727. *The Synthesis of Certain Chelating Ditertiary Phosphines.*

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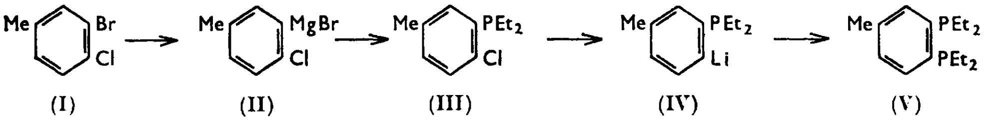
Stereochemical studies required the use of certain ditertiary phosphines which would chelate strongly to metals, and of structure such that two molecules would combine with a tetrahedral 4-co-ordinate metal to give a dissymmetric spirocyclic cation. For this purpose the synthesis of 4-methyl-*o*-phenylenebis(diethylphosphine) has been greatly improved and biphenyl-3,4-bis(diethylphosphine) and (2-diethylphosphino-5-methylbenzyl)diethylphosphine have been synthesised.

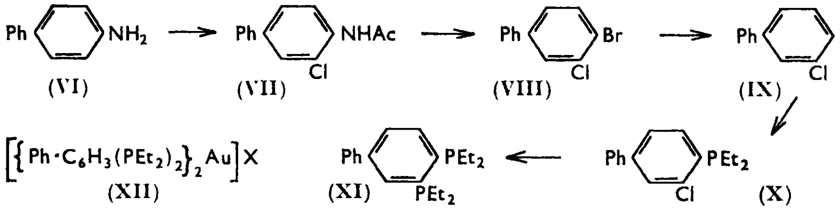
The preparation of some chelating ditertiary phosphines, required for the study of the stereochemistry of certain gold derivatives,[1] is now described.

4-Methyl-*o*-phenylenebis(diethylphosphine) (V) was first prepared by Hart and Mann,[2] 3-bromo-4-iodotoluene being treated with an excess of magnesium, followed by diethylphosphinous chloride, Et_2PCl; the yield was low and the product difficult to purify. The following greatly improved synthesis is based on Hart's method for preparing *o*-phenylenebis(diethylphosphine).[3]

3-Bromo-4-chlorotoluene (I) was treated with activated magnesium (1·07 equiv.) in ether, to give the Grignard reagent (II), which with diethylphosphinous chloride (0·9 equiv.) gave the phosphine (III) in 48% yield. This phosphine, treated in tetrahydrofuran solution at —35° with lithium (2 equiv.) and then with diethylphosphinous chloride (1 equiv.), gave the pure diphosphine (V) in 15% overall yield, calculated on the chlorobromotoluene (I) employed. The phosphine (V) was readily separated from the accompanying lower-boiling diethyl-*m*-tolylphosphine.



For our purpose, an analogue of the diphosphine (V) having a larger nuclear substituent was also required, and biphenyl-3,4-bis(diethylphosphine) (XI) was therefore prepared. 4-Nitrobiphenyl[4] was reduced to 4-aminobiphenyl (VI),[5] which when acetylated and then chlorinated in acetic acid gave 4-acetamido-3-chlorobiphenyl (VII).[4] Hydrolysis gave the 4-amino-compound, which when diazotised and subjected to the Sandmeyer reaction afforded 4-bromo-3-chlorobiphenyl (VIII). This reacted very slowly and incompletely with activated magnesium to give the Grignard reagent (IX), identified by carboxylation to 3-chlorobiphenyl-4-carboxylic acid,[6] thus confirming the positions of the halogen atoms



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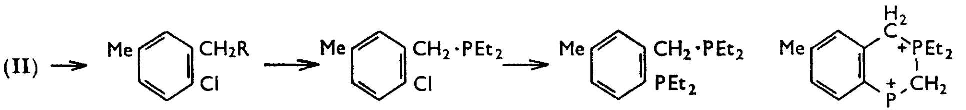
[1] Davis and Mann, following Paper.
[2] Hart and Mann, *J.*, 1957, 3939.
[3] Hart, *J.*, 1960, 3324.
[4] Bell, Kenyon, and Robinson, *J.*, 1926, 1239.
[5] Jenkins, McCullough, and Booth, *Ind. Eng. Chem.*, 1930, **22**, 31.
[6] Schoepple and Truesdail, *J. Amer. Chem. Soc.*, 1937, **59**, 372.

in the compound (VIII). The reagent (IX), treated with diethylphosphinous chloride, gave, on working up, a distillate of crude 3-chloro-4-biphenylyldiethylphosphine (X) which was difficult to purify; it was treated in turn with lithium and diethylphosphinous chloride, to give the required diphosphine (XI), some 4-biphenylyldiethylphosphine, and a small amount of biphenyl. The low yield of the diphosphine (XI) prevented its purification, but it was characterised as the highly crystalline spirocyclic bis(diphosphine)gold(I) iodide (XII; X = I) and picrate; other salts are also recorded.[1]

To obtain a diphosphine which on chelation with a metal would give a suitable six-membered ring, (2-diethylphosphino-5-methylbenzyl)diethylphosphine (XV) was synthesised. The Grignard reagent (II) on treatment with formaldehyde gave 2-chloro-5-methylbenzyl alcohol (XIII; R = OH), which with hydrogen bromide gave the bromide (XIII; R = Br). This bromide was converted into the Grignard reagent, which with diethylphosphinous chloride afforded the phosphine (XIV); some 1,2-bis-(2-chloro-5-methylphenyl)ethane, isolated at this stage, was undoubtedly a by-product during the formation of the Grignard reagent. The phosphine (XIV), when treated as before with lithium and then with diethylphosphinous chloride, gave the required diphosphine (XV), and some diethyl-3-methylbenzylphosphine. This by-product corresponds in type to the diethyl-*m*-tolylphosphine and the 4-biphenylyldiethylphosphine which accompanied the formation of the diphosphines (V) and (XI), respectively.



(XIII) (XIV) (XV) (XVI)

The origin of these similar by-products is obscure. Their comparatively high yield, when the calculated quantity of diethylphosphinous chloride is used, shows that they cannot arise by hydrolysis of unreacted lithio-derivative (as IV). Moreover, Hart[3] found that diethyl-*o*-lithiophenylphosphine, when treated in tetrahydrofuran with diethylphosphinous chloride (1 mol.), gave diethylphenylphosphine and *o*-phenylenebis(diethylphosphine) in 37 and 27% yields, respectively; the yield of the diphosphine was not increased when the chloride (1·4 mol.) was used. It is possible that some replacement of lithium by hydrogen from the solvent occurs, but there is no evidence of this process in the conditions employed.

The diphosphine (XV) combined with dibromomethane to give 1,1,3,3-tetraethyl-1,2,3,4-tetrahydro-6-methyl-1,3-diphosphonianaphthalene dibromide (XVI; X = Br), which is apparently the first phosphorus analogue of the quinazoline system to be recorded.

The diethylphosphinous chloride used in this work was prepared by the interaction of tetraethyl-lead and ethylphosphonous dichloride,[7] but a slight change in the proportion of these reagents prevented the formation of a troublesome forerun, and this increased the yield of the pure diethylphosphinous chloride from 38 to 80%.

All attempts to obtain Grignard reagents from 1-bromo-2-chloronaphthalene and 1-bromo-2-iodonaphthalene, using various conditions and solvents, failed, and a projected synthesis of 1,2-bis(diethylphosphino)naphthalene was therefore abandoned.

EXPERIMENTAL

All compounds were colourless unless otherwise described.

Diethylphosphinous Chloride.—A stirred mixture of ethylphosphonous dichloride (130 g.) and tetraethyl-lead (110 g., 0·34 mol.) was heated under nitrogen at 140—145° for 36 hr. Fractional distillation gave the pure chloride (100 g., 80%), b. p. 131—132°.

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[7] Beeby and Mann, *J.*, 1951, 411.

4-Amino-3-bromotoluene hydrochloride [8] (280 g.) was converted by the Sandmeyer reaction into 3-bromo-4-chlorotoluene (I) (230 g., 90%), b. p. 94°/3 mm. (lit.,[9] 120—125°/28 mm.).

(2-*Chloro*-5-*methylphenyl*)*diethylphosphine* (III).—A portion (100 ml.) of a solution of 3-bromo-4-chlorotoluene (I) (98·6 g.) in ether (600 ml.) was added under nitrogen to magnesium (12·56 g., 1·07 atom) followed by ethyl bromide (4·0 g., 0·073 mol.) and an iodine crystal. When the reaction started, the remainder of the solution was slowly added. The complete mixture was stirred for 1 hr., and pure diethylphosphinous chloride (53·8 g., 0·9 mol.) in ether (75 ml.) added dropwise, a brown oil slowly separating. The mixture was stirred for a further 30 min., and then hydrolysed by a saturated aqueous ammonium chloride solution (400 ml.). After removal of the solvent from the dried ethereal layer, two distillations gave the *phosphine* (III) (49 g., 48%), b. p. 99—101°/0·4 mm. (Found: C, 61·2; H, 7·4. $C_{11}H_{16}ClP$ requires C, 61·5; H, 7·5%). It gave an *ethobromide*, m. p. 181° (from ethanol) (Found: C, 48·1; H, 6·4. $C_{13}H_{21}BrClP$ requires C, 48·2; H, 6·5%), and an *ethiodide*, m. p. 188° (from ethyl methyl ketone) (Found: C, 42·2; H, 5·6. $C_{13}H_{21}ClIP$ requires C, 42·1; H, 5·7%); both salts gave the yellow *ethopicrate*, m. p. 121—122° (from ethanol) (Found: C, 48·4; H, 4·5; N, 9·0. $C_{19}H_{23}ClN_3O_7P$ requires C, 48·4; H, 4·9; N, 8·9%).

In an early preparation, in which the diethylphosphinous chloride contained some ethylphosphonous dichloride, addition of acetone to the residue from the first distillation deposited *di*-(2-*chloro*-5-*methylphenyl*)*ethylphosphine*, needles, m. p. 137—138° (from acetone) (Found: C, 61·5; H, 5·3. $C_{16}H_{17}Cl_2P$ requires C, 61·7; H, 5·5%); it gave an *ethiodide*, m. p. 218° (Found: C, 46·5; H, 4·4. $C_{18}H_{22}Cl_2IP$ requires C, 46·3; H, 4·7%), and a yellow *ethopicrate*, m. p. 175—176° (from ethanol) (Found: C, 51·0; H, 4·6; N, 7·6. $C_{24}H_{24}Cl_2N_3O_7P$ requires C, 50·7; H, 4·3; N, 7·4%).

4-*Methyl*-o-*phenylenebis*(*diethylphosphine*) (V).—Lithium foil (2·74 g., 2 atoms) was added to a solution of the phosphine (III) (42·4 g.) in tetrahydrofuran (200 ml.) maintained at *ca.* −35°. This mixture was stirred for 2½ hr., diethylphosphinous chloride (24·6 g., 1 mol.) in tetrahydrofuran (40 ml.) slowly added, and the mixture allowed to attain room temperature. After removal of the solvent from the organic layer, distillation of the residue at 0·6 mm. gave fractions: (A) b. p. 70—90° (11 g.); (B) b. p. 115—120° (16·5 g.); (C) b. p. 120—140° (3 g.).

Fraction (A) was almost wholly diethyl-*m*-tolylphosphine; it gave an *ethiodide*, m. p. 151° (from ethanol) (Found: C, 46·6; H, 6·8. $C_{13}H_{22}IP$ requires C, 46·4; H, 6·6%), and a yellow *ethopicrate*, m. p. 88° (from aqueous ethanol) (Found: C, 52·0; H, 5·5; N, 9·6. $C_{19}H_{24}N_3O_7P$ requires C, 52·1; H, 5·5; H, 9·6%). The infrared spectrum of the iodide showed clearly the 1,3-disubstituted benzene absorption bands.

Fraction (B) was the required diphosphine (V) (31%). A few drops reacted vigorously with 1,2-dibromoethane to give 1,1,4,4-tetraethyl-1,2,3,4-tetrahydro-6-methyl-1,4-diphosphonianaphthalene dibromide, which gave the dipicrate, m. p. 178·5—179° (lit.,[2] 178—179°); a second portion reacted with gold(III) chloride to give bis-[4-methyl-*o*-phenylenebis(diethylphosphine)]-gold iodide, m. p. 241—242° (lit.,[2] 240·5—242°).

4-*Bromo*-3-*chlorobiphenyl* (VIII).—4-Nitrobiphenyl (160 g.), prepared by nitration of biphenyl (250 g.) in acetic acid,[4] was reduced in benzene solution to 4-aminobiphenyl (VI) (75 g., 55%) using activated iron and water.[5] A mixture of the aminobiphenyl (83 g.), acetic acid (150 ml.), and acetic anhydride was boiled under reflux for 1 hr., cooled, and diluted with more acetic acid (1·5 l.). A slow stream of chlorine was passed through to give an increase in weight of 35·5 g. The solution was diluted with water, and after 1 hr. the deposited 4-acetamido-3-chlorobiphenyl (VII) was collected; a sample had m. p. 145° (from aqueous ethanol) (lit.,[4] m. p. 146°). A solution of the remaining crude biphenyl (VII) in boiling ethanol (300 ml.) was diluted with hydrobromic acid (150 ml., 48%), boiled under reflux for 4 hr., and cooled. The 4-*amino*-3-*chlorobiphenyl hydrobromide* (120 g., 85%) crystallised; a sample, recrystallised from ethanol containing a small amount of the acid, gave needles, m. p. *ca.* 240° (sublimes) (Found: N, 5·1. $C_{12}H_{10}ClN,HBr$ requires N, 4·9%).

A stirred suspension of the hydrobromide (119 g.) in hydrobromic acid (150 ml., 48%) was cooled to 0° and treated slowly with sodium nitrite (30 g., 1·15 mol.) in water (55 ml.). A portion of the diazotised solution, when added to an alkaline solution of 2-naphthol, deposited 3-*chloro*-4-*biphenylylazo*-2-*naphthol*, deep red plates, m. p. 202—203° (from ethyl methyl ketone) (Found: C, 72·9; H, 4·7; N, 7·9. $C_{22}H_{15}ClN_2O$ requires C, 73·6; H, 4·2; N, 7·8%). The diazotised

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[8] *Org. Synth.*, Coll. Vol. 1, 2nd edn., 1941, p. 111.

[9] Cohen and Smithells, *J.*, 1914, **105**, 1908.

solution was added slowly to a boiling solution of cuprous bromide (40 g.) in hydrobromic acid (40 ml., 48%), and the deposited heavy oil extracted with chloroform. The extract, when washed with dilute acid and alkali, dried, and distilled, gave 4-*bromo*-3-*chlorobiphenyl* (VIII) (57·5 g., 52%), b. p. 129°/0·2 mm., m. p. 42° (Found: C, 54·1; H, 3·3. $C_{12}H_8BrCl$ requires C, 53·8; H, 3·0%).

After preliminary experiments to form a Grignard reagent, two solutions were prepared: (A) the biphenyl (VIII) (75 g.) in ether (150 ml.); (B) ethyl bromide (20 g., 0·65 mol.) in ether (50 ml.). Half of solution (B) was added to magnesium (11·5 g., 1·7 atom) containing an iodine crystal, to give a vigorous reaction; solution (A) was then added to maintain gentle boiling, followed by the remainder of (B). The mixture was stirred for 30 min. and then boiled under reflux for 1½ hr. [A portion was added to solid carbon dioxide–ether, and on working up gave 3-chlorobiphenyl-4-carboxylic acid, m. p. 166—166·5° (lit.,[6] 166·5—167°) (from toluene).]

Diethylphosphinous chloride (55·9 g., 0·95 mol.) in ether (60 ml.) was added dropwise to the chilled stirred Grignard solution, followed after 30 min. by saturated aqueous ammonium chloride (*ca.* 300 ml.). After the usual working up, distillation at 0·3 mm. gave the unchanged biphenyl (VIII) (55 g., 73% recovery) and a fraction (17·6 g.), b. p. 147—163°, which was apparently a mixture of (VIII) and the required phosphine (X) (Found: C, 62·6; H, 5·4. Calc. for $C_{16}H_{18}ClP$: C, 69·3; H, 6·5%). Triethylphosphine (9 ml.), formed by the action of the ethylmagnesium bromide on the diethylphosphinous chloride, was collected in the liquid-nitrogen trap, and identified by conversion into the ethiodide, which gave *tetraethylphosphonium picrate*, yellow needles, m. p. 212° (from water) (Found: C, 44·6; H, 6·1; N, 11·0. $C_{14}H_{22}N_3O_7P$ requires C, 44·8; H, 5·9; N, 11·2%).

A few drops of the fraction, b. p. 147—163°/0·3 mm., when treated with methyl toluene-*p*-sulphonate in light petroleum (b. p. 40—60°), gave a sticky solid which after five recrystallisations from acetone–ether gave 2-*chloro*-4-*biphenylyldiethylmethylphosphonium toluene*-p-*sulphonate*, m. p. 151—151·5° (Found: C, 62·9; H, 6·6. $C_{24}H_{28}ClO_3PS$ requires C, 62·2; H, 6·2%).

3,4-*Biphenylylenebis*(*diethylphosphine*) (XI).—The impure phosphine (X), b. p. 147—163°/0·3 mm., in tetrahydrofuran was cooled to *ca.* −35°, and treated as previously described with lithium (0·63 g., 2 atom) and then with diethylphosphinous chloride (5·6 g., 1 mol.) in tetrahydrofuran (20 ml.). Working up as before gave fractions: (A) b. p. 115—122°/0·1 mm. (1·0 g.); (B) b. p. 123—133°/0·1 mm. (1·2 g.); (C) b. p. 133—153°/0·1 mm. (1·8 g.).

Tests showed that fractions (A) and (B) gave the same product with ethyl iodide; they were combined, dissolved in benzene (10 ml.), and treated with the iodide (3 g.). After 4 hr. the deposited 4-*biphenylyltriethylphosphonium iodide* (1·9 g.) was collected; it formed needles, m. p. 219—220° (from water) (Found: C, 54·6; H, 6·3. $C_{18}H_{24}IP$ requires C, 54·3; H, 6·1%), and gave a yellow *picrate*, m. p. 89° (from aqueous acetone) (Found: C, 57·6; H, 5·2; N, 8·4. $C_{24}H_{26}N_3O_7P$ requires C, 57·7; H, 5·2; N, 8·4%). The filtrate from the preparation of the iodide was taken to dryness, and the residue extracted with ether; evaporation of the extract gave biphenyl (0·6 g.), m. p. and mixed m. p. 69—70° (from ethanol).

Fraction (C) was the crude diphosphine (XI). It was added to chloroauric acid (0·4 g.) [each dissolved in ethanol (5 ml.)]. The mixture was gently warmed, cooled, and treated with aqueous potassium iodide; the waxy precipitate gave the pale yellow *di*[*biphenylylene*-3,4-*bis*(*diethylphosphine*)]*gold iodide* (XII; X = I) (0·8 g.), m. p. 313—315° (decomp.) (from ethanol) (Found: C, 48·8; H, 5·6. $C_{40}H_{56}AuIP_4$ requires C, 48·8; H, 5·7%). In acetone solution, treated with aqueous sodium picrate, it gave the yellow *picrate* (XII; X = $C_6H_2N_3O_7$), m. p. 191—192° (from aqueous acetone) (Found: C, 50·6; H, 5·3; N, 3·9. $C_{46}H_{58}AuN_3O_7P_4$ requires C, 50·9; H, 5·4; N, 3·9%).

2-*Chloro*-5-*methylbenzyl Alcohol* (XIII; R = OH).—The Grignard reagent (II) was prepared by treating magnesium (26·2 g., 1·08 atom) with ethyl bromide (2·0 g., 0·02 mol.) in ether (50 ml.) and then with 3-bromo-4-chlorotoluene (I) (205·5 g.) in ether (150 ml.). The mixture was stirred at 0° for 3 hr., and then formaldehyde, prepared by heating paraformaldehyde (50 g., 1·67 mol.) at 190°, was led through the solution, which was finally hydrolysed by the addition of ice (250 g.) and concentrated sulphuric acid (100 ml.) diluted with water (250 ml.). Distillation of the dried ethereal layer gave the *alcohol* (XIII; R = OH) (92 g., 59%), b. p. 106—108°/3 mm. (Found: C, 61·1; H, 6·0; C_8H_9ClO requires C, 61·4; H, 5·8%). It gave a 3,5-*dinitrobenzoate*, pale yellow needles, m. p. 125° [from light petroleum (b. p. 80—100°)] (Found: C, 51·6; H, 3·1; N, 8·0. $C_{15}H_{11}ClN_2O_6$ requires C, 51·4; H, 3·2; N, 8·0%).

A stirred mixture of this alcohol (86 g.) and hydrobromic acid (250 ml., 48%) was boiled under reflux for 3 hr. After cooling, the organic portion was separated, washed with water, dried, and distilled, giving the lachrymatory *bromide* (XIII; R = Br) (105 g., 87%), b. p. 87—89°/2 mm. (Found: C, 43·3; H, 3·8. C_8H_8BrCl requires C, 43·8; H, 3·8%). A mixture of the bromide (0·6 g.), thiourea (0·5 g.), and ethanol (5 ml.) was heated under reflux for 5 min. and then treated with picric acid (0·5 g.); the S-2-*chloro*-5-*methylbenzylthiouronium picrate* which rapidly separated had m. p. 234° (from ethanol) (Found: C, 40·4; H, 3·2; N, 15·8. $C_{15}H_{14}ClN_5O_7S$ requires C, 40·6; H, 3·2; N, 15·8%).

(2-*Chloro*-5-*methylbenzyl*)*diethylphosphine* (XIV).—The bromide (102·5 g.) in ether was slowly added, with stirring, to magnesium (11·6 g., 1·02 atom) containing an iodine crystal, followed by diethylphosphinous chloride (58·0 g., 1 mol.) in ether (50 ml.), a viscous brown oil separating. After 30 min., saturated aqueous ammonium chloride (300 ml.) was added. The dried ethereal layer on distillation gave the phosphine (XIV) (68 g., 64%), b. p. 123—127°/4 mm. It formed an *ethiodide*, needles, m. p. 123—123·5° (from ethanol–ether) (Found: C, 44·1; H, 5·8. $C_{14}H_{23}ClIP$ requires C, 43·7; H, 6·0%), and an *ethopicrate*, yellow needles, m. p. 91—92° (from aqueous ethanol) (Found: C, 49·2; H, 5·3; N, 8·8. $C_{20}H_{25}ClN_3O_7P$ requires C, 49·4; H, 5·2; N, 8·6%).

The residue from the phosphine distillation, when mixed with light petroleum (b. p. 40—60°), deposited 1,2-*bis*-(2-*chloro*-5-*methylphenyl*)*ethane* (1·0 g.), needles, m. p. 143° after three recrystallisations from acetone (Found: C, 69·3; H, 5·9%; *M*, 278. $C_{16}H_{16}Cl_2$ requires C, 68·9; H, 5·8%; *M*, 279); the absence of phosphorus was confirmed.

(2-*Diethylphosphino*-5-*methylbenzyl*)*diethylphosphine* (XV).—The phosphine (XIV) (60 g.) in tetrahydrofuran was stirred at *ca.* −35° with lithium (3·8 g., 2 atom), and after 2½ hr. with diethylphosphinous chloride (32·6 g., 1 mol.) in tetrahydrofuran (50 ml.). After working up as before, the residue on distillation at 1·8 mm. gave fractions: (A) b. p. 97—114° (12·9 g.); (B) b. p. 115—140° (10·6 g.).

Redistillation of fraction (B) gave the *bisphosphine* (XV) (6·5 g., 9%), b. p. 100—104°/1·2 mm. (Found: C, 66·8; H, 9·5. $C_{16}H_{28}P_2$ requires C, 68·0; H, 9·9%).

Fraction (A) was mainly diethyl-3-methylbenzylphosphine. With ethyl iodide it gave *triethyl*-3-*methylbenzylphosphonium iodide*, m. p. 133—135° (from ethanol–ether) (Found: C, 48·1; H, 7·2. $C_{14}H_{24}IP$ requires C, 48·0; H, 6·9%); this gave a yellow *picrate*, m. p. 106—107° (from aqueous ethanol) (Found: C, 53·0; H, 6·1; N, 9·4. $C_{20}H_{26}N_3O_7P$ requires C, 53·2; H, 5·8; N, 9·3%).

A mixture of fraction (A) (0·2 g.) water (50 ml.), potassium permanganate (1 g.), and sodium carbonate (1 g.) was boiled under reflux for 1 hr., cooled, and treated with sulphur dioxide until a colourless solution was obtained. Isophthalic acid separated, and, after recrystallisation from water containing *ca.* 5% of methanol, had m. p. and mixed m. p. 343—345° (decomp.); it was converted by reaction with phosphorus pentachloride and then methanol into the dimethyl ester, m. p. and mixed m. p. 64° (from aqueous methanol).

1,1,3,3-*Tetraethyl*-1,2,3,4-*tetrahydro*-6-*methyl*-1,3-*diphosphonianaphthalene Dibromide* (XVI; X = Br).—A solution of the diphosphine (XV) (1·2 g.) and dibromomethane (1·0 g., 1·25 mol.) in ethanol (40 ml.) was boiled under reflux under nitrogen for 16 hr. The ethanol was evaporated and the residue dissolved in acetone (10 ml.), to which ether was then added dropwise until crystals (0·15 g.) separated; a very small further addition of ether gave a second crop (0·1 g.), but more ether caused the deposition of an oil which did not crystallise. The united crops, after five recrystallisations from acetone–ether, gave the *dibromide* (XVI; X = Br), slightly hygroscopic needles, m. p. 308—309° (Found: C, 44·4; H, 6·8. $C_{17}H_{30}Br_2P_2$ requires C, 44·7; H, 6·6%); it gave a yellow *dipicrate*, m. p. 189° (from aqueous dimethylformamide) (Found: C, 46·1; H, 4·6; N, 11·2. $C_{29}H_{34}N_6O_{14}P_2$ requires C, 46·2; H, 4·5; N, 11·2%).

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