250. *The Synthesis and Stereochemistry of Some Tervalent Arsenic Compounds.*

By I. G. M. Campbell and R. C. Poller.

The synthesis of substituted 9-arsafluorenes by several different routes, and the optical resolution of two of them, are described. The enantiomers of 9-*p*-carboxyphenyl-2-methoxy-9-arsafluorene, $[\alpha]_D$ $\pm 160°$, are optically stable at room temperature in pyridine. Racemisation occurs in chloroform–ethanol, slowly at 70° and more rapidly at 111°; at 111° the half-life is 17 min. The catalytic effect of hydrogen chloride on the racemisation is demonstrated and shown to be less pronounced in this series than in the corresponding 9-stibiafluorenes. (+)-2-Amino-9-phenyl-9-arsafluorene possesses high optical stability, for the specific rotation, $[\alpha]_D$ $+255°$ (in ethanol), is unchanged after 1 hour's heating at 110°.

Enantiomers of simple 3-covalent arsenic compounds have not as yet been isolated although, from physical evidence, their configuration is undoubtedly pyramidal, so that compounds in which arsenic is attached to three different groups should be capable of optical resolution. Various values for the H–As–H angle in arsine have been published; one of the most recent, 91·5°, has been calculated by Nielsen from moments of inertia [1] and is in good agreement with that of 92° obtained from microwave spectra.[2] Trimethylarsine and arsenic tribromide have been examined by electron diffraction and the bond angles found to be 96° and 100° respectively.[3] Perhaps of more importance than the bond angle to the practical stereochemist is some estimate of the ease of inversion of these pyramidal molecules, and this has been given by Weston [4] who, from molecular dimensions and vibration frequencies, has calculated the potential-energy barrier to inversion. The results of this calculation are expressed as a temperature at which the half-life of "racemisation" would be 2 hr., and the value found for trimethylarsine is +107° c. If this estimate is valid, racemisation by inversion should be too slow to prevent the resolution of a dissymmetric tertiary arsine.

Nevertheless, all attempts to isolate enantiomers of suitably substituted arsines have failed [5] except in the case of the phenoxarsines,[6] where the dissymmetry may possibly arise from the folding of the molecule. In this investigation we chose to examine substituted 9-arsafluorenes, in which the arsenic atom is held in a chemically stable five-membered ring, because several members of the analogous 9-stibiafluorene series have been obtained in optically active forms,[7] and it seemed likely that the optical and chemical stability of the corresponding arsenic compounds would be even more favourable for resolution experiments.

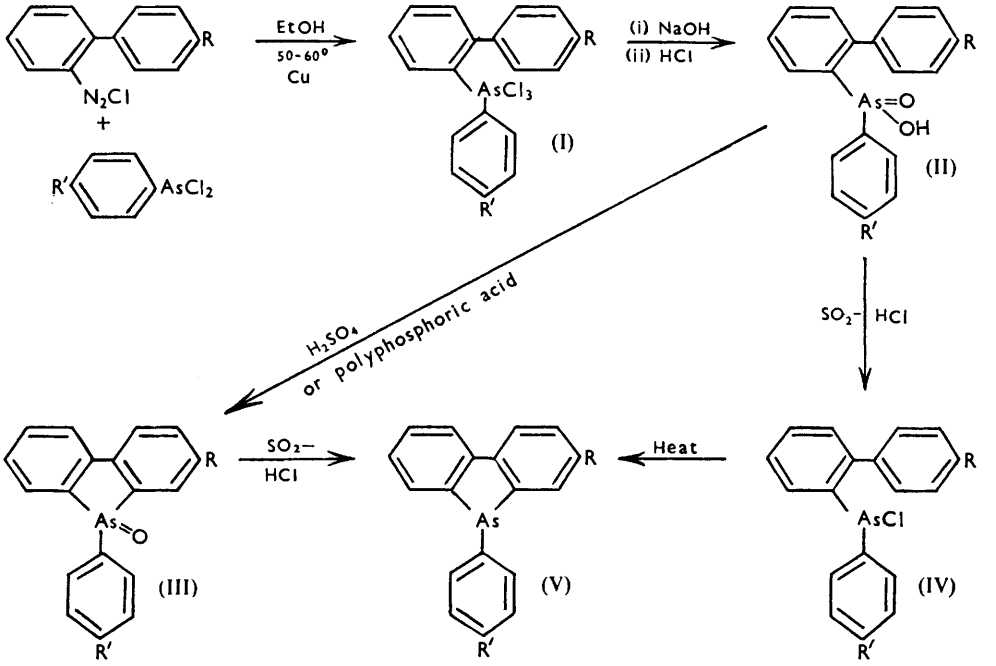
9-Arsafluorenes were first prepared by Aeschlimann *et al.*[8] by cyclisation of 2-diphenylylarsonic acid, and, more recently, Feitelsohn and Petrow,[9] and Garascia and Mattei,[10] have

[1] Nielsen, *J. Chem. Phys.*, 1952, **20**, 1955.
[2] Loomis and Strandberg, *Phys. Rev.*, 1951, **81**, 798.
[3] Allen and Sutton, *Acta Cryst.*, 1950, **3**, 46.
[4] Weston, *J. Amer. Chem. Soc.*, 1954, **76**, 2645.
[5] Kamai, *Ber.*, 1935, **68**, 960, 1893; *J. Gen. Chem.* (*U.S.S.R.*), 1940, **10**, 683; 1942, **12**, 104; 1947, **17**, 2178.
[6] Lesslie and Turner, *J.*, (*a*) 1934, 1170; (*b*) 1935, 1268; 1936, 730; Lesslie, *J.*, 1938, 1001; 1949, 1183.
[7] Campbell and Morrill, *J.*, 1955, 1662.
[8] Aeschlimann, Lees, McLeland, and Nicklin, *J.*, 1925, 66.
[9] Feitelsohn and Petrow, *J.*, 1951, 2279.
[10] Garascia and Mattei, *J. Amer. Chem. Soc.*, 1953, **75**, 4589.

shown that the arsenic ring system can withstand nitration without disruption. In this work, however, we have largely avoided substitution and have used as starting materials suitably substituted 2-aminodiphenyls and proceeded to the 9-arsafluorenes by several different routes. In the first, using standard procedures, 2-aminodiphenyl was converted into 9-chloro-9-arsafluorene [8] and the chlorine atom replaced by the *p*-tolyl group by means of the Grignard reaction. Oxidation by alkaline permanganate left the ring system intact and gave 9-*p*-carboxyphenyl-9-arsafluorene oxide, from which the oxygen was readily removed by reduction with sulphur dioxide.

The second route involved a series of reactions, outlined below, similar to those which had proved successful in the antimony series.[11]

In the preparation of the 9-stibiafluorenes, the diazonium antimony chloride double salt, prepared in aqueous acid, was isolated and caused to interact with an arylstibonous chloride in ethanol, giving the diarylstibinic trichloride corresponding to (I). Attempts to isolate the diazonium arsenic chloride double salt under the same conditions failed but, by addition of the requisite 2-diphenyldiazonium salt, prepared in ethanol under " anhydrous " conditions, to the arylarsonous chloride, a transient yellow salt was formed but rapidly decomposed to give, presumably, the trichloride (I). This trichloride could not be readily isolated in crystalline form, in contrast to the corresponding antimony compounds, but, by hydrolysis of the reaction mixture, the arsinic acid (II) was isolated in yields much higher and more consistent than those obtained under the usual alkaline Bart reaction conditions. The latter process, in our hands, gave unpredictable results despite careful control of pH of the arylarsenite solutions.



Ring closure of the diarylarsinic acids to the 9-arsafluorene oxides (III) was effected by hot concentrated sulphuric acid, except in the case of the 4'-methoxy-derivative (II; R = OMe, R' = CO_2H) where sulphonation occurred. Acetic anhydride containing a little sulphuric acid also failed to cyclise this arsinic acid and thermal elimination of hydrogen chloride from the arsinous chloride (IV; R = OMe, R' = CO_2H), though successful, also removed arsenic to some extent. Polyphosphoric acid, however, proved to

[11] Campbell, *J.*, 1950, 3109; 1952, 4448.

be a most effective cyclising agent in this series, and when the acid (II; R = OMe, R′ = CO_2H) was added to polyphosphoric acid at 160°, the reaction was complete in 3 min. and gave good yields of the oxide (III; R = OMe, R′ = CO_2H) which was readily reduced to the arsafluorene (V; R = OMe, R′ = CO_2H).

Optical resolution of 9-*p*-carboxyphenyl-2-methoxy-9-arsafluorene through the (+)- and (−)-1-phenylethylamine salts, and of 2-amino-9-phenyl-9-arsafluorene by (+)- and (−)-tartaric acids followed orthodox lines. In both cases difficulties were encountered in the separation of the diastereoisomeric salts in optically pure condition because solubility differences were small. In fact, effective resolution of the 9-*p*-carboxy-compound was impossible without an initial mechanical separation of the aggregates of prisms and fine needles which were deposited from solution almost simultaneously. The prisms proved to be the (+)-acid–(−)-base salt, which after crystallisation to constant rotation, $[\alpha]_D$ +110°, gave on decomposition (+)-acid $[\alpha]_D$ +156° (in pyridine). The rotation of the needles, (−)-acid–(−)-base salt, increased slowly to $[\alpha]_D$ −92°, but insufficient material was available for complete optical purification. This was obviously feasible, for the salts were optically stable: there was no evidence of second-order asymmetric transformation so frequently encountered with the corresponding antimony compounds. Using (+)-1-phenylethylamine with acid regenerated from intermediate fractions of salt gave (−)-acid–(+)-base salt, $[\alpha]_D$ −116°, from which (−)-acid, $[\alpha]_D$ −160·2° ± 1°, was obtained. This value made it clear that the (+)-acid, $[\alpha]_D$ +156°, was optically impure but residual (±)-acid was readily removed from it by one crystallisation from ethanol, and the pure (+)-acid had $[\alpha]_D$ +160·7° ± 1°.

Separation of the diastereoisomeric hydrogen (+)-tartrates of 2-amino-9-phenyl-9-arsafluorene was even more tedious, and again both antipodes of the resolving agent had to be used. However, this process gave the (+)-amine hydrogen (+)-tartrate, $[\alpha]_D$ +194°, from which (+)-amine, $[\alpha]_D$ +255° ± 1°, was isolated, and the corresponding hydrogen (−)-tartrate, $[\alpha]_D$ −193°, gave (−)-amine, $[\alpha]_D$ −251° ± 1°. In this case the small optical impurity could not be removed, for the (+)- and the (−)-amine separated as vitreous solids, m. p. 38—48° and 37—47°, respectively, and could not be crystallised. However, the enantiomeric acetyl derivatives, m. p. 182—184°, $[\alpha]_D^{20}$ +278·0° ± 1·2° and −279·5° ± 2·3°, were obtained optically pure. It should be noted that salt formation with tartaric acid of the same sign of rotation lowers the specific rotation of the (+)- and the (−)-amine, a feature also occurring with (+)- and (−)-2-amino-9-*p*-tolyl-9-stibiafluorenes.

The specific rotation of 9-*p*-carboxyphenyl-2-methoxy-9-arsafluorene, $[\alpha]_D$ +161°, is higher than that of the analogous stibiafluorene,[7] $[\alpha]_D$ +153°, but the calculated molecular rotations are $[M]_D$ +609° and +650° respectively. This indicates that here, as in the eutropic series of *iso*chromanium salts [12] containing asymmetric 3-covalent elements of Group VI the molecular rotation rises with increasing molecular weight of the element. Also, the optical stability of the compounds diminishes on going from arsenic to antimony, as it does with increasing molecular weight in the thio-, seleno- and telluro-*iso*chromanium salts. For instance, a solution of the (−)-arsafluorenecarboxylic acid in pyridine lost only 7·5% of its rotation after 30 days at room temperature, whereas a similar solution of the analogous antimony compound lost 50% of its activity in 41 hr. In fact, the arsafluorene showed remarkable optical stability, for, when a solution in chloroform containing 5% of ethanol (the compound is insufficiently soluble in either solvent alone) was heated in a sealed tube at 70°, the specific rotation, $[\alpha]_D$ −144°, fell barely 5%, to −137°, after 7 hours' heating. When the temperature was raised to 111°, however, the rotation dropped from $[\alpha]_D$ −143° to −13·3° in 1 hr., and, from the rate coefficients, the half-life was calculated as 17 min. It is possible, however, that the choice of chloroform–ethanol as solvent was unfortunate in this case, because of the possible generation of hydrogen chloride, a catalyst which was found to promote racemisation of the (+)-arsafluorene at room temperature. The catalytic effect of hydrogen chloride in this case was much less striking than in the stibiafluorene series. Unfortunately, racemisation data are not available for the antimony compound analogous to the arsafluorene under discussion, so

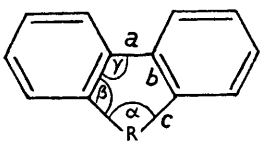
[12] Holliman and Mann, *J.*, 1945, 37.

direct comparison is not possible, but the half-life of (−)-2-carboxymethoxy-9-*p*-tolyl-9-stibiafluorene in chloroform–acetic acid containing a trace of hydrogen chloride at 26° was 5 min., whereas the half-life of 9-*p*-carboxyphenyl-2-methoxy-9-arsafluorene under similar conditions was 110 hr.

Solutions of (−)-2-amino-9-phenyl-9-arsafluorene in ethanol were optically stable at room temperature apparently indefinitely and no change in rotation was detected even after 1 hour's heating in a sealed tube at 110°. The amine, therefore, appears to be more, and the acid less, optically stable than predicted by Weston's calculations for a pyramidal molecule.[4] The half-life of the acid, 17 min. at 111°, is short compared with the value of 2 hr. at 107° calculated by Weston for the inversion (" racemisation ") of trimethylarsine, and the half-life of the (−)-amine is obviously considerably longer. Weston's model is, of course, aliphatic, and a similar assessment of the stability to inversion of an aromatic arsine would be of great interest.

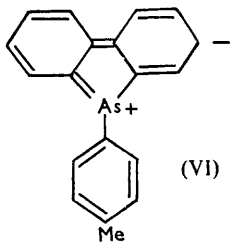
There seems little doubt that the arsafluorenes are, in fact, pyramidal molecules and evidence in support of this statement can be advanced from three sources. First, attempts to resolve 9-*p*-carboxyphenyl-9-arsafluorene have failed. This compound is symmetrical on a pyramidal model, but should be resolvable if the two benzene rings in the diphenyl residue are colinear but not coplanar.[11] Secondly, this " skew " configuration, suggested because it was considered that coplanarity of the tricyclic system could only be achieved at the expense of severe angular strain in the five-membered ring, appears unlikely in the light of geometrical calculations. Table 1 shows the probable dimensions of a 9-arsafluorene and the known dimensions of fluorene. The angles α, β, and γ were obtained by calculation using bond lengths of diphenyl obtained from electron-diffraction [13] and *X*-ray [14] measurements, and the length of the C–As bond as found in trimethylarsine.[15]

TABLE 1.



	a (Å)	*b* (Å)	*c* (Å)	α	β	γ	Reference
R = As	1·54	1·39	1·98	96°	102°	120°	*a* & *b*, 13; *c*, 15.
R = As	1·48	1·42	1·98	94	103	120	*a* & *b*, 14; *c*, 15.
R = C	1·486	1·410	1·468	105·6	109·6	107·6	16.

These figures indicate that the total angular strain in the 5-membered ring of the heterocyclic molecule, in which the tricyclic system remains planar, is less than that occurring in the five-membered ring of fluorene, recently examined by *X*-rays [16] and shown to have a maximum deviation from the plane of 0·03 Å.



(VI)

Lastly, comparison of the ultraviolet spectra of 9-*p*-tolyl-9-arsafluorene [17] and triphenylarsine [18] shows that the main absorption band of the latter has undergone a bathochromic shift of 310 Å in the heterocyclic compound. This large displacement points to a considerable lowering of energy and indicates increased conjugation between the unshared pair of electrons on arsenic and the condensed ring system. The molecule, therefore, can best be represented by the numerous canonical forms of type (VI), and the whole tricyclic system in the arsafluorene must be essentially planar. The dissymmetry of the 9-arsafluorenes, therefore, arises from the disposition of the substituent in the 9-position above or below this plane, and the properties of the optically active 9-arsafluorenes show that the bonds from the arsenic atom can retain a stable pyramidal configuration.

[13] Karle and Brockway, *J. Amer. Chem. Soc.*, 1944, **66**, 1974.
[14] Dhar, *Indian J. Phys.*, 1932, **7**, 43.
[15] Springall and Brockway, *J. Amer. Chem. Soc.*, 1938, **60**, 996.
[16] Burns and Iball, *Nature*, 1954, **173**, 635.
[17] Campbell and Poller, *Chem. and Ind.*, 1953, 1126.
[18] Mann, Millar, and Smith, *J.*, 1953, 1130.

Experimental

9-p-*Tolyl*-9-*arsafluorene*.—Diphenylyl-2-arsonic acid was prepared by the Bart reaction under conditions essentially those used by Cookson and Mann.[19] The maximum yield of the pure acid was only 27%, and this was obtained by addition of the diazonium salt solution under the surface of a large excess of aqueous sodium arsenite. After repeated crystallisation from 50% acetic acid, the compound had m. p. 216—222° (values obtained previously range from 202° to 206°), but analysis indicated that some anhydride had been formed. Cyclisation of this arsonic acid [9] by concentrated sulphuric acid at 90° gave 9-arsafluoreninic acid, m. p. 318—322° in 92% yield (m. p. 328° given in ref. 10), and this was converted into 9-chloro-9-arsafluorene, m. p. 161—162°, in 70% yield. A suspension of 9-chloro-9-arsafluorene (12·6 g.) in dry ether (45 ml.) was added slowly to *p*-tolylmagnesium bromide prepared from *p*-bromotoluene (24·8 g., 3 mols.) in ether (80 ml.), and the reaction mixture was boiled for 15 min. and filtered rapidly through glass wool. The product crystallised from this solution overnight, and recrystallisation from ethanol gave 9-p-*tolyl*-9-*arsafluorene* (V; R = H, R′ = Me), as colourless needles, m. p. 130·5—131·5° (70%) (Found: C, 71·3; H, 4·8; As, 23·5. $C_{19}H_{15}As$ requires C, 71·7; H, 4·8; As, 23·5%). From the ethereal mother-liquor a further 0·5 g. was isolated after decomposition of the excess of Grignard reagent. Attempts to characterise the arsafluorene by formation of dichloro- or dibromo-derivatives failed, because the initially crystalline dihalides were rapidly hydrolysed in moist air to the corresponding dihydroxy-compound. This also proved unsatisfactory as a derivative for it lost water at 114—130°, giving, presumably, an oxide (m. p. 206—207°). The mercurichloride, m. p. 219—222°, was deposited as colourless needles when hot ethanolic solutions of the constituents were mixed, and was found to be *bis*-9-p-*tolyl*-9-*arsafluorene trismercurichloride*, $(R_3As)_2(HgCl_2)_3$ (Found: C, 32·2; H, 2·3. $C_{38}H_{30}Cl_6As_2Hg_3$ requires C, 32·1; H, 2·1%).

9-p-*Carboxyphenyl*-9-*arsafluorene*.—When 9-*p*-tolyl-9-arsafluorene was oxidised by potassium permanganate under neutral conditions (with either magnesium sulphate or a phosphate buffer) the product obtained was largely the oxide containing little of the required carboxylic acid. The most successful oxidation occurred under alkaline conditions as follows. A mixture of crude 9-*p*-tolyl-9-arsafluorene, m. p. 127—130° (1·1 g.), potassium permanganate (2 g.), and sodium hydroxide (0·7 g.) in water (25 ml.) was boiled under reflux for 1¾ hr. The cooled mixture was decolorised by sulphur dioxide, and the product filtered off, washed, and dissolved in warm N-ammonia (40 ml.). Acidification of the filtered solution then gave 9-p-*carboxyphenyl*-9-*arsafluorene oxide* (III; R = H, R′ = CO_2H) (0·7 g.), m. p. 310—321° (decomp.), or m. p. 315—318° (decomp.) when inserted into the bath at 300° (Found: C, 62·2; H, 4·2. $C_{19}H_{13}O_3As$ requires C, 62·7; H, 3·6%). This oxide was reduced by the sulphur dioxide method,[6a] and the crude product was crystallised (twice) from ethanol. 9-p-*Carboxyphenyl*-9-*arsafluorene* (V; R = H, R′ = CO_2H) (0·4 g.) separated as colourless needles, m. p. 268—271° [Found: C, 65·5; H, 3·7; As, 21·5%; *M* (by titration in dimethylformamide with sodium methoxide), 346. $C_{19}H_{13}O_2As$ requires C, 65·5; H, 3·8; As, 21·5%; *M*, 348].

9-p-*Carboxyphenyl*-2-*methoxy*-9-*arsafluorene*.—*Method* 1. *Cyclisation of the arsonous chloride, followed by Grignard reaction.* 2-Amino-4′-methoxydiphenyl hydrochloride [20,7] (30·0 g.) in water (105 ml.) was treated with concentrated hydrochloric acid (17 ml.) and diazotised with sodium nitrite (9·6 g.) in water (18 ml.). The filtered solution was kept at 5° and added in portions under the surface of a stirred solution of sodium arsenite (33·0 g.), sodium carbonate (18·3 g.), and copper sulphate (0·6 g.) in water (165 ml.) at 60°. The tar which formed was filtered off and acidification of the filtrate gave 4′-*methoxydiphenylyl*-2-*arsonic acid*, m. p. 209—222° (12·8 g., 33%) (Found: C, 50·3; H, 4·2. $C_{13}H_{13}O_4As$ requires C, 50·7; H, 4·3%). Attempts to cyclise this acid by concentrated sulphuric acid resulted in sulphonation, so the acid was reduced by sulphur dioxide in the presence of concentrated hydrochloric acid and chloroform to 4′-methoxydiphenylyl-2-arsonous chloride, m. p. 63—67°. This crude chloride (7·7 g.) was heated at 200°, under reflux, for 2 hr. and the product dissolved in the minimum volume of boiling benzene. The solution, on cooling, deposited 9-*chloro*-2-*methoxy*-9-*arsafluorene* as yellow needles, m. p. 133—137° (3·1 g.), and a further fraction was obtained by evaporation of solvent and again heating to 200°. Recrystallisation from benzene gave the pure product, m. p. 136—137° (60%) (Found: C, 53·4; H, 3·4. $C_{13}H_{10}OClAs$ requires C, 53·4; H, 3·7%). A solution of 9-chloro-2-methoxy-9-arsafluorene (3·8 g., 1 mol.) in benzene (100 ml.)

[19] Cookson and Mann, *J.*, 1949, 2897.
[20] Copp and Walls, *J.*, 1950, 311.

was added to the Grignard reagent prepared from *p*-bromotoluene (8·9 g., 4 mols.) in ether (60 ml.). After boiling for 2·5 hr., the mixture was decomposed with 4N-hydrochloric acid, and the normal isolation procedure gave crude 2-methoxy-9-*p*-tolyl-9-arsafluorene (V; R = OMe, R′ = Me), m. p. 72—85° (5·3 g., 117% yield). Systematic crystallisation failed to remove the impurity which was almost certainly di-*p*-tolyl as steam-distillation gave a small fraction of arsenic-free material, m. p. 113—117°. Analyses of the compound (V; R = OMe, R′ = Me) were consistently poor (Found: C, 70·4; H, 4·8. Calc. for $C_{20}H_{17}OAs$: C, 69·0; H, 4·9%). Nevertheless, oxidation of the crude compound (0·5 g.) with alkaline potassium permanganate followed by reduction with sulphur dioxide gave 9-p-*carboxyphenyl-2-methoxy-9-arsafluorene* (V; R = OMe, R′ = CO_2H), m. p. 223° (0·3 g.) after crystallisation from ethanol (Found: C, 63·9; H, 4·4; As, 19·9. $C_{20}H_{15}O_3As$ requires C, 63·5; H, 4·0; As, 19·8%). An arsenic-free impurity, m. p. >340°, insoluble in ethanol, was also isolated, gave the characteristic smell of diphenyl on decarboxylation, and was probably 4 : 4′-di-*p*-carboxydiphenyl. This confirmed di-*p*-tolyl as the impurity in the tolyl compound.

Method 2. *Cyclisation of* (IV; R = OMe, R′ = CO_2H). *p*-Aminobenzoic acid (50·0 g.) was converted into *p*-carboxyphenylarsonic acid, m. p. >360° (44·3 g.), by the method of Lewis and Hamilton,[21] and this was reduced by sulphur dioxide to *p*-carboxyphenylarsonous chloride, m. p. 156—162° (31·2 g.). 2-Amino-4′-methoxydiphenyl hydrochloride (5·9 g.) in absolute ethanol (25 ml.) was treated with a saturated ethanolic solution of hydrogen chloride (6·5 ml.), cooled to 5°, and diazotised with pentyl nitrite (4 ml.) in ethanol (10 ml.). The resulting solution, at 5°, was added in portions to *p*-carboxyphenylarsonous chloride (6·0 g.), in ethanol (60 ml.) which was kept at 40—50° and vigorously stirred. Copper bronze (0·4 g.) was added during this addition. When the evolution of nitrogen ceased, ethanol was removed under reduced pressure and the crude arsinic chloride was hydrolysed by warm 4N-sodium hydroxide (30 ml.). After cooling, ether was added to dissolve arsenic-free by-products, and the mixture was acidified to Congo-red with 4N-hydrochloric acid, the crude arsinic acid being precipitated. Purification by reprecipitation from solution in sodium hydrogen carbonate gave p-*carboxyphenyl-2-4′-methoxydiphenylylarsinic acid* (II; R = OMe, R′ = CO_2H), m. p. 271—278° (decomp.) (corr.) (3·8 g., 41%). This material was used in subsequent reactions without further purification, but one crystallisation from 50% aqueous acetic acid raised the m. p. to 280—281° (decomp.) (corr.) (Found: C, 58·8; H, 4·3. $C_{20}H_{17}O_5As$ requires C, 58·3; H, 4·2%). The arsinic acid was reduced by sulphur dioxide to p-*carboxyphenyl-2-4′-methoxydiphenylylarsinous chloride* (IV; R = OMe, R′ = CO_2H), m. p. 200—204° (55%) (Found: C, 57·8; H, 4·0. $C_{20}H_{16}O_3ClAs$ requires C, 57·9; H, 3·9%). Cyclisation of this chloride (1·5 g.) by heating at 250°/14 mm. for 1 hr. gave a white sublimate, m. p. 86—89°, found to be 4-methoxydiphenyl, and a vitreous solid from which boiling ethanol extracted the compound (V; R = OMe, R′ = CO_2H), m. p. 218—222° (0·4 g.).

Method 3. *Cyclisation of* (II; R = OMe, R′ = CO_2H), *followed by reduction.* The polyphosphoric acid[22] used in this ring closure was prepared by dissolving phosphoric oxide (24 g.) in syrupy phosphoric acid (*d* 1·75; 20 ml.). When the acid (II; R = OMe, R′ = CO_2H) (1 g.) was added to polyphosphoric acid (5 g.) at 160°, the temperature of the stirred mixture dropped 10° and rose again. After 3 min. at 160°, the homogeneous solution was poured into water, and the precipitated solid was filtered off and dried. This solid, m. p. 296—302° (decomp., corr.) (0·9 g.), which was the oxide (III; R = OMe, R′ = CO_2H), was reduced by sulphur dioxide, and crystallisation of the product from ethanol gave the acid (V; R = OMe, R′ = CO_2H), m. p. 223—224° (0·7 g., 76%), unchanged on admixture with a sample made by method 1 or 2. This ring closure proceeded well with 5 g. of the arsinic acid, though the yield was somewhat lower.

2-*Amino-9-phenyl-9-arsafluorene.*—*Preparation of* 2-4′-*nitrodiphenylylphenylarsinic acid. Method* 1. *Under aqueous alkaline conditions.* This reaction was carried out under conditions essentially those used by Blicke and Webster[23] for the preparation of *m*-nitrodiphenylarsinic acid. A solution of phenylarsonous chloride (6 g.) in sodium hydroxide (4·3 g. in 30 ml. water) was slowly added to the neutralised diazonium salt solution obtained from 2-amino-4′-nitrodiphenyl[24] (5·8 g.). The recommended method of isolation failed in this case, but on neutralisation of the mixture with 4N-acetic acid a dark brown solid was obtained. Extraction of this with 4N-sodium hydroxide followed by acidification gave 4′-*nitro-2-diphenylylphenylarsinic acid* (II; R = NO_2, R′ = H), m. p. 240—243° (0·6 g.) after crystallisation from ethanol from which

[21] Lewis and Hamilton, *J. Amer. Chem. Soc.*, 1923, **45**, 758.
[22] Evans and Smith, *J.*, 1954, 798.
[23] Blicke and Webster, *J. Amer. Chem. Soc.*, 1937, **59**, 534.
[24] Scarborough and Waters, *J.*, 1927, 89.

it separated as yellow needles (Found : C, 56·2; H, 4·2. $C_{18}H_{14}O_4NAs$ requires C, 56·4; H, 3·7%). In some experiments, particularly if the neutralised diazonium and phenylarsonous oxide solutions were mixed rapidly, the main product was di-(4′-nitro-2-diphenylyl)arsinic acid, m. p. 295—299° (decomp.) (in ref. 9 the m. p. is quoted as >260°) (Found : C, 57·1; H, 4·2. Calc. for $C_{24}H_{17}O_6N_2As$: C, 57·3; H, 3·4%).

Method 2. *Reaction in absolute ethanol under acid conditions.* 2-Amino-4′-nitrodiphenyl (5·4 g.) in absolute ethanol (50 ml.) was treated with saturated ethanolic hydrogen chloride (8 ml.) and diazotised at 5° with pentyl nitrite (4 ml.) in absolute ethanol (10 ml.). The resulting solution was added dropwise to one of phenylarsonous chloride (5·6 g.) in ethanol (50 ml.) kept at 60° and vigorously stirred. At each addition a transient yellow precipitate appeared and decomposed with evolution of nitrogen. Copper bronze (0·2 g.) was added to increase the rate of decomposition. The crude product was isolated from this solution by the method used for the acid (II; R = OMe, R′ = CO_2H) and had m. p. 216—236° (decomp.) (6·7 g.). Crystallisation from ethanol or from 50% acetic acid gave the product (II; R = NO_2, R′ = H), m. p. 241—244° (3·1 g., 32%) unchanged on admixture with a sample obtained by method 1.

2-*Nitro*-9-*phenyl*-9-*arsafluorene* 9-*oxide*. The above arsinic acid (2·5 g.) was cyclised by warming it in concentrated sulphuric acid (30 ml.) at 140—150° for 1 hr. The product was isolated by pouring the cooled solution on cracked ice, and crystallisation of the precipitate from 50% acetic acid (12 ml.) gave 2-*nitro*-9-*phenyl*-9-*arsafluorene* 9-*oxide* (III; R = NO_2, R′ = H) (2·1 g.) as buff leaflets, which melted at 120°, resolidified on further heating, and remelted at 272—273° (Found : C, 59·7; H, 3·3; N, 3·8. $C_{18}H_{12}O_3NAs$ requires C, 59·2; H, 3·7; N, 4·0%).

2-*Amino*-9-*phenyl*-9-*arsafluorene*. Simultaneous reduction of the nitro-group and removal of oxygen occurred when the above oxide (5 g.) was heated with stannous chloride (17·5 g.), concentrated hydrochloric acid (17·5 ml.), and ethanol (25 ml.) under reflux for 2 hr. At 0° the solution gradually deposited the stannichloride of the base, which was isolated and decomposed with 4N-sodium hydroxide. Extraction of the amine with ether gave a glass which was converted into the *hydrochloride* (V; R = NH_3Cl, R′ = H), colourless needles, m. p. 220—224° (decomp.) (3·4 g., 69%), after crystallisation from carbon tetrachloride (Found : C, 60·5; H, 4·3. $C_{18}H_{15}NClAs$ requires C, 60·8; H, 4·3%). Base regenerated from this hydrochloride again formed a glass but a specimen regained from the (+)-tartrate [once recrystallised and consequently probably slightly enriched with (+)-base] gave a satisfactory analysis (Found : C, 68·1; H, 4·7; N, 4·0. $C_{18}H_{14}NAs$ requires C, 67·7; H, 4·4; N, 4·4%). The *acetyl derivative* (V; R = NHAc, R′ = H) had m. p. 156—157° (Found : C, 66·0; H, 4·6. $C_{20}H_{16}ONAs$ requires C, 66·5; H, 4·5%).

Attempted Resolution of 9-p-*Carboxyphenyl*-9-*arsafluorene*.—Specific rotations were measured in absolute ethanol in 2 dm. tubes unless otherwise stated.

(1) The acid (1 g.) was dissolved in boiling ethanol (110 ml.) containing (−)-1-phenylethylamine (0·7 g., 2 equivs.) and, on cooling, deposited a first fraction of salt, F1, m. p. 200—210°, $[\alpha]_D$ −6·7° ± 2° (*c* 0·255) (0·85 g.). Concentration of the mother-liquor to half volume gave a second fraction, F2, m. p. 203—208°, $[\alpha]_D$ −6·8° ± 2° (*c* 0·265) (0·35 g.). Decomposition of F2 with 0·1N-sulphuric acid at −10° gave an acid, m. p. 263—268°, which was optically inactive when examined in pyridine. F1 was recrystallised three times from ethanol, and the final *salt* (0·3 g.) had m. p. 208—210°, $[\alpha]_D$ −9·5° ± 2° (*c* 0·263) (Found : C, 69·3; H, 5·4. $C_{27}H_{24}O_2NAs$ requires C, 69·1; H, 5·2%). This increase in specific rotation was evidently caused by chemical purification for decomposition gave a specimen of acid, m. p. 268—269°, which was optically inactive.

(2) The *quinine salt*, m. p. 207—208°, $[\alpha]_D$ −87·8° ± 1° (*c* 0·458), separated in 90% yield when the acid was mixed with twice the calculated quantity of quinine in boiling ethanol (Found : C, 69·8; H, 5·8. $C_{39}H_{37}O_4N_2As$ requires C, 69·6; H, 5·5%). This salt was recrystallised five times from ethanol and showed no change in specific rotation. The final fraction, m. p. 207—208°, had $[\alpha]_D$ −86·8° ± 2·2° (*c* 0·255), and acid regained from it showed no rotation when examined in pyridine.

Resolution of 9-p-*Carboxyphenyl*-2-*methoxy*-9-*arsafluorene*.—The acid (6·5 g.) was added to (−)-1-phenylethylamine (4·16 g., 2 equivs.) in boiling ethanol (530 ml.), and the filtered solution set aside at room temperature. During the slow crystallisation, a layer of elongated prisms separated initially and clumps of fine needles were deposited above it; both forms then grew simultaneously. After 66 hr. the mother-liquor was decanted, and the crystals were separated mechanically into prisms, A1, and needles, A2. The decanted mother-liquor gave fraction A3 when kept for 48 hr., and successive fractions were obtained by concentration under reduced

pressure (see Table 2). A1 was crystallised four times from ethanol containing a little (−)-1-phenylethylamine, and the apparently pure (+)-*acid*–(−)-*base salt* obtained had m. p. 224°, $[\alpha]_D$ +110° ± 2° (*c* 0·216) (0·69 g.) (Found : C, 67·1; H, 5·2. $C_{28}H_{26}O_3NAs$ requires C, 67·3; H, 5·2%). Fractions A2, A3, and A4 were combined and recrystallised six times from ethanol but

TABLE 2.

Fraction	Wt. (g.)	$[\alpha]_D$	*c* (EtOH)	M. p.	Fraction	Wt. (g.)	$[\alpha]_D$	*c* (EtOH)	M. p.
A1	2·75	+30·0°	0·220	200—220°	A4	1·30	−45·8	0·207	—
A2	1·23	−50·6	0·240	197—200	A5	1·32	−12·4	0·237	195—202
A3	0·55	−60·7	0·224	195—202	A6	0·29	0	0·218	192—210

the most lævorotatory fraction, m. p. 206—207°, $[\alpha]_D$ −92° (*c* 0·206) (0·2 g.), had not reached optical purity. Crystallisation from ethyl acetate or *iso*propyl alcohol also failed to yield the pure (−)-acid–(−)-base salt and consequently the acid was regenerated from all intermediate fractions. This acid (3·5 g.) was treated with (+)-1-phenylethylamine (2·24 g., 2 equivs.) in hot ethanol (350 ml.). Again the diastereoisomeric salts differed characteristically in crystalline form and were separated mechanically. The prisms, $[\alpha]_D$ −68·4° (*c* 0·223) (1·4 g.), after three recrystallisations from ethanol containing a little free (+)-base gave the optically pure (−)-*acid*–(+)-*base salt*, m. p. 225—226°, $[\alpha]_D$ −116° ± 2° (*c* 0·215) (0·48 g.) (Found : C, 67·0; H, 5·3%).

Isolation of the (+)- *and the* (−)-*acid.* Addition of excess of 0·1N-sulphuric acid to a solution of the appropriate salt, dissolved in ethanol and kept at −10°, precipitated the crystalline active acid. Decomposition showed that the (+)-acid–(−)-base salt had not reached optical purity, but complete optical purification was effected when the (+)-acid liberated was crystallised once from ethanol. Details of the active acids are given in Table 3.

TABLE 3.

Resolving agent	Salt, $[\alpha]_D$	Acid, $[\alpha]_D^{21}$	Acid, $[\alpha]_{5461}$	*c* in pyridine	M. p.	Found (%) in acid C	H
(−)-CHPhMe·NH_2 ...	+110°	+156°	—	0·494	239—240°	—	—
(−)-CHPhMe·NH_2 ...	−92	−111	—	0·206	230—233	—	—
(+)-CHPhMe·NH_2 ...	−116	−160	−198	0·476	240	63·2	4·3
		+161 *	+196	0·488	240	63·0	4·0

* (+)-Acid, $[\alpha]_D$ +156°, recrystallised from ethanol.

Resolution of 2-Amino-9-phenyl-9-arsafluorene.—The amine, regenerated from the hydrochloride (7·1 g.) by addition of N-sodium hydroxide, was added to (+)-tartaric acid (3·3 g., 1·1 mol.) dissolved in boiling ethanol (120 ml.), and the solution rapidly filtered. The salt (8·35 g., 88%) which separated overnight had m. p. 158—160° (decomp.), $[\alpha]_D$ +4·0°. Rotations were measured in " AnalaR " acetone (*c* ~ 0·25). Concentration of the mother-liquor gave a small, rather discoloured second fraction, $[\alpha]_D$ −26·3°. The first fraction was recrystallised eight times from ethanol containing 1% of (+)-tartaric acid and then had m. p. 158—160° (decomp.), $[\alpha]_D$ +28·9° (4·56 g.). Resolution was obviously very slow, consequently a different solvent for crystallisation seemed advisable, despite the fact that previous small-scale experiments had indicated that the (+)-base (+)-tartrate could be obtained in essentially optically pure condition by using ethanol. Two recrystallisations from methanol (4 ml. per g. of salt) gave a fraction having $[\alpha]_D$ +51·0° (3·28 g.), and four further crystallisations from the same solvent gave pure (+)-*base* (+)-*tartrate*, as pale buff plates, m. p. 159—161° (decomp.), $[\alpha]_D$ +194° ± 2° (0·42 g.) (Found : C, 56·1; H, 4·6. $C_{22}H_{20}O_6NAs$ requires C, 56·3; H, 4·3%). In crystallisations from methanol it was found essential to prevent evaporation of the solvent or little increase in $[\alpha]_D$ occurred. Recrystallisation of lævorotatory fractions indicated that isolation of (−)-base (+)-tartrate should be possible but tedious. Consequently all intermediate fractions were decomposed, giving impure (−)-base, $[\alpha]_D$ −47·5°. The fraction of salt (3·3 g.) obtained from this base (3·5 g.) with (−)-tartaric acid (1·8 g., 1·1 mol.) in ethanol (70 ml.) had m. p. 152—155° (decomp.), $[\alpha]_D$ −47·3°. One crystallisation of this from methanol raised the rotation of the salt (1·83 g.) to $[\alpha]_D$ −121° and three further crystallisations from ethanol gave the (−)-*base* (−)-*tartrate*, m. p. 158—159° (decomp.), $[\alpha]_D$ −193° ± 2° (0·38 g.) (Found : C, 56·2; H, 4·7%).

Isolation of the (+)- *and the* (−)-*amine.* The appropriate salt was dissolved in the minimum volume of methanol, and 0·1N-sodium hydroxide was added at −10°. In this way the (+)-amine was precipitated as a colourless gum which solidified to a pale brown glass, m. p. 38—48°

(hot-stage microscope), $[\alpha]_D^{25}$ +255° ± 1°, $[\alpha]_{5461}^{25}$ +321° ± 1°, and the (−)-amine had m. p. 37—47°, $[\alpha]_D^{25}$ −251° ± 1°, $[\alpha]_{5461}^{25}$ −318° ± 1° (*c* 0·45 in EtOH) (Found: C, 67·0; H, 4·5. $C_{18}H_{14}NAs$ requires C, 67·7; H, 4·4%). Acetic anhydride at room temperature gave the corresponding (+)- and (−)-*acetyl derivative*, m. p. 187—189°, $[\alpha]_D^{20}$ +278·0° ± 1·2° (*c*, 0·205 in EtOH), and $[\alpha]_D$ −279·5° ± 2·3° (*c* 0·110 in EtOH) (Found: C, 66·1; H, 4·7. $C_{20}H_{16}ONAs$ requires C, 66·5; H, 4·5%).

Racemisation.—The results of racemisation experiments on the (−)-acid (V; R = OMe, R′ = CO_2H) are given in Table 4. " AnalaR " chloroform containing 5% of ethanol was used

TABLE 4.

Solvent	*c*	Temp.	Initial $[\alpha]_D$	Final $[\alpha]_D$	Time	10^2k
Pyridine	0·467	20—22°	−160°	−160°	6 days	—
$CHCl_3$–EtOH	0·254	70	−144	−137	7 hr.	—
$CHCl_3$–EtOH	0·251	111	−143	−42·4	30 min	4·1
$CHCl_3$–EtOH	0·251	111	−143	−13·3	60 min.	4·0

$k = (\ln \alpha_0/\alpha_t)/t$ in min.$^{-1}$.

as solvent, because it was impossible to dissolve 50 mg. of the (−)-acid in 20 ml. of any of the common neutral organic solvents. Solutions were sealed in glass bulbs which were heated in a thermostat for the periods stated. The bulb was then cooled rapidly and the solution examined polarimetrically at 20°. Acid regained from the solution with $[\alpha]_D$ −13·3° had m. p. 219—221° and had m. p. 221—224° when mixed with (±)-acid. The catalytic effect of hydrogen chloride was demonstrated when a glass rod which had been in contact with ethanolic hydrogen chloride was dipped into a solution of the (+)-acid. The initial rotation, α_D +0·72°, fell to α_D +0·36 in 110 hr. and reached zero after about 500 hr. at room temperature. This racemisation did not follow the unimolecular rate law.

Solutions of the (+)-amine (V; R = NH_2, R′ = H) in ethanol were heated in sealed bulbs at 110°. No change in rotation was detected after 15 or 60 min.

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