The Configuration of Heterocyclic Antimony Compounds. Part III. Resolution and Racemisation of New Members of the 9-Stibiafluorene Series.*

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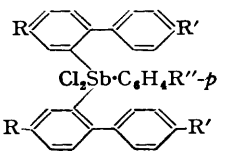
The synthesis and resolution of three new 9-stibiafluorenes is described. The specific rotation of these compounds varies considerably with the substituent present in the 2-position. Racemisation of 2-carboxymethoxy-9-*p*-tolyl-9-stibiafluorene observed in pyridine at four temperatures leads to an energy of activation of 14·4 kcal./mole, a value almost identical with that obtained for the corresponding 2-amino-compound in benzene. Unfortunately, it has not proved possible to prevent adventitious catalysis of the racemisation, a phenomenon shown by the amine and by both of the new acids examined. The cause of the dissymmetry of the stibiafluorenes is discussed, and further evidence in favour of a planar rather than a skew configuration of the tricyclic system is presented.

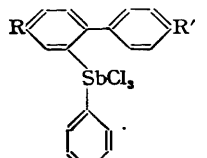
EARLIER papers in this series * described the synthesis and optical resolution of 2-carboxy- and 2-amino-9-*p*-tolyl-9-stibiafluorene and recorded unsuccessful attempts to obtain enantiomers of 9-*p*-carboxyphenyl-9-stibiafluorene (III; R′ = H, R″ = CO_2H) in which the tricyclic portion of the molecule is unsubstituted. The two compounds previously resolved have the salt-forming group at position 2 and have specific rotations of the same

* Parts I and II, *J.*, 1950, 3109; 1952, 4448.

order. It was considered desirable to study how changes in the position of polar substituents affected rotatory power and optical stability, and to synthesise an active stibiafluorene sufficiently soluble for convenient investigation of its racemisation rate, but not subject to the adventitious catalysis observed in the earlier work.



(I)



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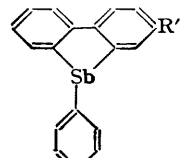


(III)

The first compound chosen was 9-*p*-carboxyphenyl-2-methyl-9-stibiafluorene (III; R′ = Me, R″ = CO_2H), an isomer of the compound (III; R′ = CO_2H, R″ = Me) in which this type of dissymmetry was first demonstrated. The acid was synthesised through the intermediate (II) by the method described in Part I (*J.*, 1950, 3109), and the (−)-1-phenylethylamine salt gave immediate evidence of resolution. The isolation of the optically pure enantiomers, however, proved difficult because the solubilities of the diastereoisomeric salts were too close for ready separation, and free acid frequently separated from the salts despite the presence of excess of free (−)-amine in the solvents used for recrystallisation. Ephedrine was more effective as a resolving agent and the (+)-acid (−)-ephedrine salt, $[\alpha]_D$ +48·5°, was readily obtained, but second-order asymmetric transformation prevented the isolation of the more soluble salt in an optically pure condition. In one resolution fractions representing 85% of the salt separated with $[\alpha]_D$ +20° to +28°, giving acid with $[\alpha]_D$ +40° to +50°, and decomposition of the residual 15% of salt gave inactive acid. The specific rotation of the (+)-acid, $[\alpha]_D$ +78·0°, is low compared with that of the positional isomer (III; R′ = CO_2H, R″ = Me), which has $[\alpha]_D$ +245°. Evidently the rotatory contribution of the tricyclic residue is considerably reduced when the carboxyl group is replaced by methyl.

In the second compound examined (III; R′ = OMe, R″ = CO_2H), the *p*-carboxy-group was retained but methyl was replaced by the more polar methoxy-group. 2-Amino-4′-methoxydiphenyl required for the synthesis of this compound was obtained by nitration of 4-diphenylyl benzoate (cf. Jones and Chapman, *J.*, 1952, 1829) followed by hydrolysis, methylation, and reduction. In the course of the nitration a new mononitrophenol was obtained and shown to be 4-hydroxy-2-nitrodiphenyl (Campbell and Morrill, *Chem. and Ind.*, 1953, 1229). The position of the nitro-group in the compound follows from its oxidation to benzoic acid and its conversion, through the same series of reactions, into the same stibiafluorene (III; R′ = OMe, R″ = CO_2H) as was obtained from 4′-methoxy-2-nitrodiphenyl. For this acid also, ephedrine proved the most effective resolving agent, and, in contrast to all the other acids examined, the salts were optically stable in solution. (+)-1-Phenylethylamine used in the first attempts to resolve the acid gave successive fractions of salt with $[\alpha]_D$ +20·5°, +9·5°, and −85·9°, but crystallisation of the first of these from ethanol, ethyl acetate, or *n*-butanol failed to raise the specific rotation. Repeated crystallisation from chloroform, however, gave a salt, $[\alpha]_D$ +80·2°, obviously still optically impure and, from analysis, probably contaminated with free acid. The specific rotation of the more soluble fraction rose to $[\alpha]_D$ −103·4° on crystallisation, and (−)-acid obtained from it had $[\alpha]_D$ −145·5° ±2°. That this had not reached optical purity was proved by resolution with ephedrine, which gave a (+)-acid (−)-ephedrine salt, $[\alpha]_D$ +93·5°, yielding (+)-acid, $[\alpha]_D$ +153·0° ±1°. This value is effectively double that of (III; R′ = Me, R″ = CO_2H), and again illustrates the striking effect of the polar methoxy-group on the rotatory power of stibiafluorenes. Though the solubility of this acid in chloroform and in benzene was greater than that of (III; R′ = Me, R″ = CO_2H) it was still too low for a convenient study of racemisation in these solvents. A preliminary examination of the (−)-acid in pyridine indicated a half-life of 41·3 hours at 22° and 26·3 hours at 38°, when calculated from the initial rate constants, but, after racemisation had

proceeded to the extent of 20—25%, the rate became progressively slower, and, as insufficient active acid was available for a detailed study, no further work on it was done.

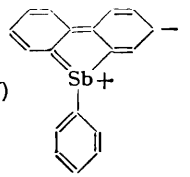
The search for a compound more suitable for determination of racemisation rates led to the study of 2-carboxymethoxy-9-*p*-tolyl-9-stibiafluorene (III; R′ = O·CH_2·CO_2H, R″ = Me), as introduction of the oxyacetic acid residue in place of carboxyl was expected to increase solubility, and the properties of the (±)-acid justified the choice. Initially attempts were made to obtain it through (III; R′ = OMe, R″ = Me) by demethylation, but this proved impracticable as antimony was eliminated and 4-methoxydiphenyl was the sole product, an illustration of the characteristic sensitivity of stibiafluorenes to halogen acids. Eventually the compound was obtained by the interaction of *p*-tolylstibonous chloride with diazotised 2-amino-4-ethoxycarbonylmethoxydiphenyl, followed by the usual cyclisation process. Resolution of the (±)-acid with ephedrine gave the less soluble (−)-acid (−)-ephedrine salt, $[\alpha]_D$ −147·5°, and the more soluble (+)-acid (−)-ephedrine salt, $[\alpha]_D$ +110·1°, and from these the active acids, $[\alpha]_D$ ±112·0° (*c* 0·3 in pyridine), were obtained. Isolation of the more soluble salt required considerable care as recrystallisation from boiling alcohol caused asymmetric transformation.

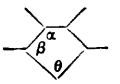
The specific rotation of this acid was considerably influenced by concentration, a characteristic not observed in any of the other stibiafluorenes. For example, values of $[\alpha]_D$ ranging from −112° to −145° were obtained when the acid was examined in pyridine at concentrations varying from 0·3 to 0·9 g. per 100 ml. Racemisation of the (−)-acid was initially followed in chloroform solution but consistent results could not be obtained despite rigorous precautions. For instance, a specimen of acid, $[\alpha]_D$ −112·0°, when examined in "AnalaR" chloroform not specially purified, had $[\alpha]_D$ −20·6° when first examined, and this fell to zero in 70 minutes. In carefully purified chloroform at 46·5°, two different specimens of optically pure acid gave racemisation rates of 1·7 and 1·8 × 10^{-3} min.$^{-1}$, and the rotation of (−)-acid in chloroform–acetic acid (1 : 1) at 26°, which had undergone only 15% racemisation in 29 hours, fell to zero in 55 minutes after the introduction of a trace of hydrochloric acid. The rate of this catalysed racemisation was 1·41 × 10^{-1} min.$^{-1}$ (half-life 5 minutes). Consistent results were obtained when the racemisation of portions of the same batch of acid was observed in pure pyridine at the same concentration, although a significant drop in rate occurred towards the end of the racemisation. Under these conditions the rate constants observed at 30°, 38°, 44°, and 46° were 3·8, 6·5, 10·4, and 12·7 × 10^{-4} min.$^{-1}$ respectively, and the resulting Arrhenius plot led to an energy of activation of 14·4 ± 0·5 kcal./mole, slightly lower than the value of 14·8 ± 0·5 obtained for the (+)-amine (III; R′ = NH_2, R″ = Me) when racemisation rates were measured in benzene (Part II, *loc. cit.*).

Weston (*J. Amer. Chem. Soc.*, 1954, **76**, 2645) has concluded, from calculations based on a potential-energy function derived from known vibrational frequencies and molecular dimensions, that optically active derivatives of tervalent antimony should be stable at room temperature. In assessing the stability of the pyramidal molecule to inversion, Weston calculated the half-life of "racemisation" of trimethylstibine to be two hours at 67°, and, despite the vast structural difference between trimethylstibine and the stibiafluorenes, we considered that comparison of the calculated with an experimentally determined value would be of interest. Using the slope of the Arrhenius plot, in each case, we found that the half-life of the (−)-oxyacetic acid (III; R′ = O·CH_2·CO_2H, R″ = Me) was 115 minutes at 67°, and that of the (+)-amine (III; R′ = NH_2, R″ = Me) was 116 minutes. This remarkable agreement must, unfortunately, be regarded as fortuitous because, on investigating the (−)-acid (III; R′ = CO_2H, R″ = Me) (Part I, *loc. cit.*) we found that the half-life, determined in pyridine at 70°, was 89 hours, and it seems improbable that introduction of CO_2H in place of O·CH_2·CO_2H should exert such a pronounced stabilising effect if the inversion of the pyramidal molecule were the sole mechanism of racemisation. Further, Weston calculated the maximum energy of activation for the "racemisation" to be 26·7 kcal./mole, whereas our value is only 15 kcal./mole, and the difficulty we have experienced in obtaining reproducible results with all the active stibiafluorenes examined indicates that adventitious catalysis cannot be excluded with certainty.

As yet, no firm answer can be given to the question whether the dissymmetry of the

stibiafluorenes results from the stable pyramidal arrangement of the bonds round antimony or from a skew configuration of the benzene rings in the diphenyl system. But additional evidence, indicating that the whole tricyclic system is planar, has been obtained by comparison of the ultraviolet spectra of triphenylstibine and 9-*p*-tolyl-9-stibiafluorene (Campbell and Poller, *Chem. and Ind.*, 1953, 1126). The main absorption band of the stibiafluorene shows a bathochromic shift of 320 Å compared with that of triphenylstibine, indicating considerably increased conjugation between the antimony atom and the condensed ring system. If this interpretation is correct, the molecule is best represented by the numerous canonical forms of type (IV), in which every bond in the five-membered ring will have some double-bond character and the C–Sb bond will be shorter than the normal 2·11 Å.

(IV) 



(V)

Scale drawings indicate that the five-membered ring can remain planar if α is 120°, β 107°, and θ 86° as in (V) (Part I, *loc. cit.*), but when the C–Sb bond length is shortened arbitrarily to 2·05 Å, the antimony bond angle becomes 89·6°, nearer the preferred value, and if α remains at 120°, β becomes 105°. Further, geometrical calculation shows that, if the benzene rings in the diphenyl system are rotated relative to one another, the total angular distortion in the five-membered ring will increase as shown in the Table 1. Obviously, the easing of

TABLE 1.

Angle between benzene rings	0°	10°	20°	30°
Total angular distortion	30°	33·4°	41·4°	51·3°
θ (Sb bond angle)	86°	86·4°	87·2°	88·6°

the strain at the antimony angle, θ, is small compared with the total strain in the other four angles of the five-membered ring, and it therefore seems unlikely that the stibiafluorene nucleus will show any serious deviation from the planar configuration. This conclusion is supported by the results of the recent *X*-ray crystal analysis of fluorene (Burns and Iball, *Nature*, 1954, **173**, 635) in which the maximum deviation from the plane is found to be 0·03 Å and the angles are α 107·6°, β 109·6°, and θ 105·6°.

A final decision on this problem should be possible through *X*-ray examination, and preliminary measurements on 9-*p*-ethoxycarbonylphenyl-9-stibiafluorene have been made by Mr. B. Chaudhuri, through the kindness of Dr. Lipson, Manchester. Crystal data so far available are included in the Experimental section and it is hoped that further work may give precise information on the shape of the stibiafluorene molecule.

EXPERIMENTAL

Substituted 2-Nitro- and 2-Amino-diphenyls.—4-Methyl-2-nitrodiphenyl was prepared by a modification of the method used by Ritchie (*J. Proc. Roy. Soc. New South Wales*, 1945, **78**, 169). 2-Nitro-*p*-toluidine (NH_2 = 1) (76 g.) was finely ground, stirred into a mixture of concentrated hydrochloric acid (180 ml.) and water (70 ml.), and diazotised with a saturated solution of sodium nitrite (35 g.). The diazonium salt solution was filtered and poured into ice-cold benzene (1100 ml.), followed by a solution of sodium acetate (180 g.) in water (350 ml.). The mixture was stirred vigorously for 3 hr. at 10° and then for 48 hr. at room temperature. The upper layer was separated, the benzene removed by distillation, and the residual oil extracted several times with light petroleum (b. p. 40—60°). The extracts were filtered through a short column of alumina, the dark impurities remaining as a slowly-moving band, while the required compound appeared in the filtrate. Removal of the solvent from this filtrate left a pale orange-yellow, viscous oil which rapidly crystallised. From light petroleum (b. p. 40—60°), containing a trace of methylene chloride, this separated as pale yellow crystals, m. p. 48·5—50° (Found: C, 73·3; H,

5·4; N, 6·4. Calc. for $C_{13}H_{11}O_2N$: C, 73·2; H, 5·2; N, 6·6%). This compound has previously been reported as an oil, b. p. 208°/11 mm. (Ritchie, *loc. cit.*). It was reduced by the method recommended in *Org. Synth.*, Vol. II, p. 448, for the reduction of 2-nitrofluorene. The amine was isolated as the hydrochloride (m. p. 194—200°), and gave an acetyl derivative, m. p. 147—148°, which corresponds to the reported value for 2-acetamido-4-methyldiphenyl (Ritchie, *loc. cit.*).

Nitration of 4-Diphenylyl Benzoate.—A mixture of acetic anhydride (60 ml.) and fuming nitric acid (30 ml.) was added slowly to a well-stirred suspension of 4-diphenylyl benzoate (55 g.) in acetic anhydride (400 ml.) at 20—30°. Stirring was continued for a further 4 hr. The mixture was then filtered and the solid (A), a mixture of 2'- and 4'-nitro-4-diphenylyl benzoates, washed with water and dried. When the filtrate was diluted cautiously with water (180 ml.) below 25°, a yellow crystalline solid (B) slowly separated.

Fraction (A) was extracted with hot acetone (400 ml.), leaving a residue of 4'-nitro-4-diphenylyl benzoate, m. p. 208—212° (20·5 g.), and the filtrate, on cooling and dilution with a little water, gave yellow crystals of 2'-nitro-4-diphenylyl benzoate, m. p. 145—155° (11·4 g.) (Jones and Chapman, *J.*, 1952, 1829, record m. p. 212° and m. p. 156—157° respectively).

The mixture (B) was not easily separable by crystallisation and accordingly the benzoates were hydrolysed by boiling potassium hydroxide (10% in 70% ethanol) (5 min.). The deep red solution was cooled and filtered from a solid residue consisting mainly of potassium salts of polynitro-compounds. The filtrate was just acidified with dilute hydrochloric acid and neutralised with excess of saturated sodium hydrogen carbonate solution. The oily phenols which separated were extracted with ether and the extracts washed once with saturated sodium hydrogen carbonate solution. The ether solution was then extracted twice with 16% sodium hydroxide solution. Addition of excess of acetic anhydride to the combined alkaline extracts caused almost instantaneous acetylation, and, from the mixture of acetates deposited, boiling ethanol (2 × 75 ml.) extracted 2'-nitro-4-diphenylyl acetate, m. p. 122—124° (6·8 g.) (Copp and Walls, *J.*, 1950, 311, record m. p. 122°). The insoluble residue on recrystallisation from acetone, or better, ethyl acetate, gave *2-nitro-4-diphenylyl acetate*, m. p. 169° (4·0 g.), as transparent chunky prisms (Found: C, 65·4; H, 4·1. $C_{14}H_{11}O_4N$ requires C, 65·4; H, 4·3%).

Characterisation of 2-Nitro-4-diphenylyl Acetate.—The compound was hydrolysed by boiling 10% alcoholic potassium hydroxide (5 min.) and the *phenol* was recrystallised from 1 : 1 benzene–light petroleum (b. p. 60—80°); it had m. p. 141—143° (Found: C, 67·1; H, 4·4. $C_{12}H_9O_3N$ requires C, 67·0; H, 4·2%). It gave a *benzoate*, m. p. 105—106° (Found: C, 71·5; H, 4·1. $C_{19}H_{13}O_4N$ requires C, 71·4; H, 4·2%), and a methyl ether, m. p. 72° (Found: C, 68·1; H, 5·0%. Calc. for $C_{13}H_{11}O_3N$: C, 68·1; H, 4·8%). Copp and Walls (*loc. cit.*) report 4-methoxy-2-nitrodiphenyl, m. p. 75—77°.

Oxidation of the phenol (1·5 g.) in sodium hydroxide with potassium permanganate gave benzoic acid (0·5 g.), m. p. and mixed m. p. 121—122°. This proves that the nitro- and the hydroxyl group are present in the same ring, and as the known, steam-volatile 4-hydroxy-3-nitrodiphenyl has m. p. 66°, the present compound, m. p. 141—143°, must be 4-hydroxy-2-nitrodiphenyl. This has been substantiated by conversion of both this compound and the isomeric 4-hydroxy-2'-nitrodiphenyl into the same heterocyclic antimony compound, 9-*p*-ethoxycarbonylphenyl-2-methoxy-9-stibiafluorene (see p. 1667 and Table 2).

Attempted Reduction of 2'-Nitro-4-diphenylyl Benzoate.—The reduction of this compound with iron and acetic acid, stannous chloride and hydrochloric acid, or palladised charcoal and *cyclo*hexene was unsuccessful; only unchanged starting material or brightly coloured decomposition products were isolated. Reduction in dilute acetic acid or in ethanol with zinc dust gave a poor yield of a *compound*, m. p. 127°, which analysed correctly for the required amine (Found: C, 79·0; H, 5·5. $C_{19}H_{15}O_2N$ requires C, 78·9; H, 5·2%), but which could not be diazotised under normal conditions and did not form a stannichloride or a satisfactory acetyl derivative.

2'-Amino-4-methoxydiphenyl—2'-Nitro-4-diphenylyl benzoate was hydrolysed by boiling 10% alcoholic potassium hydroxide (5 min.), and the phenol, m. p. 113—116°, was methylated in sodium hydroxide with methyl sulphate giving 4-methoxy-2'-nitrodiphenyl, m. p. 58—62° (Jones and Chapman, *loc. cit.*, recorded m. p. 64°; Copp and Walls, *loc. cit.*, gave m. p. 60—60·5°). Reduction by zinc dust in neutral solution (*Org. Synth.*, Vol. II, p. 448) gave 2-amino-4'-methoxydiphenyl, characterised as the benzoyl derivative, m. p. 84—85°, a value considerably lower than that recorded by Copp and Walls (*loc. cit.*) who found m. p. 108° (Found: C, 79·2; H, 5·8. Calc. for $C_{20}H_{17}O_2N$: C, 79·2; H, 5·7%), and the *p*-nitrobenzoate, m. p. 163—164° (Copp and Walls, *loc. cit.*, give m. p. 164—165°).

2-Amino-4-methoxydiphenyl.—This was prepared from the corresponding nitro-compound by a similar reduction, isolated as the hydrochloride, and characterised as the *p*-nitrobenzoate, m. p. 168—169°, and the *benzoyl derivative*, m. p. 144—145° (Found: C, 78·8; H, 5·7. $C_{20}H_{17}O_3N$ requires C, 79·2; H, 5·7%).

2'-Nitro-4-diphenylyloxyacetic Acid.—4-Hydrozy-2'-nitrodiphenyl (18·2 g.) was dissolved in a solution of sodium hydroxide (12 g.) in water (35 ml.). To this solution was added monochloroacetic acid (16 g.) and sodium hydroxide (6·9 g.) in water (18 ml.), and the whole heated for 2 hr. on a boiling-water bath. A further portion of monochloroacetic acid (16 g.) was then added followed by sodium hydroxide solution (16%) until the red colour of the phenoxide ion was restored, and heating was continued for a further hour. The product consisted of unchanged phenol (4 g.) and crude 2'-nitro-4-diphenylyloxyacetic acid, m. p. 147—156° (17·3 g.). Two recrystallisations from ethyl acetate–light petroleum (b. p. 60—80°) (2 : 1) gave the pure *acid*, m. p. 160—161° (13 g.) (Found: C, 61·6; H, 4·1%; equiv., 273·5. $C_{14}H_{11}O_5N$ requires C, 61·5; H, 4·1%; equiv., 273·2).

Ethyl 2'-Amino-4-diphenylyloxyacetate.—Esterification of 2'-nitro-4-diphenylyloxyacetic acid (55 g.) in absolute ethanol (500 ml.) containing dry hydrogen chloride gave a viscous yellow oil (56 g.), b. p. 180—185°/8 × 10^{-4} mm., which failed to crystallise. This was reduced in neutral solution with zinc dust, and the crude *amino-ester* (37·6 g.) was distilled, having b. p. 172—180°/8 × 10^{-3} mm., m. p. 55—56° (Found: C, 70·5; H, 6·4. $C_{16}H_{17}O_3N$ requires C, 70·8; H, 6·3%). The aqueous mother-liquor from the reduction, on cooling to 0°, deposited the amino-acid (9 g.), which was esterified with absolute ethanol and dry hydrogen chloride, giving the amino-ester hydrochloride, m. p. 180—186° (8 g.).

Preparation of Diarylstibinic Chlorides (II).—Compounds of this type were obtained in 20—35% yield by the reaction described in Part I (*J.*, 1950, 3109). The diazoniúm antimony chloride double salt obtained from the required amine was decomposed in the presence of a molecular proportion of either *p*-ethoxycarbonylphenyl- or *p*-tolyl-stibonous chloride in ethanol by addition of a catalytic quantity of copper bronze. Any triarylstibine dichloride (I) formed usually crystallised from the mixture at this stage and was removed, and the diarylstibinic chloride (II) was isolated from the filtrate by precipitation with hydrochloric acid or by crystallisation, after evaporation (vacuum) of most of the ethanol. In this way, the double salt prepared from 2-amino-4-methyldiphenyl hydrochloride (8 g.) gave p-*ethoxycarbonylphenyldi-(4-methyl-2-diphenylyl)stibine dichloride* (I; R = Me, R' = H, R'' = CO_2Et), m. p. 252° (2 g.) (Found: C, 62·4; H, 4·9. $C_{33}H_{31}O_2Cl_2Sb$ requires C, 62·2; H, 4·6%), and p-*ethoxycarbonylphenyl-4-methyl-2-diphenylylstibinic chloride* (II; R = Me, R' = H, R'' = CO_2Et), m. p. 164—166° (4 g.) (Found: C, 48·0; H, 3·7. $C_{22}H_{20}O_2Cl_3Sb$ requires C, 48·5; H, 3·7%). Both compounds were recrystallised from carbon tetrachloride. Reduction of (II) with stannous chloride in ethanol gave the corresponding *stibinous chloride*, m. p. 121—122° (Found: C, 55·5; H, 4·3. $C_{22}H_{20}O_2ClSb$ requires C, 55·8; H, 4·3%). When 2-amino-4'-methoxydiphenyl hydrochloride (15 g.) was coupled with *p*-tolylstibonous chloride, a negligible quantity of insoluble dichloride separated and was not characterised. Evaporation of the filtrate gave *4'-methoxy-2-diphenylyl-p-tolylstibinic chloride* (II; R = H, R' = OMe, R'' = Me), m. p. 153—154° (5·1 g.) (Found: C, 47·6; H, 3·5. $C_{20}H_{18}OCl_3Sb$ requires C, 47·8; H, 3·6%). The same amine hydrochloride (10·9 g.) with *p*-ethoxycarbonylphenylstibonous chloride gave p-*ethoxycarbonylphenyldi-(4'-methoxy-2-diphenylyl)stibine dichloride* (I; R = H, R' = OMe, R'' = CO_2Et), m. p. 247—248° (1 g.) (Found: C, 58·8; H, 4·6. $C_{35}H_{31}O_4Cl_2Sb$ requires C, 59·4; H, 4·4%), and p-*ethoxycarbonylphenyl-4'-methoxy-2-diphenylylstibinic chloride*, m. p. 169—170° (II; R = H, R' = OMe, R'' = CO_2Et) (5·2 g.) (Found: C, 46·5; H, 3·5. $C_{22}H_{20}O_3Cl_3Sb$ requires C, 47·1; H, 3·6%). Similarly, the isomeric 2-amino-4-methoxydiphenyl hydrochloride (12 g.) gave only traces of dichloride and p-*ethoxycarbonylphenyl-4-methoxy-2-diphenylylstibinic chloride* (II; R = OMe, R' = H, R'' = CO_2Et), m. p. 139—141° (5·5 g.), after crystallisation from light petroleum (b. p. 100—120°) (Found: C, 47·6; H, 3·6%). Ethyl 2'-amino-4-diphenylyloxyacetate (27 g.) reacted with *p*-tolylstibonous chloride to give the insoluble *di-4'-carboxymethoxy-2-diphenylyl-p-tolylstibine dichloride* (I; R = H, R' = $O{\cdot}CH_2{\cdot}CO_2Et$, R'' = Me), m. p. 196—197° (3·5 g.) (Found: C, 58·5; H, 4·9. $C_{39}H_{37}O_6Cl_2Sb$ requires C, 59·0; H, 4·7%), and addition of hydrochloric acid to the filtrate precipitated *4'-ethoxycarbonylmethoxy-2-diphenylyl-p-tolylstibinic chloride* (II; R = H, R' = $O{\cdot}CH_2{\cdot}CO_2Et$, R'' = Me), m. p. 131—132° (10 g.), after recrystallisation from benzene–light petroleum (b. p. 60—80°) (1 : 2) (Found: C, 48·5; H, 4·2. $C_{23}H_{22}O_3Cl_3Sb$ requires C, 48·1; H, 3·9%). On evaporation of the mother-liquor at room temperature (vacuum) a further fraction of crystalline material (5 g.) separated. On crystallisation from benzene–light petroleum (b. p. 60—80°),

this gave *4'-ethoxycarbonylmethoxy-2-diphenylylstibonous chloride*, m. p. 142—143° (Found: C, 43·6; H, 3·7; Sb, 27·0. $C_{16}H_{15}O_3Cl_2Sb$ requires C, 42·9; H, 3·4; Sb, 27·2%).

Preparation of 9-Stibiafluorenes (III).—The diarylstibinic chlorides were converted into the corresponding acids by addition, in acetone solution, to aqueous sodium acetate. The precipitated acids, after thorough drying at room temperature (vacuum) were cyclised by dehydration in acetic anhydride containing sulphuric acid, and the crude 9-stibiafluorene oxides were isolated by dilution with a large volume of water. The oxides were not characterised but were reduced, while still moist, with stannous chloride in acetone (*J.*, 1952, 4448). The pure 9-stibiafluorenes were obtained in 50—65% yield, usually after one crystallisation. The properties of the *compounds* are listed in Table 2.

TABLE 2. *9-Stibiafluorenes* (III).

				Found (%)				Required (%)		
R'	R''	M. p.	Solvent	C	H	Sb	Formula	C	H	Sb
Me	CO_2Et	155—156°	EtOAc–EtOH	60·0	4·4	—	$C_{22}H_{19}O_2Sb$	60·4	4·4	27·9
Me	CO_2H	240	AcOH	58·4	3·7	29·6	$C_{20}H_{15}O_2Sb$	58·7	3·7	29·8
OMe	Me	117—118	MeOH	60·6	4·3	30·9	$C_{20}H_{17}OSb$	60·8	4·3	30·8
OMe	CO_2Et	147—148	EtOAc–EtOH	58·0	4·5	—	$C_{22}H_{19}O_3Sb$	58·3	4·2	26·9
OMe	CO_2H	231	AcOH	57·0	3·6	28·6	$C_{20}H_{15}O_3Sb$	56·5	3·6	28·6
$O{\cdot}CH_2{\cdot}CO_2Et$	Me	132—133	EtOH	59·8	4·1	—	$C_{22}H_{21}O_2Sb$	59·1	4·5	26·1
$O{\cdot}CH_2{\cdot}CO_2H$	Me	164—165	AcOH	57·1	3·9	27·8	$C_{21}H_{17}O_3Sb$	57·4	3·9	27·7

The free acids were obtained from the corresponding esters by hydrolysis with 5% alcoholic potassium hydroxide. An attempt to demethylate (III; R' = OMe; R'' = Me) by hydrobromic acid in acetic acid or by aluminium chloride in benzene resulted in extensive decomposition, and the only product isolated from either experiment was 4-methoxydiphenyl, m. p. and mixed m. p. 88—89°.

Resolutions of 9-p-Carboxyphenyl-2-methyl-9-stibiafluorene.—Rotations were measured at room temperature in " AnalaR " chloroform (*c* 0·2—0·5) in 2-dm. tubes, unless otherwise stated.

Preliminary experiments showed that the acid formed salts with cinchonine, quinine, ephedrine, and (−)-1-phenylethylamine. The cinchonine salt was separated into three fractions varying in specific rotation from $[\alpha]_D$ + 63·5° to 69·8°, but acid regained from them was optically inactive. The *quinine salt*, m. p. 205—206°, $[\alpha]_D$ − 67·4° (Found: C, 65·1; H, 5·6. $C_{20}H_{15}O_2Sb,C_{20}H_{24}O_2N_2$ requires C, 65·5; H, 5·4%), proved equally ineffective as a resolving agent, and the quinidine salt separated as a syrup and did not crystallise. Results obtained with (−)-1-phenylethylamine were initially encouraging for, when the acid (5 g., 0·012 mole) and (−)-amine (3 g., 0·025 mole) were dissolved together in ethyl acetate (900 ml.) the first crop of crystals (5·36 g.) had $[\alpha]_D$ −6·7° and the second crop (0·76 g.) had $[\alpha]_D$ +15·8°. However, even after eight recrystallisations of the first fraction from chloroform–ethanol (1 : 2), the *salt* obtained (0·1 g.; $[\alpha]_D$ −79·3°) was not optically pure (Found: C, 63·4; H, 4·9. $C_{20}H_{15}O_2Sb,C_8H_{11}N$ requires C, 63·4; H, 4·9%). Recrystallisation of the second crop, $[\alpha]_D$ +15·8°, gave two fractions, comprising all the material, but these had $[\alpha]_D$ −7·9° and −16·1°, indicating that second-order asymmetric transformation had occurred. A second attempt using (+)-1-phenylethylamine was even less satisfactory, the most dextrorotatory salt obtained having $[\alpha]_D$ +59·2°. It was essential to recrystallise the salts from solvent containing free amine, otherwise the solid which separated was contaminated with free acid. The m. p.s of all fractions were indeterminate, ranging from 200° to 215°.

Resolution with ephedrine. The acid (8·2 g., 0·02 mole) was suspended in boiling ethanol (150 ml.), and ephedrine hydrate (4·0 g., 0·022 mole) added. Addition of chloroform (20 ml.) gave an almost clear solution, which was filtered and set aside overnight. The first fraction of salt (5·5 g.) had $[\alpha]_D$ +7·5°, and three recrystallisations of this from the minimum volume of ethanol gave the pure *(+)-acid (−)-base salt*, m. p. 200—201°, $[\alpha]_D$ +48·5° (1·8 g.), as flat needles (Found: C, 62·3; H, 5·3. $C_{20}H_{15}O_2Sb,C_{10}H_{15}ON$ requires C, 62·7; H, 5·3%). The second fraction of salt (1·25 g.) obtained by evaporation (vacuum) of the mother-liquor to 80 ml. had $[\alpha]_D$ −34·4°, but contained free acid, and recrystallisation of this, and also of the third fraction (1·75 g.), $[\alpha]_D$ −6·1°, failed to give the optically pure (−)-acid (−)-base salt. The most lævorotatory fraction obtained had $[\alpha]_D$ −52·3°.

In a second resolution ephedrine (4·5 g., 0·025 mole) was added to the acid (8·2 g., 0·02 mole) in ethanol (200 ml.) and chloroform (20 ml.). The first fraction was separated after 24 hr., and later fractions were obtained by evaporating the filtrate (vacuum) at room temperature

until crystallisation started and then warming it to effect solution again. This procedure separated the salt into fractions: 4·5 g., $[\alpha]_D$ +28·3; 1·45 g., $[\alpha]_D$ +21·5°; 1·05 g., $[\alpha]_D$ +19·7°; 1·55 g., $[\alpha]_D$ +27·2°; and 1·8 g., $[\alpha]_D$ +25·2°. From the residual mother-liquor acid regained (0·92 g.) was optically inactive. Three recrystallisations of the first fractions gave pure (+)-acid (−)-base salt (1·9 g.), m. p. 200—201°, $[\alpha]_D$ +48·6°, and a further 1·1 g. were obtained from later fractions. Again all attempts to obtain the (−)-acid (−)-base salt in optically pure condition failed, but one small fraction isolated had $[\alpha]_D$ −64·7° (Found: C, 62·4; H, 5·7%).

Resolution of 9-p-*Carboxyphenyl*-2-*methoxy*-9-*stibiafluorene*.—The acid formed crystalline salts with (+)-1-phenylethylamine and with ephedrine and the solubility relations of the former appeared suitable for resolution. Accordingly the acid (5 g., 0·012 mole) and the (+)-amine (1·86 g., 0·024 mole) were dissolved together in boiling ethanol (500 ml.), and a first crop of *salt*, X1, m. p. 195—196°, $[\alpha]_D$ +20·5° (1·8 g.), was collected after 2 hr. (Found: C, 61·1; H, 4·9. $C_{20}H_{15}O_3Sb,C_8H_{11}N$ requires C, 61·6; H, 4·8%). A second crop, X2, $[\alpha]_D$ +9·4° (2·7 g.), was obtained when the filtrate was kept overnight; and X3, $[\alpha]_D$ −85·9° (0·5 g.), was isolated after evaporation to 50 ml. Initially X1 appeared to be optically pure, as recrystallisation from ethanol or ethyl acetate or *n*-butanol failed to raise the specific rotation. However, on crystallisation from chloroform containing a little (+)-amine, the $[\alpha]_D$ increased slowly. X2 on crystallisation from ethanol gave a further fraction of salt, $[\alpha]_D$ +20·4°, and this was combined with X1 and recrystallised eight times from chloroform to give a salt, $[\alpha]_D$ +80·5° (0·17 g.). Obviously this was still optically impure by comparison with X3. Two recrystallisations of X3 from ethanol gave 0·12 g. of salt, m. p. 199—201°, $[\alpha]_D$ −103·4° ±3° (Found: C, 61·6; H, 5·2%), but this had not reached optical purity. The unsatisfactory results of this resolution were caused partly by dissociation of the salt and separation of free acid, and partly by second-order asymmetric transformation. Evidence for this was obtained when a fraction of salt with zero rotation was crystallised from chloroform and recovered quantitatively with $[\alpha]_D$ +18·9°.

Resolution with ephedrine. The acid (0·8 g.) was added to a solution of ephedrine hydrate (0·4 g., 1·2 equivs.) in boiling ethanol (50 ml.). After 48 hr., the first fraction of salt, $[\alpha]_D$ +14·9° (0·7 g.), was collected. Three recrystallisations of this from absolute ethanol containing 0·2% of ephedrine gave pure (+)-acid (−)-base salt, as small plates, m. p. 193—196°, $[\alpha]_D$ +93·5° ±1·2°, unchanged by further crystallisations (Found: C, 60·5; H, 5·3. $C_{20}H_{15}O_3Sb,C_{10}H_{15}ON$ requires C, 61·0; H, 5·1%). The second fraction of salt, which separated after concentration, had $[\alpha]_D$ −40°, and two recrystallisations of this gave 0·1 g. of salt, m. p. 188—191°, $[\alpha]_D$ −94·7°. Unfortunately lack of material prevented the isolation of the pure (−)-acid (−)-base salt. This should be possible as the ephedrine salts were optically stable in solution and no evidence of asymmetric transformation was observed.

Resolution of 9-*Tolyl*-9-*stibiafluorenyl*-2-*oxyacetic Acid*.—A solution of the acid (6·2 g.) and ephedrine hydrate (3·1 g., 1·2 equivs.) in boiling ethanol (50 ml.) cooled for 5 hr. deposited crop A1 (2·55 g.), $[\alpha]_D$ −128·5°, crop A2 (3·8 g.), $[\alpha]_D$ +42·4°, after a further 5 hr., and crop A3 (0·65 g.), $[\alpha]_D$ +91·0°, after concentration to 5 ml. The presence of excess of ephedrine in the mother-liquor prevented the crystallisation of the residual salt. Two recrystallisations of A1 from ethanol gave (−)-*acid* (−)-*base salt*, m. p. 184°, $[\alpha]_D$ −147° ±1·5° (1·5 g.) unchanged by further crystallisation (Found: C, 61·9; H, 5·5; Sb, 20·1. $C_{21}H_{17}O_3Sb,C_{10}H_{15}ON$ requires C, 61·6; H, 5·3; Sb, 20·1%). A second fraction from the second crystallisation had $[\alpha]_D$ −146·0°. Recrystallisation of A2 provided a further fraction of salt with $[\alpha]_D$ −147·1°, and second-order asymmetric transformation was demonstrated when a salt, $[\alpha]_D$ −3·3° (1·2 g.), was recrystallised and recovered in two fractions, $[\alpha]_D$ −147·0° ±2° (0·7 g.), and $[\alpha]_D$ −90·3° (0·4 g.). However, two recrystallisations of A3 gave (+)-acid (−)-base salt, m. p. 173°, $[\alpha]_D$ +110·1° ±2·0° (0·12 g.), which must have been substantially optically pure, though analysis indicated that it contained free acid (Found: C, 60·0; H, 5·4%). ($[\alpha]_D$ were measured in absolute ethanol, *c* 0·2 approx.)

Isolation of the Optically Active Acids.—Decomposition of an alcoholic solution of the salts with 0·1N-sulphuric acid at −20° proved the best method of isolating the active acids. Decomposition at room temperature or insufficient washing of the precipitated acid resulted in slight racemisation. Specific rotations were measured in pyridine (*c* 0·2—0·5), and the properties of the *acids* are listed in Table 3.

Racemisation of the Optically Active Acids.—The pyridine (May and Baker's pure) used for racemisation experiments was dried over potassium hydroxide and fractionally distilled. " AnalaR " chloroform was shaken with anhydrous sodium carbonate before use, a precaution which was found essential, for, when it was omitted, low values of $[\alpha]_D$ were obtained initially

and rapid racemisation occurred. The acids (0·05—0·2 g.) were dissolved in 20 ml. of solvent at the required temperature and racemisation was observed in a jacketed polarimeter tube (l = 2 dm.). Rate constants [$k = (\ln \alpha_0/\alpha_t)/t$ in min.$^{-1}$] were evaluated graphically, from the readings given in Table 4. In every case, the racemisation was followed for considerably longer

TABLE 3. *Optically active acids* (III).

R′	R″	Resolving agent	Salt, $[\alpha]_D$	Solvent	Acid $[\alpha]_D$ in pyridine	M. p.	Found (%) C	Found (%) H
Me	CO_2H	(−)-CHPhMe·NH_2	− 79·3°	$CHCl_3$	− 69·2°	225—238°	59·0	3·9
Me	CO_2H	Ephedrine	+ 48·5	$CHCl_3$	+ 78·0	224—232	58·6	3·9
OMe	CO_2H	(−)-CHPhMe·NH_2	−103·4	$CHCl_3$	−145·5	212—215	56·5	3·7
OMe	CO_2H	Ephedrine	+ 93 5	$CHCl_3$	+153·0	221—223	56·4	3·8
O·CH_2·CO_2H	Me	Ephedrine	−147·5	EtOH	−112·5	149—151	55·8	4·3 (+ H_2O)
O·CH_2·CO_2H	Me	Ephedrine	+110·1	EtOH	+112·0	149—151	55·6	4·2 (+ H_2O)

TABLE 4. *Rates of racemisation.*

Compound	Temp.	Wt. (g.) in 20 ml.	Initial α_D	Final α_D	Time (min.)	10^4k	Half-life (hours)
(III) R′ = OMe, R″ = CO_2H	22°	0·1094	+1·68°	+1·52°	340	2·8	41·3
	38	0·0625	+0·89	+0·76	360	4·4	26·3
(III) R′ = O·CH_2·CO_2H, R″ = Me	30	0·1814	−2·64	−2·03	725	3·8	30·4
	38	0·1818	−2·63	−1·80	643	6·5	17·8
	44	0·1431	−1·74	−1·11	386	10·4	11·1
	46	0·1755	−2·54	−1·41	481	12·7	9·1
	38	0·1042	+0·95	+0·64	418	9·5	12·2
(III) R′ = O·CH_2·CO_2H, R″ = Me	46·5	0·0713 *	−0·83	−0·49	320	16·7	6·9
	46·5	0·058 *	−0·50	−0·22	454	18·4	6·3
(III) R′ = CO_2H, R″ = Me	70	0·0500	−1·22	−0·94	1920	1·3	88·9

* In $CHCl_3$; other experiments in pyridine.

but the rate gradually decreased. In the last experiment tabulated, 0·2500 g. of the active acid was dissolved in 100 ml. of pyridine at 18·5°. Eight small flasks were filled with the solution, placed in a thermostat at 70°, and withdrawn at intervals, and cooled rapidly, and the readings were taken at 18·5°.

Crystal Data for 9-p-*Ethoxycarbonylphenyl*-9-*stibiafluorene*.—Triclinic; cell dimensions, a = 9·05, b = 15·68, c = 8·05 Å; α = 112·7°, β = 99·6°, γ = 113·97°. Two molecules per unit cell, space group $P\bar{1}$, d calc., 1·60 (found 1·62). The co-ordinates of the Sb atoms are x = 2·24, y = 1·70, z = 0·88 Å.

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