water and boiled. 16 g. zinc powder was added slowly to the boiling solution over a period of one hour. The solution was filtered directly into a concentrated solution of 20 g. o-iodobenzoic acid containing the equivalent amount of caustic soda (2-3 g.). The solution was then about 100 cc. on bulk. It was heated in four sealed carius tubes containing a mixture of glass wool and copper for 5-6 hours at 180-190°. The contents of the tubes were filtered, boiled and acidified with hydrochloric acid. The acid obtained was crystallised from glacial acetic acid; it came down in pale yellow crystals, m.p. 233°. Yield 17 g. i.e. 65%.

Preparation of Selenoxanthone-4-carboxylic Acid. Lesser, Ber., 1914, 47, 2515.



10 g. di-(2-carboxyphenyl-) selenide were added slowly to

100 g. concentrated sulphuric acid cooled to 0°. The brown liquid obtained was heated at 40° in a thermostat for about five hours with occasional stirring. The solution was poured into 1½ litres ice-cold water. The yellow precipitate obtained was filtered off and dissolved in a very slight excess cold dilute caustic soda (less than 1%). The solution was boiled, filtered and the acid precipitated with dilute hydrochloric acid. After crystallising from much glacial acetic acid, 6 g. were obtained as a yellow microcrystalline powder. This acid is practically insoluble in most organic solvents and was only crystallised with difficulty.

Found: C, 55.25%, H, 2.8%, $C_{14}H_8O_3Se$ requires C, 55.4%, H, 2.7%.

Investigation of the Salt-forming Properties of Seleno-xanthone-4-carboxylic Acid.

1) With Brucine. The salt was prepared by dissolving the base in a solvent, adding the acid and boiling until the latter dissolved. When alcohol was used, a gum was produced, which solidified on cooling to 0°, but became viscous again on warming up to room temperature. Crystals were obtained from amyl alcohol, but the solvent was considered too high boiling to use for resolution experiments. The salt would not come down from acetone or chloroform. Double decomposition in aqueous solution between the sodium salt of the acid and the sulphate of the base afforded only non-crystallisable solids.

2) With nor-d-ψ-Ephedrine. A slight excess of the base (1.5 g.) was dissolved in water and the acid (2.6 g.) added. The mixture had to be considerably diluted (to 200 cc.) and boiled for some time before all the acid would dissolve. On cooling rosettes of yellow needles containing three molecules of water of crystallisation separated.

3) With l-α-Phenylethylamine. 42.4 g. of the acid were

added to 3 litres of boiling alcohol containing 16.9 g. of the base. After boiling for a long time (about two hours) all the acid went into solution. On filtering and cooling, 55 g. of the salt came out in beautiful yellow prisms. The solubility of this salt was found to be very small. It was completely insoluble in benzene, chloroform, ethyl acetate and acetonitrile. In water it was very sparingly soluble and came down in fine needles. In ethyl alcohol, dioxan and epichlorhydrin it was fairly soluble in the hot, but almost completely insoluble in the cold. In aqueous alcohol and acetone it was only slightly more soluble than in alcohol alone. It was, however, soluble in ethylene glycol, and an attempt was made to see if there was any change in the rotation of the salt when it was crystallised from this solvent. The salt came down somewhat dark coloured, and because of this, and also to remove the solvent, each crop had to be crystallised from alcohol before any rotations could be observed.

The following table indicates the manner of crystallisation and the observed rotations :-

Crystallisation of the l-α-Phenylethylamine Salt of Seleno-xanthone-4-carboxylic Acid.

10 g. salt
(α_{5791} = -0.08°, c = 1.4640)

Crystallised from $(CH_2OH)_2$ and then from EtOH.

5.g. salt
(α_{5791} = -0.08°, c = 1.4500)

Crystallised twice from $(CH_2OH)_2$ and EtOH.

2.1 g. salt
(α_{5791} = -0.07°, c = 1.5310

M.L.

salt.

Crystallised from $(CH_2OH)_2$ and then from EtOH.

2.9 g. salt
(α_{5791} = -0.06°, c = 1.5080)

All the rotations were observed in ethylene glycol, l = 2. It was concluded that, if experimental errors were neglected, there would be no change in the rotation of the salt.

4) With Strychnine. This salt was prepared by adding the theoretical quantity of the acid to a boiling alcoholic solution of the base. As with all other salts the acid took some time to go into solution. The salt was quite soluble in the hot, but only slightly in the cold, i.e. the difference in solubility was too great to do fractional crystallisation experiments. These were therefore done

from acetone. The salt had m.p. 240-243°. Resolution experiments are described on the following pages.

Estimation of Selenium in the Strychnine Salt of Selenoxanthone-4-carboxylic Acid. Method of Bradt and Lyons, (J. Am. Chem. Soc., 1926, 2645). About 0.3 g. of the salt with 2 cc. nitric acid, d 1.5, were heated in a Carius tube to 250°. The contents of the tube were washed into a 150 cc. beaker with the least amount of water. The solution was then made alkaline to litmus with 50% caustic potash, and nitric acid added until it was just acid. Zinc oxide was added in slight excess, i.e. until no more would dissolve and the litmus paper was a neutral tint. The solution was then titrated with standard $\frac{N}{20}$ silver nitrate solution. Potassium Chromate was used as an indicator, and according to Bradt and Lyons, should be used externally, since if the potassium chromate was added at the beginning of the titration the red colour of the silver chromate was masked owing to adsorption on the precipitated silver selenite. The following procedure was however found more satisfactory. Towards the end of the titration after it had been well stirred, the precipitate was allowed to settle and a drop of potassium chromate was added to the supernatant liquid. At the end point the red colour of silver chromate appeared, all the selenious acid

having been converted to silver selenite according to the following equation:-

$$H_2SeO_3 + 2AgNO_3 + ZnO = Ag_2SeO_3 + Zn(NO_3)_2 + H_2O$$

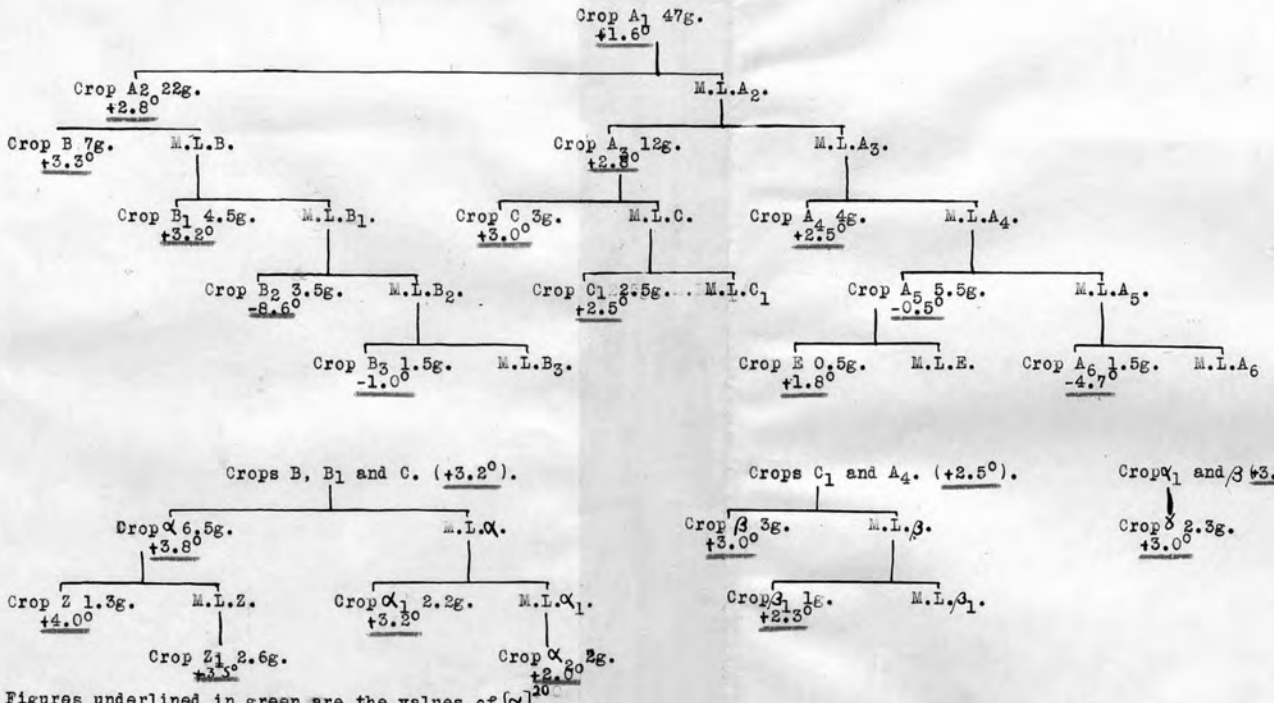
As a control about the same quantity of caustic potash and zinc oxide as was used in the above was dissolved in the same volume of water, neutralised with nitric acid and titrated with silver nitrate to see if there was sufficient halogen present to influence the end point of the above. This was not the case.

Found: Se, 12.1%, 12.25%, the strychnine salt of $C_{14}H_8O_3Se$ requires Se, 12.4%.

Strychnine Salt of Selenoxanthone-4-carboxylic Acid. Specific Rotation of the various crops obtained during its Fractional Crystallisation.

All the crystallisations were done from acetone and the crops had solvent of crystallisation attached; before their specific rotation was observed therefore, they were heated on a water bath at 100° until a constant weight was attained, and then left in an evacuated desiccator for half an hour. The rotations were measured in A.R. chloroform, $\underline{l}$ = 2 dm. The solutions were deep yellow. The readings were very small, the green mercury line being easiest to read, and as that of the yellow line was the same or merely 0.01° different, only the former is given.

FRACTIONAL CRYSTALLISATION of the STRYCHNINE SALT of SELENOXANTHONE-4-CARBOXYLIC ACID.



Figures underlined in green are the values of $[\alpha]_{5461}^{20}$

All rotations, except that of α_1, were observed using a 2 dm. tube. For α_1 a 1 dm. tube was used since the solution was very dark.

Strychnine salt of Selenoxanthone-4-carboxylic Acid. Specific Rotation of the various crops obtained during its Fractional Crystallisation. (contd.)

Crop.	c	α^{20}_{5461}	$[\alpha]^{20}_{5461}$
A_1	1.9160	+0.06°	+1.6°
A_2	1.9460	+0.11°	+2.8°
A_3	1.9540	+0.11°	+2.8°
B	1.9690	+0.13°	+3.3°
B_1	1.9655	+0.125°	+3.2°
C	1.9725	+0.12°	+3.0°
A_4	1.9990	+0.10°	+2.5°
B_2	1.9805	-0.34°	-8.6°
C_1	2.0290	+0.10°	+2.5°
B_3	1.9596	-0.04°	-1.0°
E	1.9355	+0.07°	+1.8°
A_6	1.9990	-0.19°	-4.7°
α	1.9780	+0.15°	+3.8°
β	1.9800	+0.12°	+3.0°
Z.	1.9950	+0.16°	+4.0°
α_1	1.9885	+0.125°	+3.2°
β_1	1.9940	+0.09°	+2.3°
Z_1	2.0110	+0.14°	+3.5°
α_2	1.9815	+0.04°	+2.0°
A_5	1.9820	-0.02°	-0.5°

Racemisation Experiment. 0.4 g. Crop Z_1 in 20 cc. chloroform were heated in a sealed tube at 100° for four hours, after its rotation having been observed. The latter was unchanged after heating (±0.14°).

Decomposition of Crop A_6, ($[\alpha]^{20}_{5461}$, -4.7°) and Crop Z ($[\alpha]^{20}_{5461}$, +4.0°

The melting point of Crop A_6 was 223-227°, that of Crop Z was 237-240°. They were decomposed by dissolving in chloroform and shaking with dilute ammonia. The ammonia solution was extracted twice with chloroform and once with ether. In both cases the ammonium salt was optically inactive and therefore the lower melting point of Crop A_6 was probably due to the presence of strychnine.

Rotation of the Partial Racemate in the presence of excess Acid or Base

(a) Acid : Base :: 1 ; 1.

Strychnine used, 0.1992 g.; Acid used, 0.1815 g.

Theoretical amount of acid required for 0.1992 g. of the base is 0.1807 g.

The base was dissolved in 20 cc. chloroform and the acid added. The mixture was well shaken and left overnight; there was still a small quantity of acid left undissolved.

α_{5461} = -0.03° ($\underline{l}$ = 2). ∴ $[\alpha]^{20}_{5461}$ of the salt, the calculation being based on the amount of strychnine present, = -0.8°.

(b) Acid : Base :: 2 : 1.

Strychnine used, 0.2048 g.; Acid used, 0.3748 g.

Theoretical amount of acid required for 0.2048 g. strychnine is 0.1858 g.

The base was dissolved in 20 cc. chloroform and the acid added. The mixture was well shaken until no more acid would dissolve.

$\alpha_{5461} = +0.05^{\circ}$, ($\underline{l} = 2$). $\therefore [\alpha]^{20}_{5461}$ of the salt, the calculation being based on the amount of strychnine present, $= \underline{+1.3^{\circ}}$.

(c) Acid : Base :: 1 : 2.

Strychnine used, 0.2536 g.; Acid used, 0.1162 g.

The base was dissolved in 20 cc. chloroform, the acid added and the mixture shaken until all the latter had dissolved.

$\alpha_{5461} = -1.95^{\circ}$, ($\underline{l} = 2$).

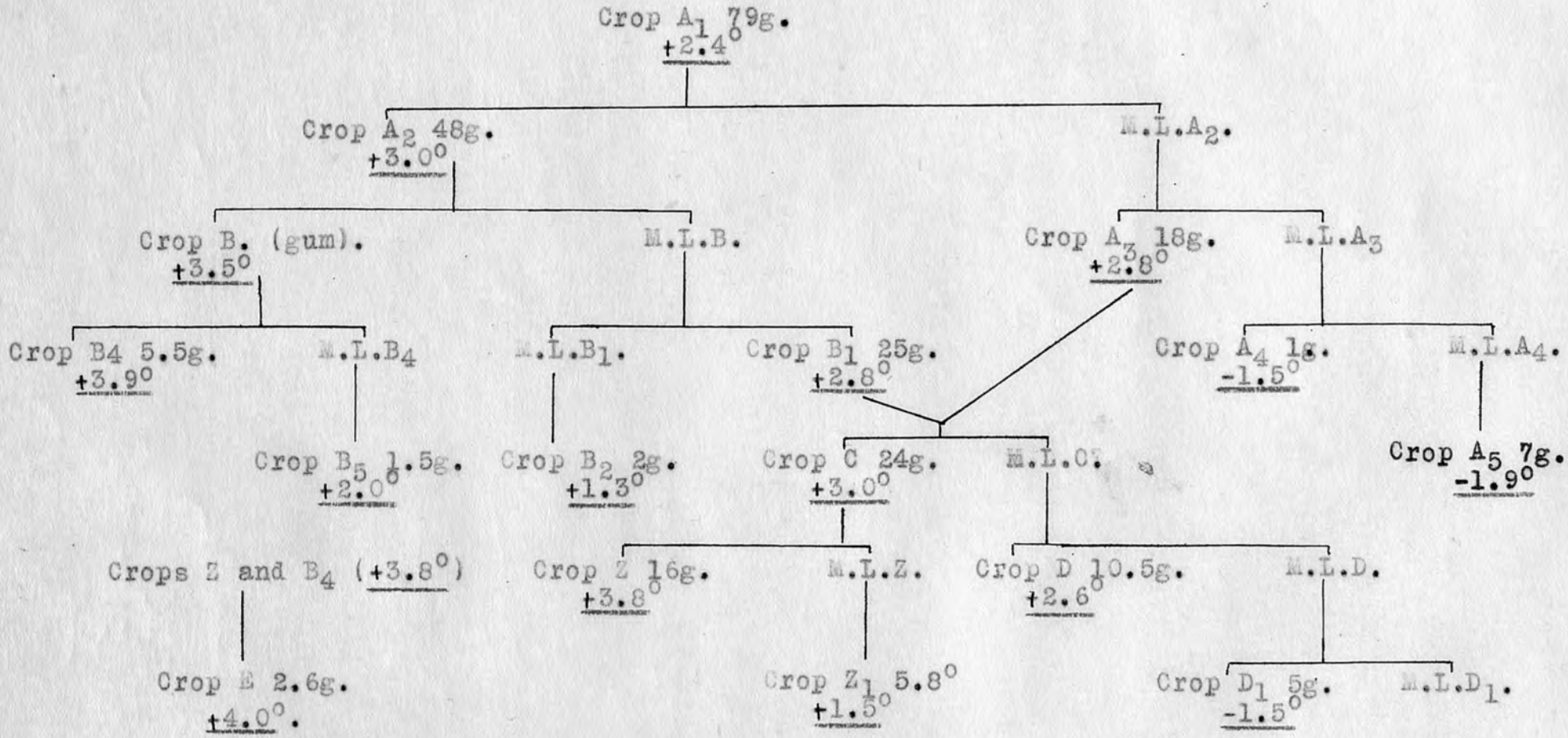
The acid present would require 0.1282 g. strychnine to form a salt. $\therefore$ there would be 0.1254 g. free strychnine present.

The rotation of strychnine in chloroform was then observed; 0.2996 g. in 20 cc. chloroform had α_{5461}, -5.07° ($\underline{l} = 2$).

$\therefore$ 0.1254 g. would have α_{5461}, $= \frac{5.07 \times 0.1254}{0.2996} = -2.12^{\circ}$.

$\therefore$ Assuming that the specific rotation of strychnine does not vary with concentration, and that the rotations of the salt and strychnine in the same solution are additive, the rotation of the salt would be $+0.17^{\circ}$. i.e. $[\alpha]^{20}_{5461}$ of the partial racemate is $+6.9^{\circ}$.

FRACTIONAL CRYSTALLISATION of the STRYCHNINE SALT of SELENOXANTHONE-4-CARBOXYLIC ACID.



The figures underlined in green are the values of $[\alpha]^{20}_{5461}$

The free acids obtained from the decomposition of crops E and D_1 were optically inactive.

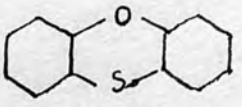
Strychnine Salt of Selenoxanthone-4-carboxylic Acid. Specific Rotation of the various crops obtained during its Fractional Crystallisation.

Crystallisation was from A.R. acetone. Solvent of crystallisation was removed by drying at 100° until a constant weight was attained and then in an evacuated desiccator for ½hr. Rotations were observed in A.R. Chloroform, l = 2 dm. Only that value for the mercury green line is given below, this being the easiest to read through the deep yellow solutions of the salt.

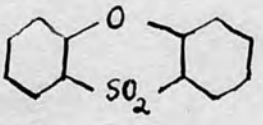
Crop.	c	α^{20}_{5461}	$[\alpha]^{20}_{5461}$	Crop.	c	α^{20}_{5461}	$[\alpha]^{20}_{5461}$
A_1	1.9990	+0.095°	+2.4°	B_5	2.0000	+0.08°	+2.0°
A_2	1.9720	+0.12°	+3.0°	B_2	1.9920	+0.05°	+1.3°
B	1.9935	+0.14°	+3.5°	C	1.9820	+0.12°	+3.0°
A_3	1.9890	+0.11°	+2.8°	Z	1.9980	+0.15°	+3.8°
B4	1.9650	+0.155°	+3.9°	Z_1	1.9870	+0.06°	+1.5°
B_1	1.9960	+0.11°	+2.8°	D	1.9855	+0.105°	+2.6°
A_4	1.9640	-0.06°	-1.5°	D_1	1.9710	-0.06°	-1.5°
A_5	1.8910	+0.07°	+1.9°	E	1.9800	+0.16°	+4.0°.

Attempted reduction of Selenoxanthone-4-carboxylic Acid.

20 g. of zinc were covered with about 100 cc. bench mercuric chloride and left over-night. The liquid was decanted off and the zinc amalgam washed with distilled water. It was then added to 1 g. of selenoxanthone-4-carboxylic acid suspended in 150 cc. hydrochloric acid. The mixture was boiled for several hours but the acid remained undissolved and retained its vivid yellow colour. It also had a very high melting point and was therefore presumed to be unchanged selenoxanthone-4-carboxylic acid.

Preparation of Phenoxthionine. 

170 g. (1 mol.) were heated to 70° and 32 g. (1 mol.) sulphur were added. 67 g. (.5 mol.) of aluminium chloride were added gradually over twenty minutes, the temperature being kept at 70°. The mixture was mechanically stirred and the temperature raised during half an hour to 100° and maintained there for 3½ hours. The mixture was then decomposed with dilute hydrochloric acid and the oil extracted with chloroform. The chloroform solution was vacuum distilled when 70 g. of diphenyl ether were recovered unchanged together with 67 g. of an oil, boiling point 177-180°/15mm. This crystallised on cooling and from it and the redistilled intermediate fraction 64 g. pure phenoxthionine were obtained as a fine white crystalline solid.

Preparation of Phenoxthionine Sulphone. 

6.5 g. of phenoxthionine were dissolved in the least possible quantity of glacial acetic acid. 20 g. of chromic acid were dissolved in 120 cc. of the same solvent and added gradually to the phenoxthionine solution. The mixture was then boiled for half an hour under reflux and the resulting dark green liquid poured into 750 cc. water. The white precipitate obtained was recrystallised from alcohol when 5.6 g.

long blunt ended prisms were obtained, m.p. 146.5-147.5°. This was the required phenoxthionine sulphone.

Action of Selenium on Phenoxthionine Sulphone.

The sulphone was mixed with the theoretical quantity of black powdered selenium required for the reaction $R_2SO_2 + Se = R_2Se + SO_2$. The mixture was heated gently to 150° in a Claisen flask and then to its boiling point. No reaction appeared to occur even when excess selenium was added or a trace of iodine. Phenoxthionine sulphone was recovered m.p. 145-147°.

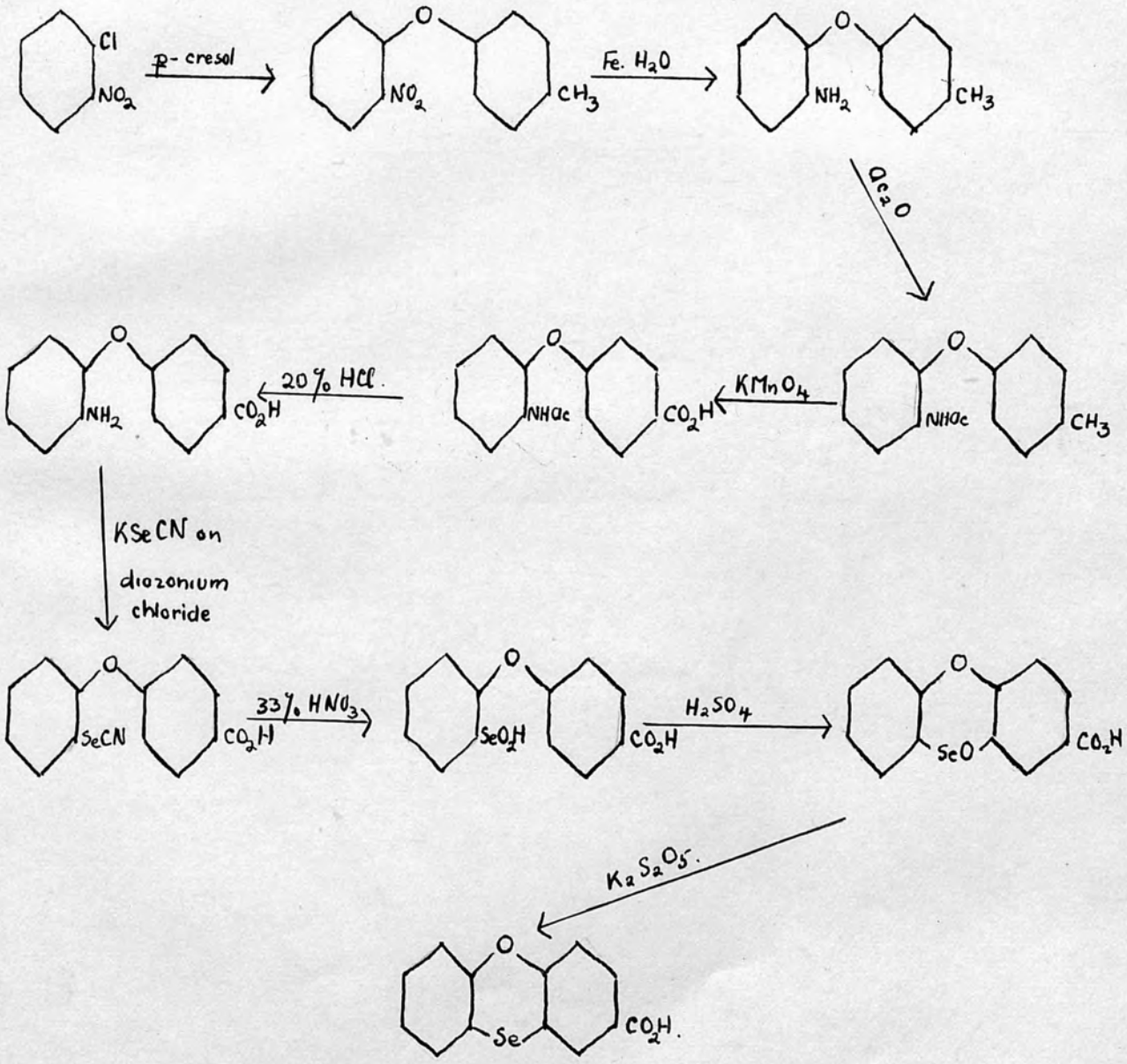
Action of Selenium on Diphenyl Ether.

79 g. (1 mol.) of selenium was added to 170 g. (1 mol.) diphenyl ether at 160°. The temperature was lowered to 120° and 67 g. (½ mol.) aluminium chloride were added gradually over twenty minutes. The temperature remained at 120° for one hour and was then raised to 170-180°. It was maintained there for three hours the mixture being mechanically stirred all the time. It was decomposed with ice and the dark crystalline solid obtained filtered off and extracted with chloroform. After removal od the free selenium, of which there was a considerable quantity, the chloroform solution was vacuum distilled and was found to contain only unchanged diphenyl ether.

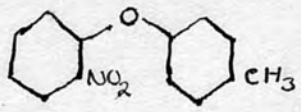
SYNTHESIS

of

PHENOXSELENINE-2-CARBOXYLIC ACID.



Preparation of o-Nitrophenyl p-Tolyl Ether.

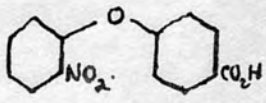


(R.V. Henley, J.C.S., 1930, 1222)

		Used
o-Nitrochlorbenzene	1 mol. 157.5 g.	315 g.
p-Cresol	2 mol. 216 g.	432 g.
KOH.	1.33 mol. 75 g.	150 g.

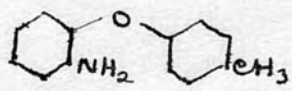
The caustic potash with six drops of water was melted in a three-litre flask. It was cooled just to the point of fusion and the cresol added. The mixture was shaken and heated until a clear liquid was obtained, and then the nitrochlorbenzene added. The flask was then fitted with a long air condenser and the mixture heated for two hours on a metal bath at 200°. After cooling slightly about five times as much water was added and about 150 cc. 25% caustic soda solution. On cooling and shaking the ether solidified in dark brown granular crystals. This was crystallised from alcohol and the ether was obtained in pale yellow crystals in a 75% yield.

Preparation of 2-Nitro 4'-Carboxy Diphenyl Ether.

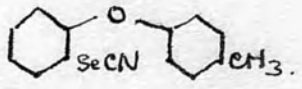


50 g. of chromic acid was added gradually over twenty minutes to 30 g. 2-nitro 4'-methyl diphenyl ether dissolved in 600 cc. glacial acetic acid. The mixture was boiled for a further twenty minutes and the dark green solution obtained poured into 1 litre of water. A sticky solid was precipitated. On attempting to recrystallise from water as described in Beilstein II, p. 906, it was found to require a very large quantity of solvent. It was therefore purified by dissolving it in caustic soda and reprecipitating with hydrochloric acid. 7.5 g. were obtained, m.p. 182°. Yield 22%.

Preparation of o-Aminophenyl p-Tolyl Ether.



150 g. iron filings were well mixed with 150 g. o-nitrophenyl p-tolyl ether and heated on a water bath in a five-litre beaker. About 3 cc. dilute acetic acid and some boiling water were added and after a few minutes the reaction began. It was often so violent that the mixture frothed to the top of the beaker. When the reaction had subsided more boiling water was added and the addition repeated until reaction ceased. The mixture was neutralised with a little ammonia and the base extracted with hot alcohol. After filtering off the iron the alcoholic solution was reduced in bulk to about 600 cc. and acidified with a large excess of concentrated hydrochloric acid. The base was thus precipitated as the hydrochloride and after being dried on a water bath was used straight away for the next synthesis. Yield, 85 per cent.

o-(p-Tolyloxy-)phenylselenocyanate. 

For both this compound and the cofresponding carboxylic acid the potassium selenocyanate was either bought of a solution prepared according to the method of Muthmann and Schroder, (Ber. 1900, 33, 1765). In the latter case it was found unnecessary to do more than digest the Potassium cyanide and Selenium, melt with the amount of water stated and then make the solution up to 50 per cent.

59g. (mol.) o-(p-Tolyloxy-)aminobenzene were diazotised in the usual manner by way of the hydrochloride. To the filtered diazo solution sufficient sodium acetate crystals were added to make the solution alkaline to congo red. The solution was then added slowly over 15 mins. to110c.c. 50% KSeCN solution (1½ mol). Reaction occurred immediately. Evolution of nitrogen was allowed to continue at room temperature until the whole of the product had collected as a dark red oil beneath the aqueous layer. The oil was extracted with chloroform, the chloroform solution dried over calcium chloride, the solvent removed and the oil left distilled under reduced pressure. About 4g b.p. 224-227°/18mm. distilled over without decomposition. This solidified on cooling and on crystallisation from alcohol colourless crystals were obtained, m.p.45°. If the compound was left standing open to the atmosphere a pink colour developed, indicating that a certain amount of decomposition with the formation of free selenium had taken place.

Oxidation of o-(p-Tolyloxy-)phenylselenocyanate.

The oxidation of the crude selenocyanate was attempted with potassium permanganate, chromic acid and strengths of nitric acid ranging from 20% to d 1.4. In all cases the yields were poor. With potassium permanganate (5mols. in 5% solution) only a black sludge was obtained, both when the starting material was the crude oil or the pure crystalline substance. Oxidation of 1g. of the pure material with 4g. chromic acid in 59c.c. glacial acetic acid gave a minute quantity of an ammonia soluble substance when the reaction mixture was poured into water and dilute HCl added. When the ammoniacal solution was acidified only a small dirty white precipitate was obtained, which was not examined further. By oxidation of the crude substance with various strengths of nitric acid products were hardly ever obtained which had the same melting points and many of them were uncrystallisable gums. Unless relatively large quantities of nitric acid were used, the crude starting material did not go into solution. Experiments such as the following were performed:-

(a) The crude selenocyanate (5g.) was added to 50g. nitric acid (d 1.4.) cooled to -15°. The oil did not go into solution. The temperature was allowed to rise slowly, but no reaction occurred until it reached 40°. It was kept at 40-60° for 2 hours and then heated on a boiling water-bath for about

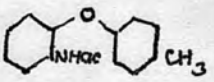
½hour. Even then only a small amount of the oil seemed to have dissolved. The mixture was poured on to ice ; a red gummy substance was obtained mixed with a small quantity of yellow solid. Both the gum and the solid were soluble in dilute ammonia, but only a gum was obtained on acidification. This could not be crystallised from alcohol and was completely insoluble in benzene and the petroleum ethers. From glacial acetic acid ,after long standing, a small quantity of a yelliw solid was obtained, m.p. 106-108°.

(b). 10 g. crude selenocyanate were boiled for 11 hours with 500 c.c. 20% nitric acid. Practically all the oil went up into solution. The solution was then diluted and on stirring and scratching an ammonia soluble precipitate was obtained, which on crystallisation from alcohol gave a dirty yellow crystalline powder. m.p. 170-174°.

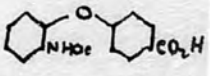
(c). 200 c.c. 25% nitric acid and 5 g. selenocyanate were boiled for 2½ hours. On dilution of the clear solution with an equal volume of water, a yellow solid was obtained which after crystallisation from acetic acid had m.p. 202-203°(decomp)

(d). 45g. crude selenocyanate were boiled with 1500 c.c. 30% nitric acid until solution was complete. On dilution a dirty yellow product was obtained m.p. 168°. On standing the mother liquor deposited an orange coloured crystalline substance which on crystallising from glacial acetic acid evolved brown oxides of nitrogen indicating that it was

probably a nitrate. After crystallisation its m.p. was 176-183°. From the acetic acid mother liquor a further quantity of a yellow substance was obtained, m.p. 205-207° (decomp.). This became white on exposure to air, but regained its colour on heating.

Preparation of 2-Acetamido-4'-methyldiphenyl ether. 

2-Amino-4'-methyldiphenyl ether hydrochloride (71 g.,1 mol.) was dissolved in glacial acetic acid. To the warm solution was added an aqueous solution of 40 g. acetic anhydride (1¼ mol.) and 50g. sodium acetate crystals. The mixture was warmed until a test portion became solid in presence of water, and then it was poured into much water. The precipitated 2-acetamido-4'-methyldiphenyl ether crystallised from light petroleum (b.p. 80-100) in needles or prisms, m.p. 92°. (Found: N. 6.0%, $C_{15}H_{15}O_2N$ requires N, 5.8%).



Preparation of 2-Acetamido-diphenyl ether 4'-carboxylic acid.

Potassium permanganate was found to decompose the synthesised carboxylic acid, and therefore many experiments had to be performed to find the conditions under which the maximum quantity of acid was obtained. These are set out overleaf. In all cases the acid was isolated by decolourising the reaction mixture with SO_2, extracting the residue with sodium carbonate and acidification of the filtered extract. The acetamido-acid formed short rods, m.p. 211° from alcohol. (Found: N, 5.1%, $C_{15}H_{13}O_4N$ requires N, 5.2%). Unchanged methyl compound was recovered from the alkali insoluble residue.

EXPERIMENTS ON THE OXIDATION OF 2-ACETAMIDO-4'-METHYLDIPHENYL ETHER BY POTASSIUM PERMANGANATE.

Expt.	Me.cpd. used in g.	$KMnO_4$ used in g.	$\frac{KMnO_4 \text{ used}}{\text{Theor. amt.}}$	Solvent	Temp. of Reaction	Yield in g.	Recovd. Me.cpd. in g.	%age Yield	
								Acid.	Recovd. Me.cpd.
A	72	96	1	Me.cpd. dissolved in 400 cc. A.R. acetone & 100 cc. H_2O. $KMnO_4$ added in 2 equal lots in 400 cc. H_2O.	80°	2	67	2	93
B	36	96	2	Me. cpd. in 120 cc. acetone added to $KMnO_4$ in 800 cc. H_2O.	80°	5	26	12	72
C	18	48	2	Me. cpd. in 160 cc. acetone & 40 cc. H_2O. $KMnO_4$ added powdered. All solvent evapd.	80°	3.7	12	19	66
D	18	48	2	$KMnO_4$ in 480 cc. H_2O. Ground Me. cpd. added.	90°	4	9	20	50
E	18	72	3	Me. cpd. added to $KMnO_4$ in 10% aq. soln.	80-90°	9	2	45	11
F	4 x 18	4 x 72	3	ditto	90-100°	27	18	33	25
G	18	96	4	ditto	80-90°	4.5	4	23	22

From the table on the previous page it therefore appears that the best yield of the acid was obtained when three times the theoretical quantity of permanganate was used. The yield varied with the scale of the operation, diminishing with increasing quantity of 2-acetamido-4'-methyldiphenyl ether used. The use of acetone as a solvent appeared to have no appreciable effect on the course of the reaction.

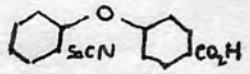
Hydrolysis of 2-Acetamido-diphenyl ether 4'-carboxylic acid.

(a) With Sulphuric Acid.

3 g. of the acetyl compound were dissolved in 9 g. concentrated sulphuric acid. The solution was warmed for a few minutes and then water added slowly. When the hot solution cooled, the sulphate of the base crystallised out as a dirty white solid.

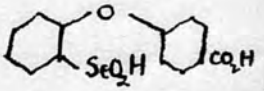
(b) With Hydrochloric Acid.

A suspension of 5 g. of the acetamido acid in 60 cc. 20% hydrochloric acid was bpiled for ¾ hour. The heavy powder present at the beginning of the experiment was gradually replaced by a mat of feathery needles of the hydrochloride of the base, from which the latter was liberated by means of concentrated sodium acetate solution. The 2-amino-diphenyl ether 4'-carboxylic acid crystallised from alcohol or benzene in square or rectangular prisms, m.p. 137°. (Found: N, 6.1%. $C_{13}H_{11}O_3N$ requires 6.1%). Mayer and Krieger (Ber. 1922, 55, 1663) state that the acid melts at 120-121, but give no analysis in support of its composition.

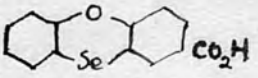


Preparation of 2-Selenocyanodiphenyl ether 4'-carboxylic acid.

26g Amino-acid hydrochloride were diazotised in the usual way. Sodium acetate was added to the filtered diazo solution until it no longer gave a blue colour with congo-red. 40 c.c. 50% potassium selenocyanate (1.33 mols.) were cooled in ice and the diazo solution added gradually. A steady evolution of nitrogen occurred. The mixture was allowed to stand for $\frac{3}{4}$ hr. at room temperature, and then heated on a water bath until the evolution of nitrogen had ceased. The precipitate was gummy when hot, but quite solid when cold. It was filtered off and extracted several times with sodium bicarbonate. The first extractions gave dark coloured precipitates on acidification which were discarded. The later ones gave pale yellow-brown acids which always went slightly pink on standing. The acids were dried and used in the crude state for oxidation to the seleninic acid. Only gummy solids were obtained on attempting to crystallise from acetic acid or alcohol. The acid was insoluble in benzene and the lower boiling P.E. fractions, but a small quantity was obtained pure for analysis and melting point determinations by two or three crystallisations from P.E. b.p. 100-120°. The selenocyanate was finally obtained as pale brownish coloured needles m.p. 178° (decomp.). (Found; C, 53.4%. H, 2.9%. $C_{14}H_9O_3NSe$ requires C, 52.8% H, 2.85%). The yield of the crude product was 79%.

Preparation of 2-(p-carboxyphenoxy-)seleninic acid. 

A solution of 3 g. 2-selenocyano diphenyl ether 4'-carboxylic acid in 90 c.c. 33% nitric acid was boiled for a few minutes. On cooling, a certain amount of tar and free selenium predipitated, was filtered off, and the solution diluted with the same volume of water. Some solid was at once precipitated and more came out on standing. On crystallising twice from glacial acetic acid a white crystalline solid was obtained, 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 concentrated nitric acid (d. 1.4) this seleninic acid crystallised as a nitrate decomposing at 120-130°.

Preparation of Phenoxselenine 2-carboxylic acid. 

In the preliminary experiment 2 g. of the above seleninic acid were added gradually to 10 g. concentrated sulphuric acid cooled to 0°. The mixture was at first reddish in colour and then darkened to an olive green. It was heated on a water bath for about 20 mins. when a fine bluish-black precipitate appeared. Water was added and the precipitate filtered off and when the latter was well washed with water the blue colour disappeared. The dirty white powder thus obtained crystallised from glacial acetic acid in which it was quite

soluble, or from benzene, in which it was only sparingly soluble, as fine white microscopic needles, m.p. 246°. The yield was very small and on analysis the product was found to be phenoxselenine-2-carboxylic acid, and not the expected phenoxselenine-10-oxide-2-carboxylic acid. (Found: C, 53.3%. H, 3.0%. $C_{13}H_8O_3Se$ requires C, 53.6% H,2.8%. $C_{13}H_8O_4Se$ requires C, 50.8%. H, 2.6%). Since concentrated sulphuric acid obviously caused some decomposition, the following experiments on ring closure were performed:-

(a) Action of Heat on 2-(p-carboxyphenoxy) seleninic acid.

---

1 g. of the seleninic acid was heated in a metal bath to its melting point, and after the evolution of steam etc. had ceased, the temperature of the bath was raised to 250°, and maintained at this temperature for ¼ hour. The melt was dissolved in alcohol, from which it would not crystallise. It was therefore precipitated with water, dried and recrystallised from benzene. 0.2 g. solid was obtained, with an ill-defined crystalline form, and m.p. 242-245°. From the mother liquor a substance was obtained m.p. 225-235°, which was unchanged when boiled with sodium carbonate solution and reprecipitated with dilute hydrochloric acid, and was therefore not an anhydride.

(b). Action of Anhydrous Oxalic Acid on 2-(p-carboxyphenoxy) seleninic Acid.

5.g. anhydrous oxalic acid were heated at about 120 for 3 hours. It was then ground in a mortar with 0.5 g. of the seleninic acid and the mixture heated in a metal bath at 190° for ½ hour. Water was given off but no fusion occurred. The mixture was digested with 40 c.c. water to remove the oxalic acid and the greenish yellow insoluble material had m.p. 235-242°. It crystallised from benzene in granular aggregates, 0.27 g. being obtained m.p. 238-245°.

As only impure phenoxselenine carboxylic acid was obtained from both (a) and (b) above, the effect of varying the concentration of the sulphuric acid, the time and the temperature of the reaction was investigated. The results are set out in the table on the following page. In all cases the reaction mixture was poured into water, left to stand for an hour, and the precipitated selenoxide carboxylic acid reduced by grinding with one part of potassium metabisulphite and a little water. After allowing to stand at room temperature for a hour, the product was recrystallised from benzene or alcohol.

The ACTION of SULPHURIC ACID on 2-(p-CARBOXYPHENOXY) SELENINIC ACID.

Expt.	Wt. of A* used in g.	Concn. of H_2SO_4	Vol. of H_2SO_4	Temp.	Time	Observations	Yield of B* in g.	%age Yield.
I	1	75%	8.5cc.	100°	15mins.	A* recovd. unchanged	Nil	Nil
II	1	85%	7 cc.	100°	10mins.	Dark blue ppt.	0.38	42
III	1	85%	7 cc.	100°	5mins.	Dark blue ppt.	0.5	56
IV	1	85%	7 cc.	110°	1min.	Intense blue ppt.	0.42	47
V	1	85%	7 cc	63°	30mins.	Slight blue ppt.	0.60	66
VI	1	85%	7 cc.	54°	30mins.	Slight blue ppt.	0.63	70
VII	1	85%	7 cc.	50°	30mins.	Olive green soln.	0.70	78
VIII	2	85%	14 cc.	49°	30mins.	Olive green soln.	1.33	74
IX	5	85%	36.5cc.	44°	40mins.	Olive green soln.	3.6	80
X	10	85%	73 cc.	42°	30mins.	Olive green soln.	7.7	85

* A is 2-(p-carboxyphenoxy) seleninic acid.
B is phenoxselenine 2-carboxylic acid.

Pure phenoxselenine-2-carboxylic acid crystallises from ethyl alcohol in pale yellow needles, m.p. 251°. The sodium salt is sparingly soluble in cold water, but quite soluble in the hot. When dissolved in glacial acetic acid, and excess bromine added, orange-red plates with a metallic lustre are precipitated. These appear to be a dibromide, m.p. 214°. (decomp., darkening gradually above 170°) which is unstable. A specimen kept in a desiccator over calcium chloride for three weeks was found to contain only 19.2% bromine when analysed in a Parr bomb. Another specimen dried for 10 mins. in an evacuated desiccator over sulphuric acid contained 33.7% bromine, ($C_{13}H_8O_3SeBr_2$ requires Br. 35.4%). In cold water the compound was immediately converted to the white phenoxselenine-10-oxide-2-carboxylic acid, identified by its m.p. of 218° (decomp.).

Decarboxylation of Phenoxselenine-2-carboxylic acid.

1 g. of the acid was refluxed for 45 mins. with about 30 cc. quinoline dried over potassium carbonate, and a small quantity of copper bronze. That residue which was insoluble in both dilute hydrochloric acid and dilute alkali was crystallised from alcohol. Long rectangular prisms were obtained, m.p. 87° either alone or mixed with a specimen of phenoxselenine given to us by Dr. H.D.K.Drew.

Salts of Phenoxselenine-2-carboxylic Acid.

The salt forming properties of some optically active bases were investigated by dissolving the phenoxselenine-2-carboxylic acid in hot ethyl alcohol and adding the base. Results were as follows:-

Strychnine. A gum was obtained which solidified on standing overnight.

Brucine. White glistening needle-shaped prisms crystallised out on top of a certain amount of yellow gum.

Morphine. A gum first came down which was transformed into hard crystals on standing for several days.

Quinidine and Cinchonine. These salts were very soluble in alcohol and only gums could be obtained when water was added.

α-Phenylethylamine. The salt crystallised out very slowly.

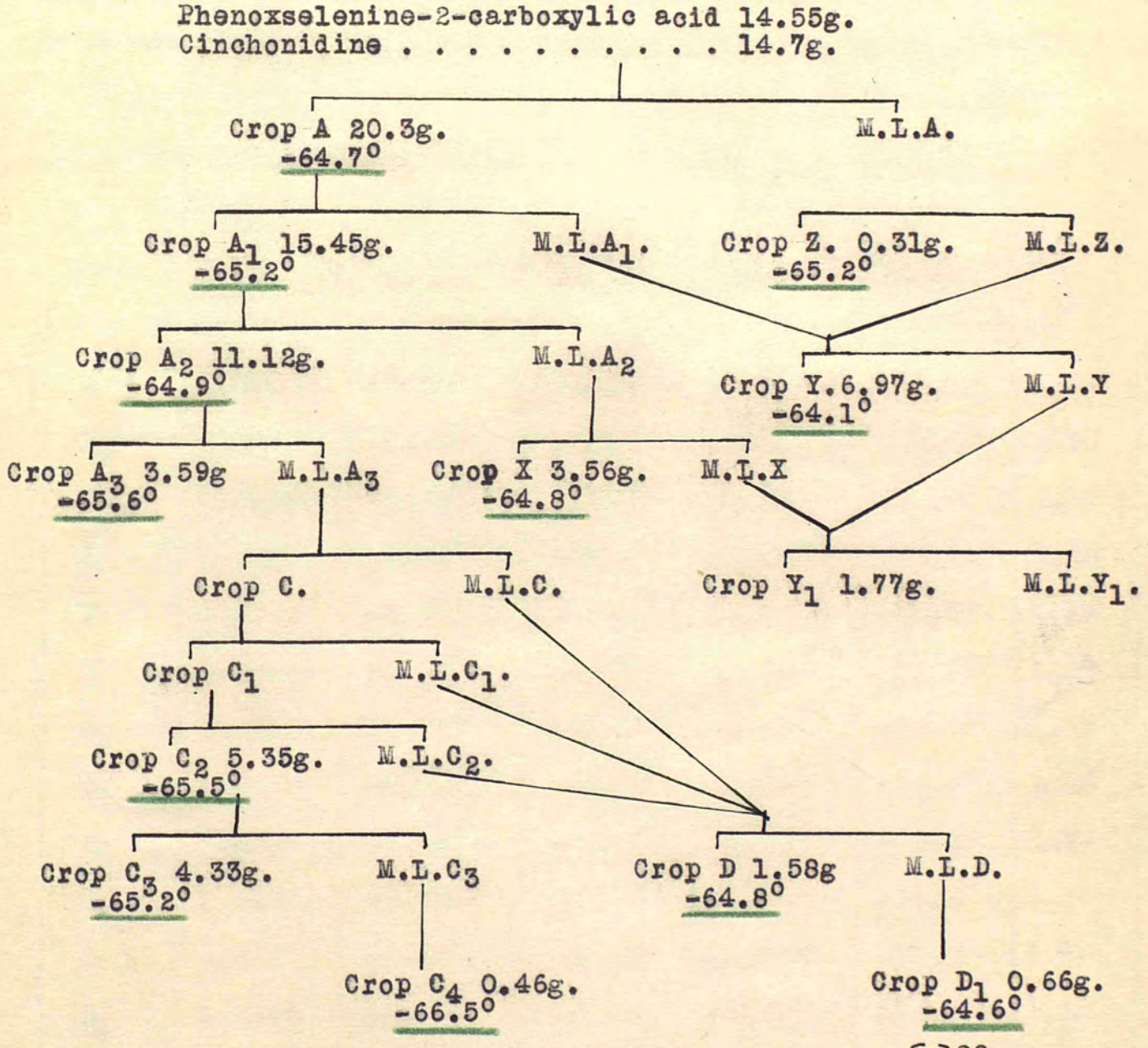
Cinchonidine. Well defined white bundles of rosettes of prisms were obtained.

Of these the optical properties of the cinchonidine, α-phenylethylamine and brucine salts were examined.

Cinchonidine Salt of Phenoxselenine-2-carboxylic Acid.

This salt crystallised readily when 14.7 g. of the base was added to an equivalent quantity (14.5 g.) of the acid dissolved in about 600 c.c. hot absolute ethyl alcohol. Elongated white prisms were obtained, m.p. 211°, whose specific rotation did not change during repeated crystallisation, except within the limits of experimental error.
(Found, C, 66.3%. H, 5.3%. $C_{32}H_{30}O_4N_2Se$ requires C, 65.6% H, 5.2%.)
The full experimental details of the attempted resolution of the salt will be found on the two following pages.

FRACTIONAL CRYSTALLISATION of the CINCHONIDINE SALT of PHENOXSELENINE-2-CARBOXYLIC ACID.



The figures underlined in green are the values of $[\alpha]_{5461}^{20}$

The rotation of D_1 was again observed after 24 hours. There was no mutarotation.

Crop A_3 and M.L.Y_1 gave inactive acids when decomposed.

Cinchonidine Salt of Phenoxselenine-2-carboxylic Acid. Specific Rotation of the Crops obtained during its Fractional Crystallisation.

All rotations measured in A.R. chloroform. $\underline{l}$ = 2dm.

Crop.	$\underline{c}$	α_{5791}	$[\alpha]^{20}_{5791}$	α_{5461}	$[\alpha]^{20}_{5461}$	
A	1.2755	-1.65°	-64.7°	-1.88°	-73.7°	1.14
A_1	1.2810	-1.67°	-65.2°	-1.91°	-74.5°	1.14
A_2	1.3005	-1.69°	-64.9°	-1.91°	-73.5°	1.13
Z	1.2880	-1.68°	-65.2°	-1.91°	-74.15°	1.14
X	1.2890	-1.67°	-64.8°	-1.88°	-72.9°	1.13
Y	1.2945	-1.66°	-64.1°	-1.88°	-72.6°	1.13
C_2	1.2985	-1.70°	-65.5°	-1.94°	-74.3°	1.14
C_3	1.3040	-1.70°	-65.2°	-1.94°	-74.4°	1.14
C_4	1.2700	-1.69°	-66.5°	-1.93°	-76.0°	1.14
A_3	1.3140	-1.725°	-65.6°	-1.96°	-74.6°	1.14
D	1.2890	-1.67°	-64.8°	-1.90°	-73.7°	1.14
D_1	1.2845	-1.66°	-64.6°	-1.89°	-73.6°	1.14

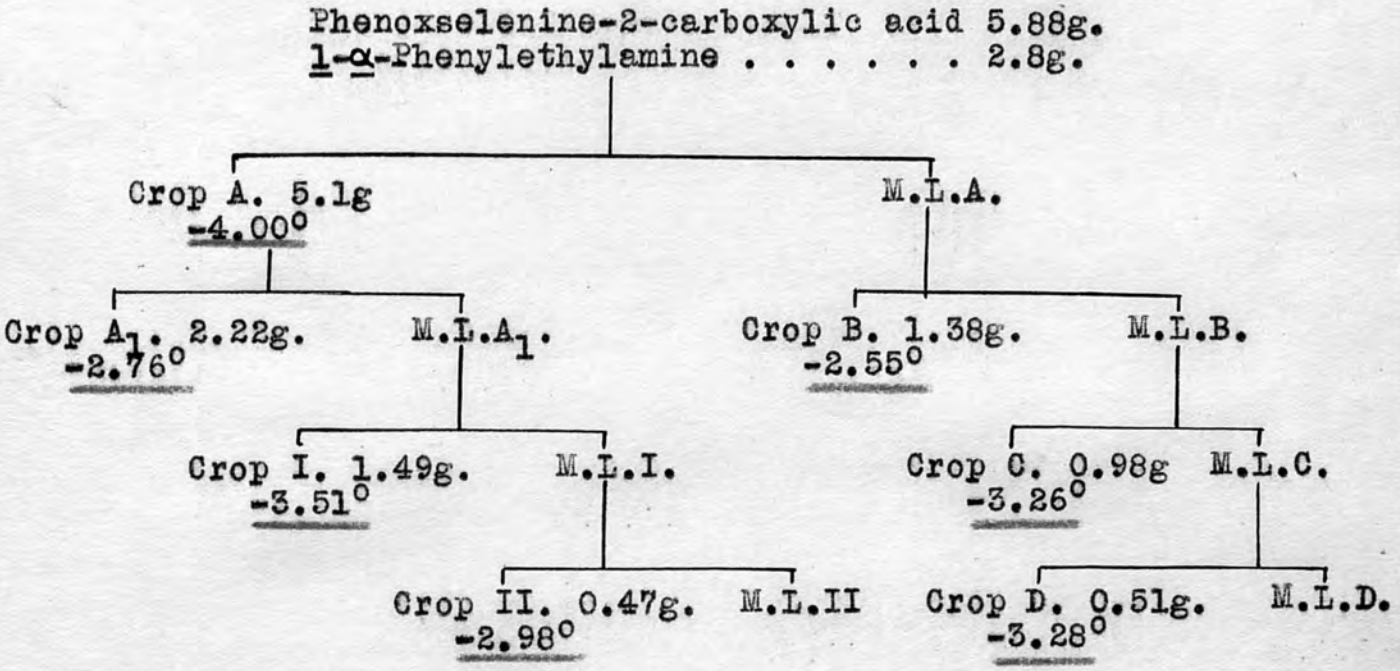
l-α-Phenylethylamine Salt of Phenoxselenine-2-carboxylic Acid.

This salt was prepared by adding slightly more than the equivalent quantity of the base to a hot solution of the acid in absolute alcohol. Needle shaped prisms were obtained, m.p. 207°, insoluble in acetone and chloroform, slightly soluble in hot water, and soluble in methyl alcohol. The specific rotation of the salt appeared to remain constant within the limits of experimental error during repeated crystallisation from absolute alcohol. Some of the crops on decomposition yielded an acid giving slightly positive values of α (+0.02° and +0.03°), but this was attributed to defective end plates.
(Found: C, 60.7%. H, 4.7%. $C_{21}H_{19}O_3NSe$ requires C, 61.15%. H, 4.7%).

Full experimental details of the attempted resolution of the salt will be found on the two following pages.

FRACTIONAL CRYSTALLISATION of the l-α-PHENYLETHYLAMINE SALT of

PHENOXSELENINE-2-CARBOXYLIC ACID.



The figures underlined in green are the values of $[\alpha]_{5791}^{20}$

Acid obtained from the decomposition of crop A_1 had α_{5791} + 0.02° ✱

" " " " " " " I " " + 0.02° ✱

" " " " " " M.L.II. " " + 0.03° ✱

" " " " " " M.L.D. " " + 0.02° ✱

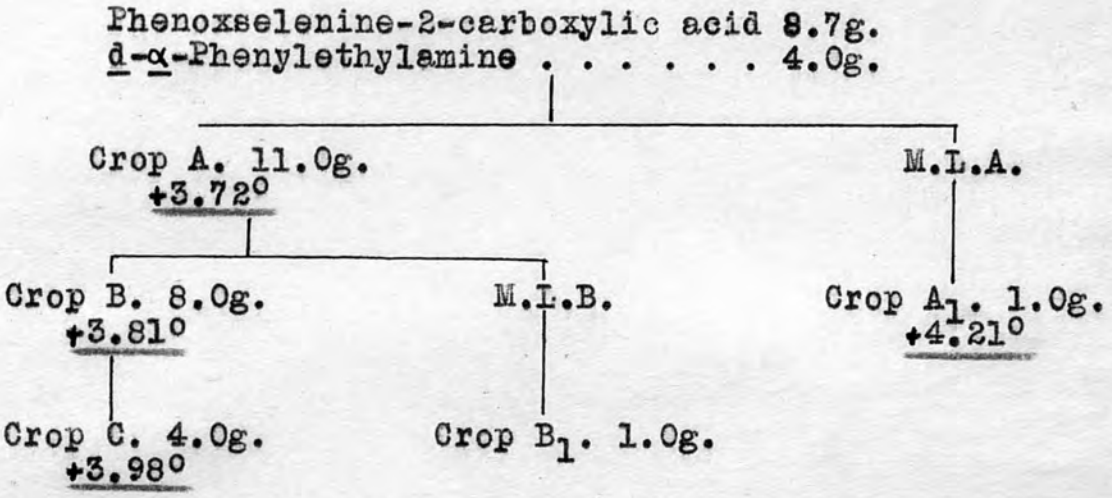
✱ These values are for a concentration of roughly 0.2g. in 20 cc. absolute alcohol. l = 2 dm.

l-α-Phenylethylamine Salt of Phenoxselenine-2-carboxylic Acid. Specific Rotation of the Crops obtained during its Fractional Crystallisation.

All rotations measured in methyl alcohol. l = 2dm.

Crop.	c	α_{5791}	$[\alpha]^{20}_{5791}$	α_{5461}	$[\alpha]^{20}_{5461}$	δ
A	2.0010	-0.16°	-4.00°	-0.17°	-4.25°	1.06
B.	1.9605	-0.10°	-2.55°	-0.11°	-2.81°	1.1
A_1	1.9930	-0.11°	-2.76°	-0.11°	-2.76°	1.0
C	1.9920	-0.13°	-3.26°	-0.14°	-3.51°	1.08
I	1.9970	-0.14°	-3.51°	-0.15°	-3.76°	1.07
D	1.9790	-0.13°	-3.28°	-0.14°	-3.53°	1.08
II	2.0150	-0.12°	-2.98°	-0.13°	-3.22°	1.08

Fractional Crystallisation and Optical Properties of the d-α-Phenylethylamine Salts of Phenoxselenine-2-carboxylic Acid.



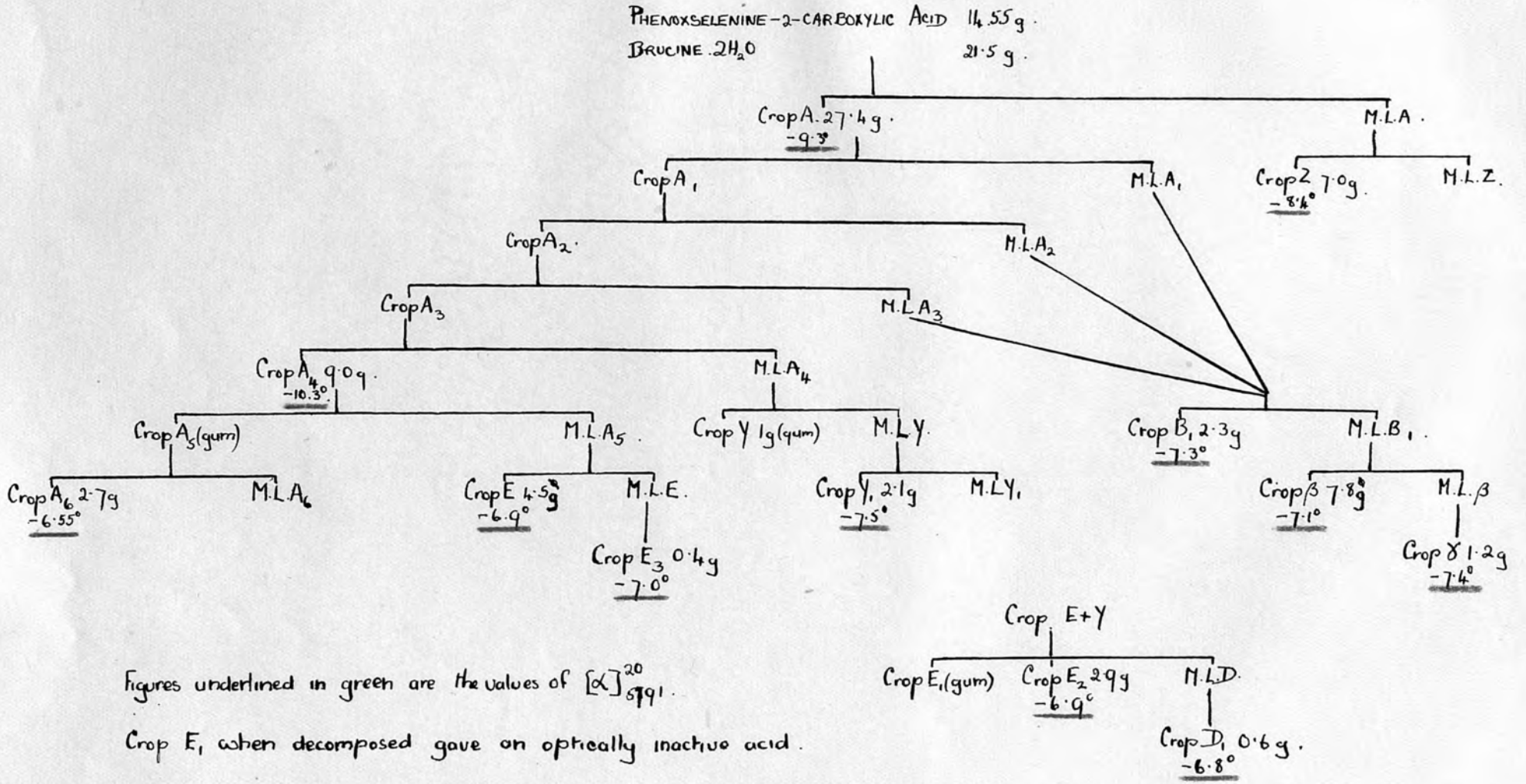
Figures underlined in green are the values of $[\alpha]^{20}_{5791}$.

The free acids obtained from the decomposition of crops B. and C. were optically inactive.

Crop.	c	α_{5791}	$[\alpha]^{20}_{5791}$	α_{5461}	$[\alpha]^{20}_{5461}$	δ
A	2.0175	+0.15°	+3.72°	+0.17°	+4.21°	1.13
B	1.9670	+0.15°	+3.81°	+0.17°	+4.32°	1.13
A_1	2.0185	+0.17°	+4.21°	+0.18°	+4.46°	1.06
C	1.8845	+0.15°	+3.98°	+0.16°	+4.24°	1.07

All rotations measured in methyl alcohol. l = 2 dm.

Fractional Crystallisation of the Brucine Salt of Phenoxselenine-2-carboxylic Acid.



Figures underlined in green are the values of $[\alpha]_{5791}^{20}$.

Crop E_1 when decomposed gave an optically inactive acid.

Brucine Salt of Phenoxselenine-2-carboxylic Acid. Specific Rotation of the Crops obtained during its Fractional Crystallisation.

All rotations measured in A.R. acetone. $\underline{l}$ = 2 dm.

Crop.	$\underline{c}$	α_{5791}	$[\alpha]^{20}_{5791}$	α_{5461}	$[\alpha]^{20}_{5461}$	δ
A	2.0120	-0.39°	- 9.7°	-0.48°	-11.9°	1.23
Z	2.0885	-0.35°	- 8.4°	-0.45°	-10.8°	1.29
A_4	1.9885	-0.41°	-10.3°	-0.51°	-12.8°	1.25
β	1.9685	-0.28°	- 7.1°	-0.34°	- 8.6°	1.22
B_2	1.9760	-0.29°	- 7.3°	-0.37°	- 9.4°	1.28
Y_1	1.9875	-0.30°	- 7.5°	-0.38°	- 9.6°	1.27
E	1.9605	-0.27°	- 6.9°	-0.34°	- 8.7°	1.26
Y	2.0075	-0.25°	- 6.2°	-0.31°	- 7.4°	1.24
A_6	1.9845	-0.26°	- 6.55°	-0.33°	- 8.32°	1.27
γ	2.0240	-0.30°	- 7.4°	-0.38°	- 9.4°	1.27
E_3	1.9920	-0.28°	- 7.0°	-0.36°	- 9.0°	1.28
E_2	2.0220	-0.28°	- 6.9°	-0.36°	- 8.9°	1.28
D_1	1.9910	-0.27°	- 6.8°	-0.34°	- 8.5°	1.26

Decomposition of Crop A_6

1 g. was dissolved in alcohol at room temperature, and the solution cooled in ice. Dilute hydrochloric acid was added slowly, and the precipitated acid filtered off and well washed with cold water, and dried by leaving overnight in an evacuated desiccator over calcium chloride. (Found; C, 53.2%, H, 2.9%. $C_{13}H_8O_3Se$ requires C, 53.56%, H, 2.8%.) 0.15 g. were dissolved in 20 cc. absolute alcohol and the rotation observed. This was found to remain constant at room temperature over a period of four days, but became zero after boiling the solution for 35 minutes.

α_{5791} on dissolving in alcohol was +0.05°

" after four days +0.05°

" after boiling soln. 35 mins. +0.00°

Racemisation of Crop A_6.

The rotation of an acetone solution, $\underline{c}$ = 1.9765; $\underline{l}$ = 2, was observed both before and after heating for two hours in a sealed tube at 100°. Readings were as follows:-

	α^{20}_{5791}	α^{20}_{5461}
Before heating.	0.27°	0.35°
After heating	0.31°	0.38°

Variation of the Specific Rotation of the Brucine Salt of Phenoxselenine-2-carboxylic Acid with Concentration.

As may be seen from the following table, the rotation of the solutions of the salt in acetone, ($\underline{l}$ = 2) decreased with increasing concentration.

$\underline{c}$	α^{20}_{5791}	$[\alpha]^{20}_{5791}$	α^{20}_{5461}	$[\alpha]^{20}_{5461}$	$\underline{S}$
1.704	-0.29°	-8.51°	-0.36°	-10.56°	1.24
2.008	-0.29°	-7.22°	-0.36°	-8.97°	1.24
2.208	-0.27°	-6.11°	-0.34°	-7.47°	1.22
2.223	-0.26°	-5.85°	-0.34°	-7.41°	1.27

The brucine salt of phenoxselenine-2-carboxylic acid crystallised from alcohol in white needle-shaped prisms containing three molecules of water. If there was insufficient water in the alcohol only a gum was obtained.

Analysis of Crop A_6:- Found: C, 58.1%, H, 5.5%. $C_{36}H_{34}O_7N_2Se,3H_2O$ requires C, 58.4%, H, 5.5%. On heating 1.0794 g. in an air oven at 140° for 3½ hours, the loss in weight was 7.0%. Percentage of water in $C_{36}H_{34}N_2O_7Se,3H_2O$ is 7.3.

Preparation of Phenoxselenine-10-oxide-2-carboxylic Acid.

A solution of 1.8 g. phenoxselenine-2-carboxylic acid in the least amount of hot glacial acetic acid was treated with 20 cc. hydrogen peroxide solution (20 vols.). Immediate oxidation occurred and, on cooling, a microcrystalline solid separated, more being obtained on 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, 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.C.S. 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%. $C_{13}H_8C_4Se$ requires C, 50.8%, H, 2.6%).

Examination of the salt-forming properties of Phenoxselenine-10-oxide-2-carboxylic acid with some optically active bases.

(1) With l-α-Phenylethylamine. When the acid was added to a solution of the base in water, even when the latter was in excess, a free acid first crystallised out which proved to be a mixture of the oxide-acid and phenoxselenine-2-carboxylic acid. On leaving a more dilute aqueous solution containing approximately equimolecular quantities of acid and base for several days, hair-like needles were obtained, m.p. 162° (decomp.). But the salt apparently split up so easily that it was not considered suitable for optical experiments.

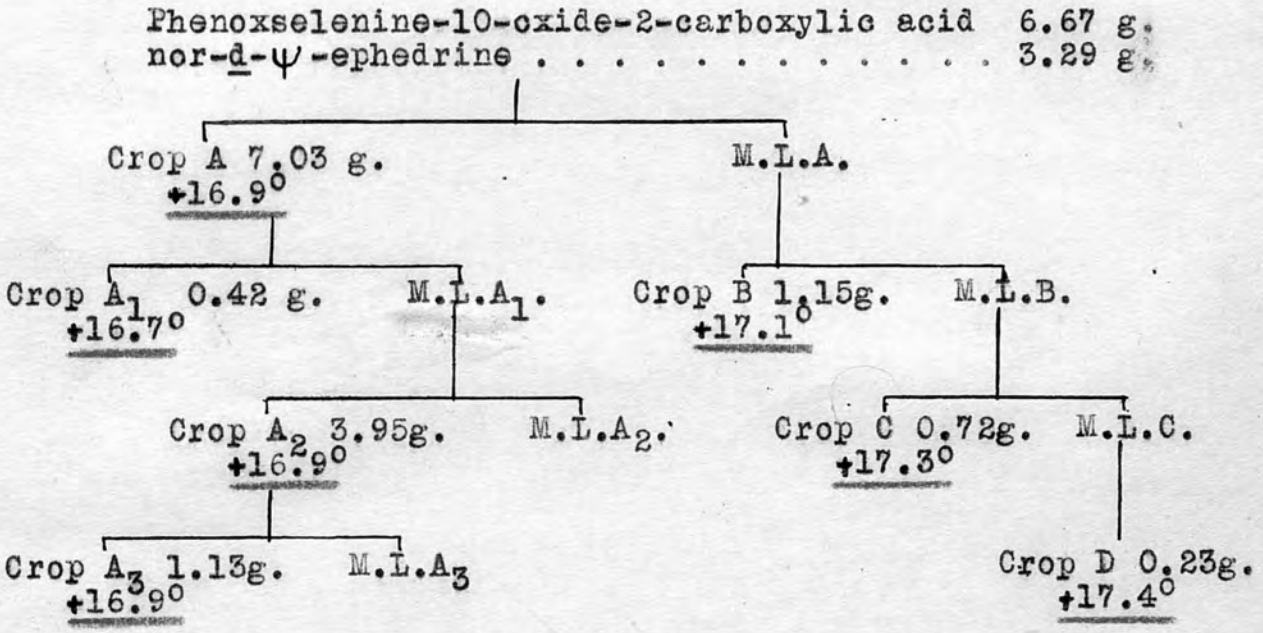
(2) With Strychnine. 12 g. of strychnine were dissolved in absolute alcohol and 11 g. of phenoxselenine-10-oxide-2-carboxylic acid added. A considerable quantity of alcohol (2½ litres) had to be added to the boiling mixture before solution was complete. On standing 1.5 g. of a white solid crystallised out which softened at 210° and finally melted at 245°. On heating with hydrogen peroxide in acetic acid a solid m.p. 218° (decomp.) was obtained. It therefore appeared that the oxide-acid would not form a strychnine salt and is partly reduced to phenoxselenine-2-carboxylic acid when

boiled with an alcoholic solution of strychnine.

(3) With Brucine. When an equimolecular quantity (1.72 g.) of the acid was added to an alcoholic solution of brucine (2.4 g.) only mixtures of the original acid and phenoxselenine-2-carboxylic acid could be recovered. The presence of the two acids was confirmed as described under the attempted preparation of a strychnine salt.

(4) With nor-d-ψ-Ephedrine. 6.67 g. of the selenoxide-acid was added to a hot aqueous solution of nor-d-ψ-ephedrine (3.29 g.). On cooling well defined granular crystals appeared. If crystallisation occurred from a hot solution needle shaped prisms were obtained which did not appear to have any different optical properties. This salt could be recrystallised from water and its m.p. was 180° (decomp. softening at 175°).
The salt was insoluble in acetone, chloroform and carbon tetrachloride. It was scarcely soluble in ethyl and methyl alcohol but more soluble in aqueous alcoholic mixtures.
(Found; C, 57.8 %, H, 4.4%. $C_{22}H_{21}O_5NSe$ requires C, 57.6%, H, 3.7%.)
Full experimental details of the attempted resolution of this salt will be found on the following two pages.

FRACTIONAL CRYSTALLISATION of the nor-d-ψ-EPHEDRINE SALT OF PHENOXSELENINE-10-OXIDE-2-CARBOXYLIC ACID.



Figures underlined in green are the values of $[\alpha]^{20}_{5791}$

The free acid obtained by decomposition of Crop D was completely inactive.

nor-d-ψ-Ephedrine Salt of Phenoxselenine-10-oxide-2-carboxylic Acid. Specific rotation of crops obtained during its fractional crystallisation.

All measurements in 50% aqueous methyl alcohol. l = 2 dm.

Crop	c	α^{20}_{5791}	$[\alpha]^{20}_{5791}$	α^{20}_{5461}	$[\alpha]^{20}_{5461}$	δ
A	1.3100	+0.44°	+16.9°	+0.49°	+18.7°	1.11
B	1.4020	+0.48°	+17.1°	+0.54°	+19.3°	1.13
C	1.3260	+0.46°	+17.3°	+0.52°	+19.6°	1.13
A_1	1.3160	+0.44°	+16.7°	+0.50°	+19.0°	1.14
A_2	1.4535	+0.49°	+16.9°	+0.56°	+19.3°	1.14
D	1.1190	+0.39°	+17.4°	+0.44°	+19.7°	1.13
A_3	1.3930	+0.47°	+16.9°	+0.54°	+19.4°	1.12

Attempted Preparation of 2-Carboxyphenoxselenine-10-sulphide

1 g. phenoxselenine-10-oxide-2-carboxylic acid was suspended in about 50 cc. water and a slow stream of Hydrogen sulphide passed through it for half an hour. After drying on a water bath the product melted at 215-240° with some decomposition indicating that it was ammixture of the starting material and some phenoxselenine-2-carboxylic acid.

PREPARATION of SELENANTHREN.

Preparation of Thianthren. (Fleischer and Stemmer. Ann., 1917, 422, 267.)

To a mixture of 120 g. sulphur monochloride in 200 g. benzene was added gradually 100 g. of aluminium chloride, but the speed at which it was added was sufficient to cause a very vigorous reaction. The mixture was cooled under the tap occasionally. When addition was complete the mixture was heated for two hours on a water bath and then decomposed by pouring on to ice. After passing steam through for three hours the mixture was filtered and well pressed so that any oil was sucked off as completely as possible. The solid was then crystallised, first from benzene and then from alcohol with charcoal. 60 g. of thianthren were obtained as colourless white crystals.

Preparation of Thianthrendisulphone.

6 g. of thianthren were dissolved in boiling glacial acetic acid, and 12 g. of chromic acid suspended in 100 cc. of the same were added gradually. The mixture was refluxed for half an hour during which time the sulphone was partly precipitated. The mixture was poured into cold water

and the precipitated solid recrystallised from much glacial acetic acid. 6 g. were obtained, m.p. 321°.

Preparation of Selenanthren. (Krafft and Kaschau, Ber., 29, 443.)

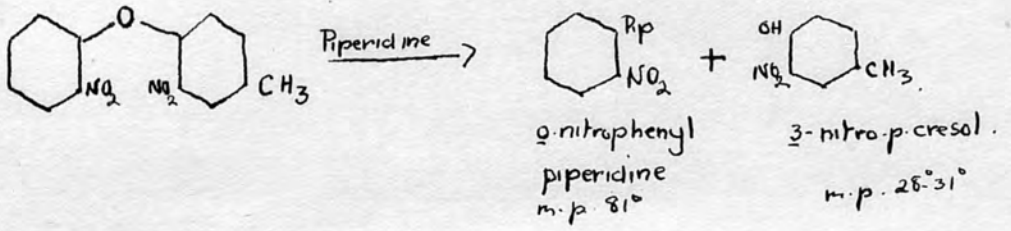
22 g of thianthrendisulphone and 12.5 g. of powdered black selenium were intimately mixed and heated in a metal bath in a Claisen flask. At 350° (bath temperature) the mixture had melted but there was no apparent reaction. It was then heated with a free flame for twelve hours, during which time there was a gradual evolution of sulphur dioxide. The mixture was then vacuum distilled. 9 g. of a reddish oil were obtained, b.p. 223-240°/18 mm., together with other lower boiling by-products. The oil solidified on cooling and was recrystallised several times from alcohol to remove free selenium and other impurities. Selenanthren was finally obtained as pale brownish needle-shaped prisms.

Nitration of o-Nitrophenyl p-Tolyl Ether.

5 g. of the ether was added to a mixture of 50 g. HNO_3. d 1.5 and 50 g. glacial acetic acid. On addition the temperature rose from 40° to 65°. The mixture was left to stand for three or four minutes and then heated on a gauze to 100°. The mixture was then poured into 300 cc. of water when a yellow precipitate was obtained which was recrystallised from alcohol. Pale yellow crystals were obtained, m.p. 106° (cf. Cook, Amer. Chem. J., 25, 64. gives m.p. 100°).

The constitution of the dinitro compound thus obtained was investigated by doing a Piperidine Scission. 2 g. of the compound were heated with 5 cc. piperidine for about twenty minutes at 100°. The resulting liquid was poured into dilute alkali when a red solid separated. This was filtered off, washed with water and dried in a vacuum to free it from as much piperidine as possible. After crystallising twice from alcohol and water its melting point and mixed melting point with o -nitrophenyl piperidine was 81°. The alkaline filtrate was made strongly acid and then steam distilled. The phenol was extracted from the distillate with ether and after removal of the ether a solid was obtained, m.p. 28-31°, and was therefore most probably 3-nitro p-cresol the melting point of which has been given values ranging between 31° and 36°.

Therefore, the dinitro compound obtained from the nitration of o-nitrophenyl p-tolyl ether is 4-methyl-22'-dinitro-diphenyl ether, which is split by piperidine thus:-



o-nitrophenyl piperidine m.p. 81°

3-nitro-p-cresol. m.p. 28-31°

Experiments on the Nitration of Phenoxselenine-2-carboxylic Acid and the corresponding Selenoxide.

1) 10 g. glacial acetic acid
10 g. Nitric Acid, d 1.5.
1 g. Phenoxselenine-10-oxide-2-carboxylic Acid.

The mixture was boiled for about 10 minutes and then water added. The white crystals which were obtained were reduced with potassium metabisulphite. On crystallising the pale yellow product from alcohol its melting point and mixed melting point with phenoxselenine-2-carboxylic acid was 249°. i.e. there had been no reaction.

2) 10 g. Glacial acetic acid,
20 g. Nitric acid d 1.5
.75 g. Phenoxselenine-10-oxide-2-carboxylic acid.

The mixture was heated on a water bath for 5 minutes, and then treated as described in 1). After crystallisation from alcohol the product melted at 253°; this rose to 255° on recrystallisation. The bulk of the product had remained in the mother liquor and when this was evaporated down, a substance came down which melted at 215-235° , indicating the nitration had produced a mixture of substances.

When the same nitration mixture was heated for two hours on a water bath and then treated as in 1), a small quantity of a reddish-yellow solid was produced when the product was crystallised from alcohol. When its melting point was being observed its red colour disappeared at 160-180° and it finally melted at 261°. Only a mixture of substances with a very indefinite melting point could be extracted from the mother liquor.

3) 10 g. Nitric acid, d 1.5.

0.5 g. Phenoxselenine-2-carboxylic acid.

The mixture was heated for one hour on a water bath and then treated as in 1). 0.4 g. yellow solid was obtained which after crystallisation from alcohol melted 241-261° (0.3 g.). The melting point was unchanged after the substance had been recrystallised.

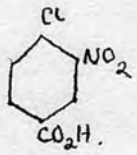
4) 10 g. Sulphuric acid (conc.)

10 g. Nitric acid, d 1.5.

1 g. Phenoxselenine-2-carboxylic acid.

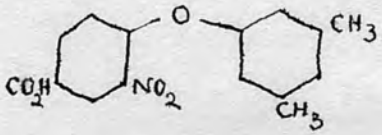
The phenoxselenine-2-carboxylic acid was added slowly to the nitration mixture cooled in ice. After warming a few minutes at 100°, the mixture was poured on to ice. The product was reduced with potassium metabisulphite and on crystallisation from alcohol substances were obtained melting above 300°, and at 240- 280°.

Preparation of p-chlor-m-nitro-benzoic acid.



20 g. of p-chlorbenzoic acid were added gradually to 140 cc. nitric acid (density 1.5) so cooled that its temperature did not rise above 30° during the addition. It was then heated to 55-60° for ten minutes and the product poured into water. After allowing it to stand for half an hour it was filtered and the white crystalline solid obtained recrystallised from aqueous alcohol. Yield, 24 to 25 g. (96%) m.p. 184°.

Preparation of 3:5-dimethyl-2'-nitro-diphenyl ether-4'-carboxylic acid.



(1) Using sodium acetate as a condensing agent. 20 g. of chlornitrobenzoic acid were dissolved in 400 cc. of alcohol. 17 g. (2 mol.) fused sodium acetate and 15 g. (1.2 mol.) m-xylenol were added and the mixture boiled under reflux for one hour. The mixture was poured into water and acidified and the solid which separated out treated with sodium bicarbonate; on acidifying the alkaline solution the chlornitrobenzoic acid was recovered unchanged.

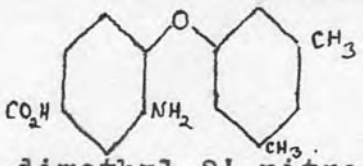
(2) Using caustic potash. 15 g. (2 mol.) of caustic potash were melted with three drops of water. 37 g. (3 mol.)

of m-xylenol were added and the mixture well shaken and heated until a clear melt was obtained. 20 g. (1 mol.) chlornitrobenzoic acid were introduced and the pasty mass thus produced was heated on a metal bath for one and a quarter hours at 170-180°. The mixture was then cooled, treated with about 500 cc. water, and the whole saturated with carbon dioxide. The excess m-xylenol which then separated out went solid on standing and was filtered off, the filtrate being extracted with ether to remove the remainded. On acidifying the queous liquor an acid was precipitated which crystallised from alcohol in short rods, m.p. 179-181°. Mixed m.p. with 4-chlor-3-nitro-benzoic acid, 150-170°. Yield 20 g.

(Found: N, 4.6%, $C_{15}H_{13}O_5N$ requires 4.9% N.)

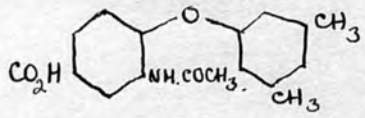
The yield was not appreciably changed when 4 mols. m-xylenol were used instead of three.

Preparation of 3:5-Dimethyl-2'-amino diphenyl ether 4'-carboxylic acid.



36g. (1 mol.) 3:5-dimethyl 2'-nitro diphenyl ether 4'-carboxylic acid were dissolved in 200cc. .880 ammonia (more than 10 mols.) diluted with an equal volume of water. To this hot solution was added 300g. ferrous sulphate crystals (9 mols.) dissolved in 300 cc. water and slightly acidified with sulphuric acid. At the end of the reaction the colour of the mixture changed from that of ferric hydroxide to black or very dark brown. After allowing to stand for about 15 minutes, the iron residue was filtered off, and the filtrate acidified; the quantity of acid contained in the latter was very small, (some times there was none at all); The iron was then extracted with boiling dilute caustic soda, and when the alkaline solution was acidified, the hydrochloride of the base was precipitated. The free base was obtained from the latter by adding sodium acetate until the solution was alkaline to congo-red. The base was crystallised from alcohol when it was obtained in short rods m.p.173°, mixed m.p. with nitro compound, 142°. The base is not very strong, only a part of it being converted into the hydrochloride, when treated with fairly concentrated hydrochloric acid. The yield from the above reaction was practically theoretical. Found: N, 5.5%. $C_{15}H_{15}O_3N$ requires N, 5.5%.

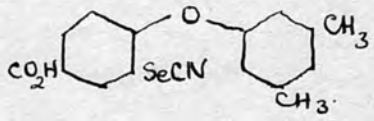
Preparation of 3:5-Dimethyl 2'-acetamido diphenyl ether 4'-carboxylic acid.



This was prepared by adding excess acetic anhydride to a solution of the corresponding amino-acid in glacial acetic acid. After allowing to stand for half an hour, the solution was poured into water. The precipitated acetyl derivative was crystallised from alcohol when it was obtained in fine needles, m.p. 219°.

(Found N, 4.7%. $C_{17}H_{17}O_4N$ requires 4.7%)

Preparation of 3:5-Dimethyl 2'-selenocyano diphenyl ether 4'-carboxylic acid.



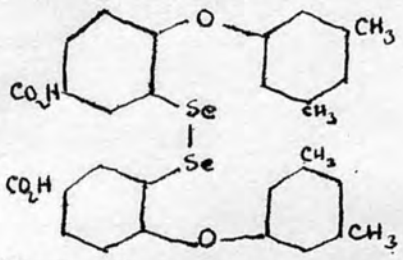
10 g. (1 mol.) 3:5-dimethyl 2'-amino diphenyl ether 4'-carboxylic acid were dissolved in a solution of 2 g. caustic soda (slightly more than 1 mol.) in 300cc.water. 4 g.(1.5 mols.) sodium nitrite were added and the mixture added gradually to 40 cc. concentrated hydrochloric acid diluted with an equal volume of water and cooled in a freezing mixture. The diazonium salt began coming out when about half the mixture of sodium salts had been added. When diazotisation was complete, sodium acetate crystals were added until the

mixture was no longer acid to congo-red; at this stage the diazonium was then added to a 50% solution of potassium selenocyanate containing 13 g. (1.5 mols.) of the latter. There was an immediate evolution of nitrogen and a brownish-red solid was precipitated mixed with free selenium which was at first bright red but darkened when the mixture was heated to a 100° to drive off the nitrogen. The light-brwon solid was filtered off and crystallised from alcohol, when very pale brown diamond shaped plates were obtained, m.p. 233° (decomp.).

(Found: C, 55.5%, H, 4.1%. $C_{16}H_{13}O_3NSe$ requires C, 55.2% H, 3.8%).

The compound could also be crystallised quickly from glacial acetic acid, but if it was boiled for any length of time with this solvent, decomposition occurred with the evolution of prussic acid and the formation of a dark coloured amorphous product which dissolved in alkali giving a bright blue solution.

Preparation of Di-5-carboxy-2-(3:5-xylenoxy-)phenyl Diselenide.



3:5-dimethyl 2'-selenocyano diphenyl ether 4'-carboxylic acid was boiled with dilute caustic soda for 15 mins. After cooling the solution was acidified with dilute hydrochloric acid when an exceedingly hydrated acid was precipitated. This was dried on a water bath and crystallised from glacial acetic acid. Pale yellow plates were obtained, m.p.239-243°. The latter did not become any sharper even after repeated cyystallisation. This compound was extremely soluble in alcohol and from nitric acid d, 1.4 a highly crystalline substance was obtained, which was probably a nitrate. The diselenide crystallised from acetic acid with one molecule of solvent of crystallisation. Found; C, 54.9%, H,4.5% $C_{30}H_{26}O_6Se_2$, $1CH_3COOH$ requires C, 54.8%, H, 4.2%. When 1 g. was heated in an air oven for 2 hours at 150° the loss in weight was 8.55%. The theoretical percentage of acetic acid in the molecule is 8.6%.

Experiments on the Oxidation of 3:5-Dimethyl 2'-selenocyano diphenyl ether 4'-carboxylic acid.

1) With Caro's Acid. Caro's acid was prepared by adding 20 parts of concentrated sulphuric acid to 18 parts of potassium persulphate over a period of 1 hour and without allowing the temperature to rise above 15°. The mixture was then added to about 100 g. ice, and this boiled with 0.5 g. of the selenocyanate for one hour. At the end of this time, the selenocyanate, identified by its very characteristic crystalline form and its melting point, was recovered unchanged.

2) With Perhydrol. The slenocyanate was recovered unchanged when 0.5 g. were dissolved in acetone and boiled for half an hour with either the approximately theoretical quantity of perhydrol or a large excess of it.

3) With Concentrated Nitric Acid in Glacial Acetic Acid. When 1 g. of the selenocyanate was boiled for 5 minutes with 10 cc. nitric acid d 1.4 diluted with 16 cc. acetic acid, and the resulting liquid poured into cold water, a yellow solid was obtained, m.p. 233° (decomp.), mixed m.p. with the selenocyanate 207°. This, from its colour, was obviously a nitrated product. When this same mixture was left for

a few minutes at 0°, 50° or 100°, there was no reaction.

4) With aqueous Nitric Acid Solutions.

(a) 25% nitric acid (25 cc. HNO_3 d 1.4, in 40 cc. H_2O.). About 60 cc. of this acid, 10 cc nitrobenzene and 1 g. of the selenocyanatewere boiled in a bolt-head flask for a few minutes. After about 10 minutes reaction occurred suddenly. Much water was then added and the nitrobenzene removed in steam. The yellow solid which appeared was crystallised from glacial acetic acid when its m.p. was 233°(decomp.) and was most likely a nitrated product.

(B) 26% Nitric Acid. When 1 g. of the selenocyanate was boiled with 90 cc. of this acid for 15 mins., the former would not go into solution and was unchanged at the end of the experiment.

(c) 30% Nitric acid.(20 cc. HNO_3 d 1.4 in 23 cc. H_2O). 0.5 g. selenocyanate, 43 cc. of the acid and 5 cc. nitrobenzene were boiled together for 15 minutes. After diluting the mixture with water, and removal of the nitrobenzene with steam, the precipitated solid was crystallised from alcohol. It was extremely soluble and only came down with difficulty. On leaving to crystallise slowly, a mixture of needle-shaped prisms and cubic crystals was obtained. It was considered probable that this might have been a mixture of the diselenide and the required seleninic acid, but when the experiment was repeated, and the mixture boiled for a longer time, the

selenocyanate was recovered unchanged.

(d) WIth 40% Nitric Acid. 0.5 g. of the selenocyanate were boiled with 32 cc. for 1 hour. Solution was complete in about 20 mins. Cubic crystals were obtained which had a very indefinite melting point. This substance wwas extremely soluble in alcohol and crystallised very badly from an aqueous mixture. Well-defined needles were obtained in one experiment, but this could not be repeated. A similar result was obtained when 50% nitric acid was used.

(e) With Nitric Acid, d 1.4. When the selenocyanate was boiled with concentrated nitric acid for half an hour, only yellow nitrated products were obtained.

(f) With Nitric Acid, d 1.5. 0.5 g. of the selenocyanate were treated with the acid (I) at 0° for half an hour, (II) at 20° for $1\frac{3}{4}$ hours, (III) by warming until solution was complete. In all cases yellow nitrated products were obtained.

5) Action of Bromine.

(a) Action of Bromine followed by hydrolysis with water. 3.5 g. of the selenocyanate were dissolved in hot chloroform, and 3.2g. bromine were added. The reaction caused the chloroform to boil and a small amount of an orange-coloured precipitate appeared. The chloroform was

removed by leaving the solution in an evacuated desiccator, and the residue was boiled with water for 15 minutes. The product was crystallised from alcohol. A substance of indefinite crystalline form, which melted 240-250°, first appeared; on recrystallisation the m.p. rose to 262°. From the mother liquor a substance which crystallised in white feathery needles was obtained which melted sharply and without decomposition at 271-272°. This was not the required seleninic acid, since the latter would decompose at its melting point. A similar mixture was obtained when dilute caustic soda was used instead of water to hydrolise the bromine complex.

(b) Action of sodium hypobromite. 1 g. of the selenocyanate was suspended in water and a solution of bromine in caustic soda added. The solution was at first pale yellow, but after boiling for a considerable time, it became considerably darker. After two hours the solution was acidified and a free acid was obtained so very much hydrated as to be a gel; this was dried on a water bath, and the resulting product was insoluble in alcohol, and scarcely soluble in glacial acetic acid. From the latter a substance was obtained, m.p. 257° (decomp.). From the mother liquor there was deposited a substance whose melting point was above 320°. The lower melting insoluble product was probably the seleninic acid, but because of the poor

yield and its low solubility, it was not considered worth while to prepare it in sufficient quantity to continue with the synthesis of 1:3-dimethyl-8-carboxy-phenoxselenine.

6) Action of Mercuric Oxide. A solution of the selenocyanate in absolute alcohol was boiled with freshly prepared mercuric oxide for one hour. The selenocyanate was recovered unchanged,

Attempted Oxidation of Di-5-carboxy-2-(3:5-xylenoxy-) phenyl Diselenide.

1) When the diselenide was heated for half an hour on a water bath with concentrated nitric acid, a pale yellow substance was obtained with a very high melting point (above 320°).

2) Bromine in excess was added to a solution of the diselenide in glacial acetic acid. The orange crystals precipitated were filtered off and treated with cold dilute caustic soda. The yellow flocculent substance produced on acidification was dried on a water bath and crystallised from glacial acetic acid in which it was only sparingly soluble. The resulting solid had m.p. 228-230° (decomp.). The substance was insoluble in alcohol.

My Thanks are due to Dr. E. E. Turner for much advice and encouragement during this work.

Mary C. Thompson.

Bedford College for Women,
Regent's Park, N.W.1.
July 1937.