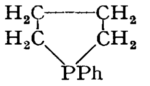
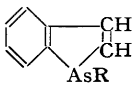
480. *The Synthesis of 1-Substituted Phosphindolines.*

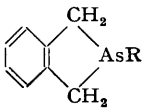
By Frederick G. Mann and Ian T. Millar.

Synthesis of 1-ethylphosphindoline is described by a method that should be applicable to many 1-alkyl(or aryl)-phosphindolines.

Hitherto the only recorded compound containing a five-membered ring system consisting solely of carbon and phosphorus atoms has been 1-phenyltetramethylenephosphine (I) (Grüttner and Krause, *Ber.*, 1916, **49**, 438). In contrast, a much greater variety of compounds containing a five-membered carbon–arsenic ring system is known : for example, the arsenic analogue of (I) (Grüttner and Krause, *loc. cit.*), the 1-substituted arsindoles (II) (Das Gupta, *J. Indian Chem. Soc.*, 1937, **14**, 231, 349, 397, 400) and the corresponding arsindolines (Turner and Bury, *J.*, 1923, **123**, 2489), and the *iso*arsindolines (III) (Lyon and Mann, *J.*, 1945, 30; Lyon, Mann, and Cookson, *J.*, 1947, 662; Beeby, Cookson, and Mann, *J.*, 1950, 1917). We have now developed a synthesis of 1-alkylphosphindolines (IV) which is closely parallel to that already employed for 1-alkyltetrahydrophosphinolines (V) by Beeby and Mann (*J.*, 1951, 411).


(I.)


(II.)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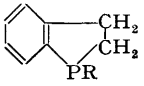
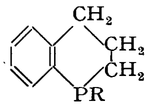
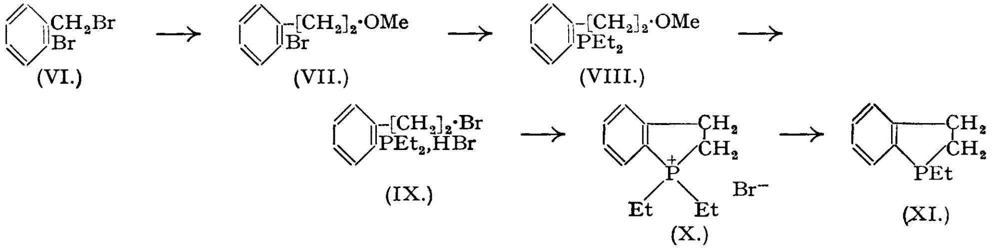

(IV.)


(V.)

For this purpose, *o*-bromobenzyl bromide (VI) was converted as before by the action of one atomic proportion of magnesium into *o*-bromobenzylmagnesium bromide, which when treated with chloromethyl methyl ether gave 2-*o*-bromophenylethyl methyl ether (VII). This compound was converted into a Grignard reagent by the entrainment method using activated magnesium, and this reagent with diethylchlorophosphine, furnished diethyl-(*o*-2-methoxyethylphenyl)phosphine (VIII), as a colourless liquid which was characterised by the preparation of its crystalline methiodide and its dibromopalladium derivative $[(C_{13}H_{21}OP)_2PdBr_2]$.


(VI.) (VII.) (VIII.) (IX.) (X.) (XI.)

The phosphine (VIII), when treated in boiling acetic acid solution with hydrogen bromide, undoubtedly first gave the hydrobromide of diethyl-(*o*-2-bromoethylphenyl)phosphine (IX) without immediate cyclisation. The evidence for the existence of this intermediate is similar to that for the corresponding compound in Beeby and Mann's synthesis (*loc. cit.*), namely, that, when the acetic acid had been evaporated under reduced pressure, treatment of the water-soluble residue with sodium hydrogen carbonate liberated an oil. This oil was insoluble in water but dissolved readily in chloroform with evolution of heat and the formation of the water-soluble 1 : 1-diethylphosphindolinium bromide (X) ; the oil therefore was the uncyclised tertiary phosphine corresponding to the hydrobromide (IX), and on dissolution in chloroform underwent exothermic cyclisation to the phosphonium bromide (X), which could then be readily re-extracted with water.

The aqueous extract thus obtained, when treated with sodium picrate, deposited 1 : 1-diethylphosphindolinium picrate, which after recrystallisation was converted into the corresponding chloride. The latter when heated gave a distillate consisting of 1-ethylphosphindoline and its hydrochloride, undoubtedly with the simultaneous liberation of ethylene : this distillate, when made alkaline and worked up in the usual way, gave 1-ethylphosphindoline (XI) as a colourless liquid, b. p. 104—106°/13 mm., which was readily oxidised on exposure to air. The phosphine was characterised by the preparation of various derivatives : in particular, its crystalline ethiodide was converted into the ethopicrate, which was identical with that employed for the preparation of the phosphindolinium chloride. It is clear therefore that the destructive distillation of the latter had left the ring system unchanged.

We are now investigating the use of phenylphosphine, $Ph{\cdot}PH_2$, for the synthesis of the corresponding *iso*phosphindolines and other cyclic derivatives of phosphorus.

EXPERIMENTAL.

2-o-*Bromophenylethyl Methyl Ether* (VII).—The preparation of this Grignard reagent and its treatment with chloromethyl ether were performed in an atmosphere of nitrogen. A solution of *o*-bromobenzyl bromide (250 g.) in ether (570 c.c.) was added with stirring to magnesium (25·1 g., 1·03 atoms) under ether (75 c.c.) during 3 hours; a crystal of iodine was added to start the reaction, which was then controlled as usual to prevent ebullition of the ether. The solution was then stirred for 2 hours at room temperature, cooled to 0—5°, and vigorously stirred whilst chloromethyl ether (80·5 g., 1 mol.) in ether (100 c.c.) was added dropwise during 1 hour. Stirring was continued for a further 3 hours, the mixture being allowed to attain room temperature meanwhile, and a solution of sulphuric acid (85 c.c.) in water (1 l.) being then added.

The ethereal layer was separated, washed with sodium hydrogen carbonate solution, dried, and distilled; fractionation gave 2-o-*bromophenylethyl methyl ether* (VII) as a colourless liquid, b. p. 64—67°/0·7 mm., having a pleasant odour (Found : C, 49·9; H, 4·8; Br, 37·1. $C_9H_{11}OBr$ requires C, 50·2; H, 5·1; Br, 37·2%) (98 g., 46%). A small fraction, b. p. 170—190°/0·02 mm., gave 2 : 2′-dibromodibenzyl, m. p. 84° (alone and mixed) (cf. Beeby and Mann, *loc. cit.*).

Diethyl-(o-2-*methoxyethylphenyl*)*phosphine* (VIII).—This preparation was carried out under nitrogen with activated magnesium (Holliman and Mann, *J.*, 1942, 739). A solution of the ether (VII) (21·5 g.) and ethyl bromide (5·5 g., 0·5 mol.) in ether (70 c.c.) was added to magnesium (3·83 g., 1·58 atoms) under ether (20 c.c.) at such a rate that the ether boiled gently. The complete mixture was then boiled under reflux for 3 hours, cooled, and chilled in ice-water whilst a solution of diethylchlorophosphine (12·5 g., 1 mol.) in benzene (70 c.c.) was added dropwise with vigorous stirring. The mixture was then boiled for 2 hours, cooled, and hydrolysed with aqueous ammonium chloride. The organic layer, when separated, dried, and distilled, gave the phosphine (VIII) as a colourless oil, b. p. 119—133°/26 mm. (15 g., 67%). The phosphine frothed so persistently on distillation that complete purification was not attempted. It gave a *methiodide*, colourless crystals after recrystallisation from methyl iodide and of m. p. 95·5—96° (Found: C, 45·9; H, 6·3. $C_{14}H_{24}OIP$ requires C, 45·9; H, 6·55%), and also, when treated with an alcoholic solution of potassium palladobromide, *dibromobis*[*diethyl*-(o-2-*methoxyethylphenyl*)*phosphine*]-*palladium*, orange crystals (from alcohol), m. p. 178° (Found: C, 43·8; H, 5·6. $C_{26}H_{42}O_2Br_2P_2Pd$ requires C, 43·7; H, 5·9%).

1 : 1-*Diethylphosphindolinium Picrate.*—A mixture of acetic acid (250 c.c.) and hydrobromic acid (constant b. p.; 250 c.c.) was saturated with hydrogen bromide, added to the phosphine (VIII) (15 g.), and then boiled under reflux for 3 hours whilst a current of hydrogen bromide was passed through. The solvent was removed under reduced pressure, and the residue treated with an excess of sodium hydrogen carbonate solution. The mixture was shaken vigorously with chloroform, which became warm. The aqueous layer when treated with sodium picrate solution deposited the yellow phosphindolinium picrate; a further crop was obtained by evaporation of the chloroform, and treatment of an aqueous solution of the residue with sodium picrate. The united crops after crystallisation from alcohol gave the *picrate* (8·25 g., 29%), as yellow crystals, m. p. 145—145·5° (Found: C, 51·0; H, 4·4; N, 9·9. $C_{18}H_{20}O_7N_3P$ requires C, 51·3; H, 4·75; N, 10·0%).

1-*Ethylphosphindoline* (XI).—The picrate (7 g.) was decomposed with hydrochloric acid, the picric acid extracted with ether, and the aqueous solution evaporated under reduced pressure. The residual chloride (as X), which slowly crystallised, was thoroughly dried and then decomposed by being heated at 350—370°/12 mm. in a nitrogen atmosphere. The viscous semi-crystalline distillate, consisting of the phosphine (XI) and its hydrochloride, was treated with aqueous sodium hydrogen carbonate solution, and the liberated phosphine extracted with benzene. The dried extract on fractionation in a nitrogen atmosphere gave the *phosphine* (XI) (2 g., 75%) as a colourless liquid, b. p. 104—106°/13 mm. (Found : C, 73·7; H, 8·0. $C_{10}H_{13}P$ requires C, 73·2; H, 7·9%). The phosphine has an odour closely resembling that of 1-ethyl-1 : 2 : 3 : 4-tetrahydrophosphinoline and readily darkens on exposure to air.

The phosphine combined with ethyl iodide to give 1 : 1-*diethylphosphindolinium iodide* (as X), colourless crystals, m. p. 123°, after recrystallisation from light petroleum (b. p. 80—100°) containing a small proportion of alcohol (Found : C, 45·1; H, 5·4. $C_{12}H_{18}IP$ requires C, 45·0; H, 5·6%). A sample of this iodide gave the corresponding picrate, identical with that employed for the preparation of the chloride. Treatment of the phosphine with potassium palladobromide furnished *dibromobis*-1-*ethylphosphindolinepalladium*, which separated from alcohol as pale yellow crystals of the *alcoholate*, m. p. 147° (Found : C, 41·1; H, 4·95. $C_{20}H_{26}Br_2P_2Pd,C_2H_6O$ requires C, 41·2; H, 5·0%); at 85°/0·2 mm. for 6 hours this gave the solvent-free *compound* of unchanged m. p. (Found : C, 40·4; H, 4·6. $C_{20}H_{26}Br_2P_2Pd$ requires C, 40·4; H, 4·4%).

We gratefully acknowledge a grant provided by the Department of Scientific and Industrial Research (I. T. M.).

UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, May* 10*th*, 1951.]