406. *Synthesis and Stereochemistry of Heterocyclic Phosphorus Compounds. Part II.* Loss of Optical Activity in the Reduction of (+)-2-Carboxy-9-phenyl-9-phosphafluorene 9-Oxide.*

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The preparation of a group of 9-phenyl-9-phosphafluorene 9-oxides by cyclisation of 2-biphenylylphenylphosphinic acids, and the reduction of two of these oxides to 9-phenyl-9-phosphafluorenes are described. 2-Carboxy-9-phenyl-9-phosphafluorene 9-oxide has been resolved by separation of the diastereoisomeric amides obtained from (+)- and from (—)-1-phenylethylamine. Reduction of the (+)-oxide, $[\alpha]_D$ +126°, with lithium aluminium hydride gave 2-hydroxymethyl-9-phenyl-9-phosphafluorene with complete loss of optical activity. This result and the retention of activity observed in the reduction of the azaphosphaphenanthrene oxide (Part I) are discussed.

In Part I of this series we described the reduction of the (+)- and the (—)-form of 10-*p*-dimethylaminophenyl-9,10-dihydro-9-aza-10-phosphaphenanthrene 10-oxide to the active phosphines with reversal of the sign of rotation. Unfortunately, these phosphines were unsuitable for racemisation experiments as they were sensitive to atmospheric oxygen in solution at room temperature, and consequently no estimate of the optical stability of this type of 3-covalent phosphorus compound could be obtained. An additional disadvantage of the molecule was the complicating factor of the nitrogen–phosphorus ring which, if rigidly puckered, might cause dissymmetry. To avoid these difficulties we decided to study 9-phenyl-9-phosphafluorene system (V) in which the phosphorus atom occurs at the apex of a simple pyramidal molecule. It was hoped that compounds of this type would sufficiently resemble aromatic phosphines to be unaffected by air at low temperatures and consequently, if resolution were successful, measurement of the rates of racemisation would provide an estimate of the optical stability of tercovalent phosphorus compounds.

The 9-phenyl-9-phosphafluorenes were prepared by the routes shown. The 2-biphenylylphenylphosphinic acids (III) were obtained from the corresponding 2-aminobiphenyls (I) either by Doak and Freedman's diazonium fluoroborate method [1] or through the Grignard reagent from the iodide (II) by the method of Burger and Dawson.[2] The latter method where applicable gave considerably better yields.

Cyclisation of the phosphinic acids to the oxides (IV) presented considerable difficulty. As stated in a preliminary note,[3] reagents and conditions which caused ring closure of the corresponding arsinic and stibinic acids were without effect on the phosphinic acids, and the use of aluminium chloride as catalyst in the normal Friedel–Crafts reaction on the chloride of the acid (III; R = R′ = R″ = H) also failed. But the use of a large excess

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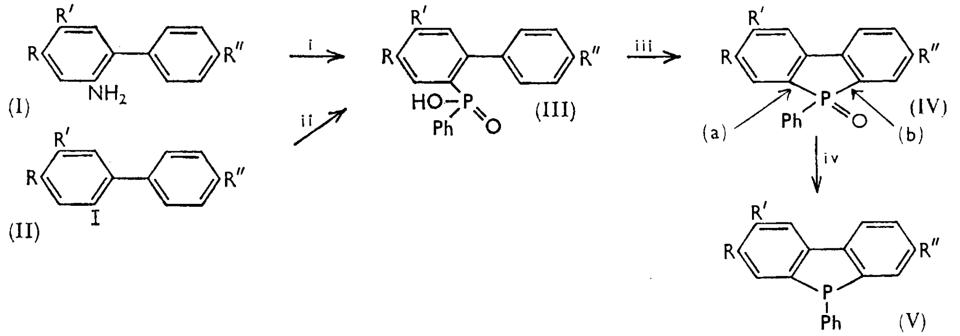
* Part I, *J.*, 1960, 5034.

[1] Doak and Freedman, *J. Amer. Chem. Soc.*, 1952, **74**, 2884.
[2] Burger and Dawson, *J. Org. Chem.*, 1951, **16**, 1250.
[3] Campbell and Way, *Proc. Chem. Soc.*, 1959, 231.

of phosphorus pentachloride in nitrobenzene at temperatures ranging from 160° to 180° for 4—10 hr. effected the intramolecular cyclisation and the 9-phenyl-9-phosphafluorene 9-oxides (IV) were obtained in 20—80% yields.

Although the mechanism of this reaction was not studied in detail, the characteristic features of an electrophilic substitution were obvious—a methyl group in the biphenylyl system facilitated cyclisation and a nitro-group impeded it. Optimum yields were obtained when three molecular proportions of phosphorus pentachloride were used and we suggest that the phosphinyl chloride, Ar_2POCl, first formed is converted in the high-temperature reaction into the trichloride, Ar_2PCl_3, which, in the presence of phosphorus pentachloride, is encouraged to ionise as $[Ar_2PCl_2]^+[PCl_6]^-$. Cyclisation by attack of the positive phosphorus on the adjacent benzene ring of the biphenylyl system would then follow.



Reagents: (i) Diazonium fluoroborate + $PhPCl_2$ in EtOAc. (ii) Mg in Et_2O, then $PhPCl_2$, followed by H_2O_2. (iii) PCl_5 in $PhNO_2$, then H_2O. (iv) $LiAlH_4$ in Bu^n_2O and C_6H_6.

This conversion, $Ar_2POCl \longrightarrow Ar_2PCl_3$, has apparently not been described although triarylphosphine dichlorides, Ar_3PCl_2, are obtained by the reaction of phosphorus pentachloride on triarylphosphine oxides.[4] The few known diarylphosphine trichlorides are not well characterised and have been made by addition of chlorine to monochlorides or by chlorination of dithiophosphinic acids.[5] They are described as crystalline solids, very easily hydrolysed, and similar in property to phosphorus pentachloride. As the latter is known to exist as $[PCl_4]^+[PCl_6]^-$, the suggested ionisation of the diarylphosphine trichlorides is not improbable, and self-ionisation $[Ar_2PCl_2]^+[Ar_2PCl_4]^-$ may also be possible.

In the cyclisation of 5-bromo-2-biphenylylphenylphosphinic acid, halogen exchange occurred and the product was 3-chloro-9-phenyl-9-phosphafluorene 9-oxide in place of the 3-bromo-compound. The chloro-oxide was obtained in 65% yield and the acid recovered (10%) was the original bromo-acid. Presumably, therefore, halogen exchange occurs, either in the reacting species when the phosphorus atom becomes positively charged and attack at the *para*-position is facilitated, or after cyclisation is completed.

Examination of the infrared spectra of the phosphinic acids and of the oxides confirms the structure of both. In addition to the bands expected for 1,2-, 1,4-, and 1,2,4-substituted benzenoid compounds (where appropriate), the characteristic P–Ph absorption occurs in both types between 1435 and 1445 cm.$^{-1}$; the strong P=O band occurs for the acids in the range 1180—1225 cm.$^{-1}$ but in a much narrower range, 1200—1210 cm.$^{-1}$, for the oxides [6] other than the 2-carboxy- and 2-hydroxymethyl derivatives where hydrogen-bonding lowers the frequency to 1170 cm.$^{-1}$. Of the three broad absorption bands at 1540—1760, 2260—2460, and 2500—2800 cm.$^{-1}$ present in all the phosphinic acids

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[4] Collie and Reynolds, *J.*, 1915, **107**, 367.

[5] Michaelis, *Annalen*, 1901, **315**, 43; Higgins, Vogel, and Craig, *J. Amer. Chem. Soc.*, 1955, **77**, 1864.

[6] Bellamy, " The Infra-red Spectra of Complex Molecules," Methuen, London, 1958.

examined [absorption which has been ascribed [7] to the group X:O(OH) where X = P, As, S, or Se], the two higher frequency bands do not occur in the spectra of the oxides. Further, all five phosphinic acids show a consistent medium-strong band at 950 or 960 cm.$^{-1}$, and no absorption in this region is shown by any of the oxides of this series except the carboxylated member. Bellamy and Beecher [8] have tentatively assigned absorption at 980 cm.$^{-1}$ to a P–O stretching vibration of quinquevalent phosphorus compounds containing the group $>$PO·O$^-$ and $>$PS·O$^-$, and our results appear to corroborate this view, particularly as the P–O–C linkage, also said to absorb in this region,[9] is absent for the compounds examined.

2-Carboxy-9-phenyl-9-phosphafluorene 9-oxide, the compound chosen for resolution experiments, was obtained in good yield by oxidation of the 2-methyl oxide (IV; R = Me, R′ = R″ = H) with potassium permanganate in pyridine under conditions similar to those used by Morgan and Herr [10] for the oxidation of *p*-tolyl- to *p*-carboxyphenyl-phosphine oxides. Unfortunately, the acid failed to give crystalline salts with any of the wide variety of alkaloids tested or with (−)-1-phenylethylamine or (+)-amphetamine (see Experimental section). However, the resolution was successfully carried out by fractional crystallisation of the (+)- or (−)-1-phenylethylamides. These were obtained by heating the acid with an excess of the active amine at its boiling point for 6—8 hr. No optical activity was observed in the small amounts of acid regained from amide formation. The product from the reaction with the (−)-amine was a mixture of amides, $[\alpha]_D$ +51·2°, which was separated by crystallisation from ethanol into the less soluble (−)-acid–(−)-amide, $[\alpha]_D$ −37·9°, and (after dilution with water and further crystallisation) the (+)-acid–(−)-amide, $[\alpha]_D$ +211·5°. Similarly, the (+)-amine gave a mixture of amides, $[\alpha]_D$ −51·9°, separated into (+)acid–(+)-amide, $[\alpha]_D$ +38·6°, and (−)-acid–(+)-amide, $[\alpha]_D$ −212·0°. The isolation of the less soluble amide in optically pure state was relatively easy; but careful control of the conditions of crystallisation was necessary if the more soluble amide was not to be contaminated by the less soluble isomer, in which case it required repeated recrystallisation before reaching optical purity.

Considerable difficulty was met in the isolation of the optically active acids from the amides. In the first attempts, the amide, $[\alpha]_D$ +211·5°, was heated with aqueous-methanolic potassium hydroxide for an hour and gave, on acidification, a product with $[\alpha]_D$ +31·4°, but the diastereoisomeric amide, $[\alpha]_D$ −37·9°, on similar treatment also gave dextrorotatory material, $[\alpha]_D$ +32·6°. The products appeared to be hydrated acids which could not be satisfactorily recrystallised. On analysis they showed the correct carbon content for the phosphafluorene oxide carboxylic acid but very high hydrogen values. Repetition of this hydrolysis with the amides of $[\alpha]_D$ +38·6° and $[\alpha]_D$ −212·0° gave similar acids with $[\alpha]_D$ −32·4° and −31·2°, respectively. When all four products were found to contain nitrogen it became obvious that the resolving group had not been removed, but, instead, ring fission had occurred at either (a) or (b) in (IV) and the products were phosphinic and not carboxylic acids. Consequently, the asymmetry of the cyclic phosphine oxide had been destroyed and the rotations observed were derived from the (+)- and the (−)-1-phenylethylamido-group. This result was entirely unexpected as the carbon–phosphorus bond is comparable in strength with the carbon–carbon bond [11] and is broken only under drastic conditions such as the fusion of phosphine oxides with alkali (phosphinic acids are then obtained [12]).

In order to discover if ring fission had occurred at (a) or (b) in compound (IV; R = R′ = H, R″ = CO·NH·CHMePh) the product from the alkaline hydrolysis, having $[\alpha]_D$

[7] Braunholtz, Hall, Mann, and Sheppard, *J.*, 1959, 868.
[8] Bellamy and Beecher, *J.*, 1953, 728.
[9] Thomas, *J. Appl. Chem.*, 1957, 198.
[10] Morgan and Herr, *J. Amer. Chem. Soc.*, 1952, **74**, 4526.
[11] Huggins, *J. Amer. Chem. Soc.*, 1953, **75**, 4123.
[12] Horner, Hoffmann, and Wippel, *Chem. Ber.*, 1958, **91**, 64.

—32·4°, was further hydrolysed by prolonged heating with ethanolic hydrochloric acid. Loss of the phenylethylamido-group gave an optically inactive acid which is almost certainly 4′-carboxy-2-biphenylylphenylphosphinic acid. Its infrared spectrum closely resembles that of the acid (III; R = R′ = H, R″ = NO_2), a compound of known structure with substituents in the positions expected if the phosphafluorene ring opened at (b). Peaks at 1090, 1100, and 1140 cm.$^{-1}$, indicative of 1,2- and 1,4-disubstituted benzenes, are present in the spectra of both acids. On the other hand, the acid (III; R = Me, R′ = R″ = H) substituted similarly to a product resulting from fission at (a) shows the extra band associated with 1,2,4-substitution,[5] *i.e.*, bands at 1070, 1100, 1150, and 1165 cm.$^{-1}$. Preferential cleavage of the bond from phosphorus to the ring holding the amido-group is in line with Horner's experience [12] that the most electronegative group separates from phosphorus in the fusion of phosphine oxides with sodium hydroxide.

The isolation of the optically pure (+)- and (—)-phosphafluorene oxide carboxylic acids was finally achieved by prolonged hydrolysis with hydrochloric acid in ethanol, a method used by Marckwald [13] in his resolution of (±)-1-phenylethylamine through amide formation with quinic acid. He noted that racemic 1-phenylethyl chloride was produced in the course of hydrolysis and we have confirmed this observation, but the by-product was only a minor disadvantage in our case. By this method the amide of $[\alpha]_D$ +38·6° gave acid, m. p. 250—251°, $[\alpha]_D^{20}$ +126·0° ± 2° (in 0·1N-sodium hydroxide), in 80% yield; and from the amide of $[\alpha]_D$ —212°, the enantiomeric acid, m. p. 250—251°, $[\alpha]_D^{20}$ —126·1° ± 1·7°, was obtained in 66% yield. A large difference in solubility in ethanol between the (±)-acid and the (+)- or (—)-form made it possible to isolate optically pure acid from partly resolved specimens.

Reduction of the phosphafluorene oxides to phosphafluorenes was carried out by the method of Horner *et al.*[14] with lithium aluminium hydride in dibutyl ether and benzene at 80°. 9-Phenyl-9-phosphafluorene,[15] m. p. 90—92°, was obtained from the corresponding oxide in rather poor yield, but, contrary to the experience of others,[16] we found no evidence for the fission of a C–P bond. Preferential removal of oxygen without reduction of the carboxyl group in 2-carboxy-9-phenyl-9-phosphafluorene 9-oxide (IV; R = R′ = H, R″ = CO_2H) was not achieved—sodium borohydride had no effect on the P=O bond—and the product of reduction by lithium aluminium hydride was a mixture of 2-hydroxymethyl-9-phenyl-9-phosphafluorene and its 9-oxide. The phosphine was obtained crystalline (m. p. 52—54°) only when it retained a molecule of ethanol, and removal of this gave an amorphous residue, m. p. 38—42°, which was readily oxidised in air, particularly when in solution. The presence of traces of oxide in the product was indicated by low analytical values for carbon and by a small peak in the P=O region of the infrared spectrum.

Reduction of the *dextro*-form of the acid, $[\alpha]_D$ +126°, gave the same two products and resulted in complete loss of optical activity. The oxide must therefore result from reoxidation of the phosphine in the course of isolation, as the original acid is optically stable in alkaline solution at 100° and is not likely to be racemised under the conditions of reduction

Racemisation of the phosphafluorene is not unexpected in the light of Weston's estimate [17] that a simple pyramidal phosphine should have a half-life at 67° of only 2 hr., but is in direct contrast with our results in the reduction of the azaphosphaphenanthrene oxide (Part I). The optical activity of the phosphine isolated in the latter case could, of course, be ascribed to the asymmetry of a skew molecule, a possibility which we discussed but dismissed for several reasons. However, if the azaphosphaphenanthrene is capable

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[13] Marckwald, *Ber.*, 1905, **38**, 801.

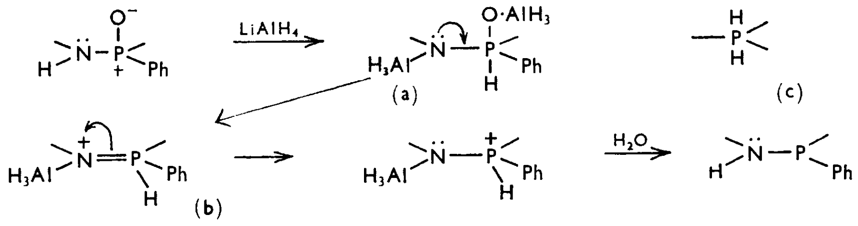
[14] Horner, Hoffmann, and Beck, *Chem. Ber.*, 1958, **91**, 1583.

[15] Wittig and Geissler, *Annalen*, 1953, **580**, 44.

[16] Issleib, Hein, and Rabold, *Z. anorg. Chem.*, 1956, **287**, 208.

[17] Weston, *J. Amer. Chem. Soc.*, 1954, **76**, 2645.

of retaining a pyramidal configuration during reduction at 80°, why is the phosphafluorene completely racemised under essentially the same conditions? We suggest that participation by nitrogen, as in the hydrogenolysis of amides,[18] results in a stereospecific reduction of the azaphosphaphenanthrene as shown in the partial formulæ annexed.



Attack by hydride ion would lead to the intermediate (a) in which phosphorus has the trigonal bipyramidal form, and loss of oxygen would occur with inversion, though hydride transfer from the $OAlH_3$ group by an $S_{\rm N}i$ reaction of the four-centre type is also possible and would result in retention. The intermediate (b) resembles a Wittig reagent which is known to retain configuration in reactions with carbonyl compounds[19] and might therefore be expected to give active phosphine on decomposition with water.

In the absence of nitrogen, an intermediate of type (b) is impossible and addition of hydride ion to the phosphafluorene oxide may occur by both $S_{\rm N}2$ and $S_{\rm N}i$ mechanisms to give a symmetrical intermediate (c) with consequent loss of activity. If, however, only one mechanism of hydrogen transfer is involved the initially active phosphine must undergo thermal racemisation. However, the azaphosphaphenanthrene can be isolated in optically active form from reduction under the same conditions, so the energy of activation of its racemisation must be considerably higher than that of the phosphafluorene. No doubt the energy barrier created by the repulsion of the lone pairs on the nitrogen and on the phosphorus would at least discourage the attainment of the planar transition state.

EXPERIMENTAL

Rotations were measured for absolute EtOH solutions in 2 dm. tubes (*c* 0·2—0·4) at room temperature unless otherwise stated. Infrared measurements were taken for Nujol mulls on the Unicam S.P. 100 spectrophotometer.

Preparation of 2-Biphenylylphenylphosphinic Acids.—(a) *Diazonium fluoroborate method.* Conditions similar to those recommended by Doak and Freedman[1] were used to prepare the phosphinic acids. For example, 2-aminobiphenyl (0·1 mole) was converted into the diazonium fluoroborate, and the dry salt was decomposed in ethyl acetate (200 ml.) in the presence of phenylphosphonous dichloride (0·1 mole) and copper bronze (2 g.). After steam-distillation to remove solvent and by-products (biphenyl and 2-chlorobiphenyl) the sticky brown residue was separated from the aqueous layer and warmed with 10% aqueous sodium hydroxide (25—30 ml.). From the filtered solution the sodium salt of the phosphinic acid crystallised as matted brown needles which were separated and washed with a little acetone. Acidification of a solution of this salt gave 2-biphenylylphenylphosphinic acid (III; $R = R' = R'' = H$),[3] m. p. 180—181° (9—10%), after crystallisation from acetic acid or ethanol–water.

Similar procedure with 2-amino-4′-nitrobiphenyl gave 4′-nitro-2-biphenylylphenylphosphinic acid (III; $R = R' = H$, $R'' = NO_2$), m. p. 234—237°, as buff needles from ethanol–water in 20—23% yield. 2-Amino-5-bromobiphenyl gave the *5-bromo-compound* (III; $R = R'' = H$, $R' = Br$), m. p. 193—194°, which separated as colourless needles from aqueous ethanol in 11%

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[18] Gaylord, " Reduction with Complex Metal Hydrides," Interscience Publ. Inc., New York, 1959, p. 545.

[19] Bladé-Font, VanderWerf, and McEwen, *J. Amer. Chem. Soc.*, 1960, **82**, 2396.

yield (Found: C, 58·1; H, 3·9. $C_{18}H_{14}BrO_2P$ requires C, 58·0; H, 3·8%). *4-Methyl-2-biphenylylphenylphosphinic acid* (III; R = Me, R′ = R″ = H), m. p. 144—145°, was obtained in only 4—5% yield by this method; it crystallised from ethyl acetate–light petroleum (b. p. 60—80°) in elongated prisms (Found: C, 73·8; H, 5·9. $C_{19}H_{17}O_2P$ requires C, 74·0; H, 5·6%).

(b) *Grignard method* (cf. ref. 2). Phenylphosphonous dichloride (4·7 g.) in ether (50 ml.) was added slowly to 2-biphenylylmagnesium iodide obtained from 2-iodobiphenyl (7 g.) and magnesium (0·6 g.) in ether (100 ml.). When the vigorous reaction had subsided the mixture was boiled for 1 hr., cooled, and treated with 2N-hydrochloric acid (25 ml.). This produced a heavy oil in addition to the aqueous and the ether layer. The aqueous layer was discarded and the ether evaporated. The residue was treated with 10% aqueous sodium hydroxide and hydrogen peroxide (5 ml.; 30-vol.); a vigorous reaction resulted in complete dissolution. Acidification gave 2-biphenylylphenylphosphinic acid, m. p. 180—181° (1·5 g., 20%) after crystallisation from acetic acid. The *ethyl ester*, m. p. 112—114° (Found: C, 73·9; H, 5·9. $C_{20}H_{19}O_2P$ requires C, 74·5; H, 5·9%), and the *anilide*, m. p. 202—204° (Found: C, 77·5; H, 5·4. $C_{24}H_{20}NOP$ requires C, 78·0; H, 5·5%), were obtained by treatment of the acid with thionyl chloride followed by ethanol or aniline, respectively.

2-Iodo-4-methylbiphenyl, b. p. 110—112°/0·3 mm., was obtained from the corresponding amine by the method of Zaheer and Faseeh [20] in 46% yield. Phenylphosphonous dichloride (7 ml.) in ether (75 ml.) was added to the filtered Grignard reagent prepared from 2-iodo-4-methylbiphenyl (17 g.) and magnesium (1·4 g.) in ether (100 ml.). During the addition (15 min.) the mixture was stirred rapidly and when the vigorous reaction had subsided heating was continued for 45 min. After cooling, the mixture was shaken with 2N-sulphuric acid (50 ml.), and hydrogen peroxide (5 ml.; 100-vol.) was added dropwise. After 30 minutes' stirring, the organic layer was separated and evaporated. The dark residue was extracted with hot 10% aqueous sodium hydroxide containing a little hydrogen peroxide. The sodium salt separated from the filtered solution on cooling, and was filtered off and washed with ether. Acidification of a solution of this salt gave the crude acid (7·7 g.) which, after crystallisation from ethyl acetate–light petroleum (b. p. 60—80°), had m. p. 144—145° (5·9 g., 33%).

Cyclisation of 2-Biphenylylphenylphosphinic Acids.—(*a*) 2-Biphenylylphenylphosphinic acid was regained from polyphosphoric acid after being heated at 120° for 30 min., but at 160° some decomposition occurred and biphenyl (10%) was isolated in addition to unchanged acid.

(*b*) Concentrated sulphuric acid at 110° (20 min.) apparently caused sulphonation of the phosphinic acid, for complete dissolution occurred on addition of the reaction mixture to water. Attempts to isolate sulphonated acids by formation of the magnesium or barium salts failed.

(*c*) The phosphinic acid (1 g.) was converted into the acid chloride by warming it with an excess of thionyl chloride in chloroform, and the viscous oil obtained was heated in carbon disulphide (20 ml.) with aluminium chloride (0·5 g.) for 3 hr. The mixture was shaken with N-hydrochloric acid, water, and saturated sodium hydrogen carbonate solution. Evaporation of the carbon disulphide gave a small sticky residue and acidification of the alkaline extract gave unchanged acid of m. p. 175—180° (0·8 g.). This experiment was repeated with nitrobenzene (10 ml.) as solvent and heating at 160° for 4 hr. The cooled mixture was poured into water and steam-distilled to remove nitrobenzene. The black residue was soluble in aqueous sodium hydrogen carbonate. Acidification gave unchanged acid, m. p. 170—180° (0·6 g.).

(*d*) A mixture of the acid (III; R = R′ = R″ = H) (1 g.) and phosphorus pentachloride (1·5 g.) was heated for 4 hr. under reflux, with exclusion of moisture, at 170—180°. The cold mixture was poured into water and steam-distilled to remove nitrobenzene. The sticky residue was separated from the aqueous layer and extracted with 10% aqueous sodium hydroxide, leaving a brown solid (0·4 g.) which was crystallised from aqueous ethanol and gave 9-phenyl-9-phosphafluorene 9-oxide, m. p. 167—168° (0·25 g.) (Found: C, 78·0; H, 4·75. Calc. for $C_{18}H_{13}OP$: C, 78·25; H, 4·7%). Acidification of the alkaline extract gave unchanged acid (0·5 g.).

The oxide formed a *cadmium iodide complex* in aqueous ethanol which separated from ethyl acetate containing a trace of ethanol in diamond-shaped plates, m. p. 200—202° [Found: C, 46·9; H, 2·8. $(C_{18}H_{13}OP)_2CdI_2$ requires C, 47·1; H, 2·85%]. The *mercuric chloride complex* made similarly had m. p. 145—147°, and contained the constituents in different proportions [Found: C, 48·5; H, 2·75. $(C_{18}H_{13}OP)_3(HgCl_2)_2$ requires C, 48·6; H, 2·8%].

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[20] Zaheer and Faseeh, *J. Indian Chem. Soc.*, 1944, **21**, 27.

Treatment of the acid (III; R = R′ = H, R″ = NO_2) (0·8 g.) by process (*d*) gave 2-*nitro*-9-*phenyl*-9-*phosphafluorene* 9-*oxide* (IV; R = R′ = H, R″ = NO_2) (0·15 g.), m. p. 203° (Found: C, 67·0; H, 4·1. $C_{18}H_{12}NO_3P$ requires C, 67·3; H, 3·8%), and unchanged acid (0·48 g.).

By process (*d*) but with the quantity of phosphorus pentachloride increased to 2 g. and the period of heating to 8 hr. at 160—170°, the acid (III; R = R″ = H, R′ = Br) (1 g.) gave a cyclic oxide, m. p. 227—228° (0·65 g.), and 0·1 g. of acid was regained. The oxide was found to contain chlorine but no bromine, and was presumably 3-*chloro*-9-*phenyl*-9-*phosphafluorene* 9-*oxide* (IV; R = R″ = H, R′ = Cl) (Found: C, 69·4; H, 4·3; Cl, 11·7; P, 10·3. $C_{18}H_{12}ClOP$ requires C, 69·6; H, 3·9; Cl, 11·4; P, 10·0%).

2-*Methyl*-9-*phenyl*-9-*phosphafluorene* 9-*Oxide*.—The acid (III; R = Me, R′ = R″ = H) (2 g.) was suspended in " AnalaR " nitrobenzene (12 ml.) and cyclised by heating it with phosphorus pentachloride (4 g.) at 160—165° for 6 hr. The product was isolated as described under (*d*) and was obtained as a glass (1·5 g.) which crystallised with difficulty from ethyl acetate–light petroleum (b. p. 60—80°), giving the pure *oxide* (IV; R = Me, R′ = R″ = H), m. p. 146—147° (Found: C, 78·5; H, 5·0. $C_{19}H_{15}OP$ requires C, 78·6; H, 5·2%). A depression of 27° was observed in a mixed m. p. determination with the uncyclised acid, m. p. 144—145°. Unchanged acid (75 mg.) was regained.

2-*Carboxy*-9-*phenyl*-9-*phosphafluorene* 9-*Oxide*.—The crude 2-methyl-9-phenylphosphafluorene oxide (10 g.) was heated in pyridine (45 ml.) and water (25 ml.) on a water-bath. Potassium permanganate (19·5 g.) was added to the hot solution in small portions during 2—3 hr. A further 30 ml. of water were added to keep the mixture fluid. Heating was continued for 5 hr., then pyridine was removed by steam-distillation, and manganese dioxide by filtration, and the alkaline solution was acidified. The precipitated acid crystallised from aqueous ethanol, and 2-*carboxy*-9-*phenyl*-9-*phosphafluorene* 9-*oxide* (II; R = CO_2H, R′ = R″ = H), m. p. 309—313° (darkening) (5·9 g.), separated as colourless needles. Recrystallisation raised the m. p. to 323—326° (Found: C, 70·9; H, 4·1. $C_{19}H_{13}O_3P$ requires C, 71·25; H, 4·1%). 2-Methyl-9-phenylphosphafluorene oxide (0·9 g.) was recovered from the precipitated manganese dioxide after reduction.

Optical Resolution of 2-*Carboxy*-9-*phosphafluorene* 9-*Oxide*.—All attempts to resolve the acid by salt formation with optically active bases failed. Salts made by dissolving the acid with the equivalent weight of quinine, quinidine, ephedrine, brucine, or strychnine, in various solvents, separated as gums. Solutions of the acid with one or two equivalents of (—)-1-phenylethylamine or (+)-amphetamine in ethanol deposited oils on addition of ether, and crystals which separated (after several weeks) from the attempt with (—)-1-phenylethylamine proved to be acid, m. p. 310°

(a) *Resolution through the* (—)-1-*phenylethylamide*. The acid (1 g.) and (—)-1-phenylethylamine (3 ml.) were heated together at the b. p. for 3 hr., cooled, and poured into 4N-hydrochloric acid (20 ml.). The solid which separated was extracted with saturated sodium hydrogen carbonate solution, leaving the amide (0·75 g.) undissolved. The acid (0·35 g.) was regained from the alkaline extract. The amide, $[\alpha]_D$ +51·2°, crystallised from ethanol and gave a first fraction (0·25 g.) with $[\alpha]_D$ —28·9°. Two further crystallisations of this gave the (—)-*acid-amide* (0·14 g.), as rosettes of needles, m. p. 263—265°, $[\alpha]_D$ —37·9° (Found: C, 76·0; H, 5·3. $C_{27}H_{22}NO_2P$ requires C, 76·6; H, 5·2%).

Dilution of the filtrate from the first separation with water gave a second fraction of amide (0·23 g.), $[\alpha]_D$ +189·3°, which when recrystallised from ethanol gave optically pure (+)-*acid amide* (0·14 g.), m. p. 273—275°, $[\alpha]_D$ +211·5°, as highly refracting prisms (Found: C, 75·9; H, 5·3%). Amide which separated as a third fraction from the original crystallisation was contaminated by a yellow gum.

(b) *Resolution through the* (+)-1-*phenylethylamide*. The acid (2 g.) was suspended in (+)-1-phenylethylamine (5 ml.; $[\alpha]_D$ +34·7° in chloroform) and heated at the b. p. for 5 hr. The cooled liquid was poured into 2N-hydrochloric acid (50 ml.), and the solid obtained was filtered and extracted with saturated aqueous sodium hydrogen carbonate. Acid (0·22 g.) was regained from the extract. The amide (2·25 g.) had $[\alpha]_D$ —51·9° and when crystallised from ethanol (15 ml.) gave a first fraction (0·65 g.) with $[\alpha]_D$ +34·5° which was raised to $[\alpha]_D$ +38·6° by one further crystallisation. This optically pure (+)-*acid*–(+)-1-*phenylethylamide* (0·45 g.) had m. p. 265—266° and separated as stout needles (Found: C, 76·7; H, 5·0; N, 3·3. $C_{27}H_{22}NO_2P$ requires C, 76·6; H, 5·2; N, 3·3%). A second fraction of amide (0·72 g.) was obtained from the mother-liquor by dilution with water (15 ml.) and had $[\alpha]_D$ —171·9°. One crystallisation of this from ethanol gave the pure (−)-*acid*-(+)-1-*phenylethylamide*, m. p. 274—275°, $[\alpha]_D$ −212·0° (0·50 g.), as heavy prisms (Found: C, 76·55; H, 5·1; N, 3·45%). A third fraction of amide, $[\alpha]_D$ −43·4° (0·27 g.), and a fourth, $[\alpha]_D$ −7·8° (0·25 g.), were separated but optically pure material was not obtained from them.

A repetition of this resolution with 2·4 g. of acid gave (+)-acid-amide, $[\alpha]_D$ +37·5° (0·61 g.), and (−)-acid amide, $[\alpha]_D$ −211·0° (0·31 g.).

Hydrolysis of the Active Amides.—The (+)-acid–(−)-amide, $[\alpha]_D$ +211·5° (0·14 g.), was boiled with a 25% solution (5 ml.) of potassium hydroxide in methanol–water (3 : 1) for 1 hr. The solution was chilled, diluted, and acidified with N-sulphuric acid at 0°. The precipitated *acid* (0·14 g.), m. p. 140—145° (decomp.) softening at 105°, $[\alpha]_D$ +32·4°, appeared to be hydrated (Found: C, 71·25; H, 5·2. $C_{19}H_{13}O_3P$ requires C, 71·25; H, 4·1%).

The (−)-acid–(−)-amide, $[\alpha]_D$ −37·9° (0·1 g.), gave, on similar treatment, an *acid* (85 mg.) which had $[\alpha]_D$ +32·6° and m. p. 140—150°, softening at 108° (Found: C, 71·2; H, 5·2%).

Hydrolysis of the (+)-acid–(+)-amide, $[\alpha]_D$ +38·5° (0·2 g.), by the same method gave an *acid* (0·17 g.), $[\alpha]_D$ −32·4°, while the (−)-acid–(+)-amide, $[\alpha]_D$ −212·0° (0·2 g.), gave an *acid* (0·17 g.), $[\alpha]_D$ −31·2° (Found: C, 71·0; H, 5·2; and C, 71·1; H, 5·2%, respectively). Both products had the same indefinite m. p. 140—150° with previous softening, and could not be recrystallised satisfactorily. Both gave a positive test for nitrogen. The acid of $[\alpha]_D$ −32·4° (0·1 g.) was dissolved in ethanol (1 ml.) and hydrolysed by boiling concentrated hydrochloric acid (2 ml.) for 5 hr. Dilution of the cooled mixture gave a solid (0·05 g.) which, after crystallisation from ethanol–water or from dilute acetic acid, had m. p. 292° (softening from 285°) and was optically inactive (Found: C, 67·25; H, 4·2. $C_{19}H_{15}O_4P$ requires C, 67·45; H, 4·5%).

Isolation of (+)- *and* (−)-2-*Carboxy*-9-*phenyl*-9-*phosphafluorene* 9-*Oxide.*—The amide, $[\alpha]_D$ +37·5° (0·65 g.), was suspended in ethanol (5 ml.) and concentrated hydrochloric acid (10 ml.) and boiled under reflux for 12 hr. The cooled mixture was poured into water, and the precipitate was collected, dissolved in 2N-sodium hydroxide, and filtered from a small sticky residue. Acidification of the filtrate gave the (+)-*acid*, m. p. 250—251°, $[\alpha]_D^{20}$ +126·0° ± 2° (*c* 0·238 in 0·1N-sodium hydroxide) (0·41 g., 83%) (Found: C, 71·1; H, 4·1%).

Similar treatment of the (−)-amide, $[\alpha]_D$ −212·0° (0·2 g.), gave the (−)-*acid*, m. p. 250—251°, $[\alpha]_D^{20}$ −126·1° ± 1·7° (*c* 0·283 in 0·1N-sodium hydroxide) (0·11 g.) (Found: C, 70·8; H, 4·1%).

A specimen of (+)-acid, $[\alpha]_D^{20}$ +81·1° (0·1 g.), obtained in this way from optically impure amide, was extracted with hot ethanol (3 ml.) and filtered. The filtrate on cooling deposited pure (+)-acid, m. p. 250—251°, $[\alpha]_D$ +125·9° ± 2·4° (45 mg.). The residue had m. p. 300° and showed a negligible rotation. The acids had $[\alpha]_D^{20}$ +107·1° and −106·3° in absolute ethanol (*c* 0·140 and 0·127 respectively) and were unchanged in rotation after 3 weeks at room temperature. A solution of the acid in 0·1N-sodium hydroxide, α_D^{19} +0·61°, was boiled under reflux for 1 hr. and cooled rapidly to 19°. The rotation of the solution was unchanged then, and also after a further 2 hours' heating.

Reduction of 9-*Phenyl*-9-*phosphafluorene* 9-*Oxides.*—(a) *Sodium borohydride.* A mixture of the oxide (IV; $R = R' = R'' = H$) (0·2 g.) and sodium borohydride (0·2 g.) in methanol (5 ml.) was warmed on a water-bath for 3 hr. Addition of water to the cold solution precipitated unchanged oxide (0·15 g.), m. p. 162—165° (after crystallisation from aqueous ethanol).

The oxide (IV; $R = R' = H$, $R'' = CO_2H$) (0·5 g.) was neutralised with 0·1N-sodium hydroxide, sodium borohydride (0·5 g.) in water (2 ml.) was added, and the mixture was kept at room temperature for 3 days. Acidification then gave unchanged oxide (0·45 g.). The oxide was also regained when the mixture was kept at 50° for 24 hr. and at 100° for 10 hr.

(b) *Lithium aluminium hydride.* The oxide (IV; $R = R' = R'' = H$) (0·47 g.), dissolved in benzene (5 ml.), was added dropwise to lithium aluminium hydride (0·2 g.) suspended in dibutyl ether (5 ml.) at 80—90°. The mixture was heated on a water-bath for 5 hr., cooled, and poured into 20% aqueous sodium hydroxide. The organic layer was separated, washed, dried (Na_2SO_4), and evaporated. The solid residue, on crystallisation from methanol gave 9-phenyl-9-phosphafluorene,[15] m. p. 90—92° (90 mg.). Its infrared spectrum was almost identical with that shown in ref. 15 (m. p. 92—94°). The main ultraviolet absorption band of 9-phenyl-9-phosphafluorene, $\lambda_{max.}$ 270 mμ (ε 14,580), $\lambda_{min.}$ 253 (ε 13,250), shows a bathochromic shift of only 10 mμ compared with that of triphenylphosphine, $\lambda_{max.}$ 260 mμ (ε 12,660). This shift is small compared with that observed for similar arsenic and antimony compounds.[21]

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[21] Campbell and Poller, *Chem. and Ind.*, 1953, 1126.

The oxide (IV; R = R′ = H, R″ = CO_2H) (0·5 g.) was suspended in benzene (10 ml.) and added in small portions to lithium aluminium hydride (0·4 g.) in dibutyl ether (10 ml.) at 80—90° during 0·5 hr. Benzene (5 ml.) was added and the whole heated on a water-bath for 4 hr. and set aside overnight. The mixture was cooled, excess of reagent was decomposed by addition of water, and the whole shaken with N-sulphuric acid (50 ml.). The organic layer was washed, dried, and evaporated *in vacuo*, giving a gum (0·32 g.). A portion (0·25 g.), crystallised from ethanol–light petroleum (b. p. 60—80°), gave solvated 2-*hydroxymethyl*-9-*phenyl*-9-*phosphafluorene* (V; R = R′ = H, R″ = $CH_2\cdot OH$), m. p. 52—54° (91 mg.) (Found: C, 75·5, 75·8; H, 6·1, 5·9. $C_{19}H_{15}OP,C_2H_6O$ requires C, 75·0; H, 6·3%). The phosphine was heated *in vacuo* at 100° for 3 hr.; the *anhydrous form* had m. p. 38—42° (Found: C, 77·4; H, 5·0. $C_{19}H_{15}OP$ requires C, 78·6; H, 5·2). Addition of ether to the filtrate from the crystallisation of the phosphine precipitated 2-*hydroxymethyl*-9-*phenyl*-9-*phosphafluorene* 9-*oxide* (IV; R = R′ = H, R″ = CH_2OH), m. p. 195—196° (50 mg.) (from ethanol–ethyl acetate) (Found: C, 74·1; H, 4·75. $C_{19}H_{15}O_2P$ requires C, 74·5; H, 4·9%). Methylation of the original gum (70 mg.) gave 2-*hydroxymethyl*-9-*phenyl*-9-*phosphafluorene methiodide*, m. p. 228—230° (30 mg.) (Found: C, 55·9; H, 3·9. $C_{20}H_{18}IOP$ requires C, 55·6; H, 4·2%).

When the reduction was repeated with the (+)-acid (0·4 g.) and lithium aluminium hydride (0·3 g.), the product (0·32 g.) was optically inactive. It (0·27 g.) was separated by crystallisation from ethanol–light petroleum (b. p. 60—80°) into the phosphafluorene alcohol (150 mg.), m. p. 51—53° (Found: C, 75·2; H, 6·2, and C, 77·8; H, 5·1% after heating *in vacuo*), and the corresponding oxide, m. p. 195—196° (60 mg.) (Found: C, 74·1; H, 4·8%). Methylation of the crude product gave the methiodide, m. p. and mixed m. p. 226—230°. The phosphine, m. p. 52—54°, when boiled in benzene for an hour gave the oxide, m. p. 195—196°, on evaporation of the solvent.

Relevant infrared bands are in the annexed Table.

Main infrared absorption bands of compounds (IV *and* V; R = R′ = H, R″ = $CH_2\cdot OH$).

Compound IV:	3260b, 3040, 1600, 1482, 1460,† 1440s, 1410w, 1350, 1205, 1175s, 1140, 1120, 1065s, 830, 770, 750s, 735s, 700
Compound V:	3330b, 3040, 1600, 1480, 1455,† 1440s, 1410, 1330, 1208, 1185s, 1140, 1120, 1060s, 895w, 830, 780s, 740s, 700s
Benzyl alcohol: *	3350b, 3030, 2920, 2880, 1500, 1460, 1212, 1090w, 1050s, 1025, 925w, 745, 700

b = broad band, mid-point; s = strong; w = weak; remainder medium. Nujol peaks, 2950b, 2890b, 1465, 1385.

* Liquid film. † The intensity of the 1465 Nujol band is increased relative to the 1385 band owing to the presence of the benzyl CH_2 group.

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