212. *Alkyl Migration in Some Organophosphorus Amidates.*

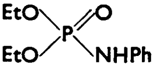
By J. I. G. CADOGAN.

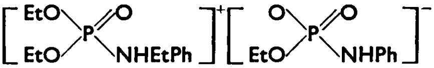
The decompositions of some organophosphorus amidates at high temperatures have been studied. The alkyl esters of the phosphoramidic and phosphonamidic acids which have been examined give tertiary amines. *P*-Alkyl-*NN'*-diphenylphosphonodiamidates, alone, are stable, but react vigorously with trialkyl phosphates to give high yields of dialkylanilines.

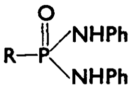
SEVERAL examples of the alkylation of amines by esters of phosphoric acid have been reported. Billman *et al.*[1] noted that trialkyl phosphates and substituted anilines, at the boiling point, gave high yields of the corresponding dialkylaniline and a mixture of phosphoric acids, this mixture indicating that each alkyl group of the ester took part in the reaction. Rueggburg and Chernack[2] later observed that morpholine is similarly alkylated at 150°. It is reasonable to suppose that the reaction involves nucleophilic attack by the amine on the α-carbon atom of the ester to give the monoalkylaniline, which, in turn, is further alkylated by the same mechanism.

In contrast to the above type of reaction, those described in this paper involve compounds containing ester and P–N–C groups in the same molecule, *e.g.*, the *N*-substituted dialkyl phosphoramidates, *e.g.*, (I). Amides of this type are not basic under normal conditions, neither are they strong nucleophils towards α-carbon atoms, but it is evident from the results described below that at high temperatures (*ca.* 250°) the nitrogen atom can be induced to attack the α-carbon atoms of ester groups in a manner similar to the reaction of aniline with trialkyl phosphates.

Diethyl *N*-phenylphosphoramidate (I), at the boiling point, decomposes very vigorously in about 30 sec. to give diethylaniline (85%) and ethylaniline (5%), both amines being partially bound as the salts of oxyacids of phosphorus. It is believed that the first step in the decomposition of the amidate involves the nucleophilic attack of the nitrogen atom on an ester group, to give ethylaniline, probably by way of the decomposition of an intermediate salt of the type (II). The secondary amine formed by this decomposition can then undergo alkylation by attacking any ester group, as in reaction of anilines and trialkyl phosphates already described.[1]


(I)


(II)


(III)

In parallel experiments it was shown that ethylaniline reacts with either triethyl phosphate or diethyl hydrogen phosphate to give diethylaniline; it is therefore not surprising that such a small amount of ethylaniline appears among the products of the decomposition of diethyl *N*-phenylphosphoramidate. The presence of such amounts of secondary amine was demonstrated by infrared analysis, using the strong band at 2·95 μ, which is attributed to the $>$NH group. All diethylaniline–ethylaniline mixtures obtained in the experiments described below were subjected to analysis of this kind, and the presence of diethylaniline was confirmed in each case by the preparation of *NN*-diethyl-*p*-nitrosoaniline.

The results described above are at variance with those of Gerrard and Jeacocke,[3] who stated that distillation of diethyl *N*-phenylphosphoramidate gave ethylaniline. No infrared evidence was however presented, and this conclusion was based on the melting point (136°) of a picrate of the basic product. It may be noted that the picrates of ethylaniline and

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[1] Billman, Radike, and Mundy, *J. Amer. Chem. Soc.*, 1942, **64**, 2977; Billman, Davis, and Thomas, *ibid.*, 1946, **68**, 895.

[2] Rueggburg and Chernack, *ibid.*, 1948, **70**, 1802.

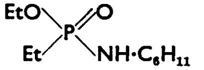
[3] Gerrard and Jeacocke, *Chem. and Ind.*, 1954, 1538.

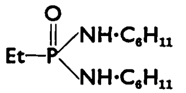
diethylaniline have similar melting points (132° and 142°) and cannot, in this case, be considered satisfactory for diagnostic purposes.

The postulated mechanism is supported by experiments with *P*-alkyl-*NN'*-diphenylphosphonodiamidates (III; R = Me and Et). These compounds contain the amidate function but no ester α-carbon atom, and self-alkylation is therefore impossible : the compounds are indeed stable. On admixture with trialkyl phosphates, however, rapid alkylation takes place at 250° to give high yields of dialkylanilines. Diphenyl *N*-phenylphosphoramidate also has no α-carbon atoms available for attack by nucleophilic centres and was found to be stable, as expected : in the presence of tri-*n*-butyl phosphate at 260°, it reacts slowly, to give a mixture of di-*n*-butylaniline and *n*-butylaniline (10% of the mixture).

The *N*-alkyl analogues which have been studied are more stable; whether this is a result of lower reaction temperatures (the boiling point of the material) or not has not been ascertained. Ethyl *P*-ethyl-*N*-*cyclo*hexylphosphonamidate (IV), after 90 min. at 230°, gave *N*-ethyl*cyclo*hexylamine (27%), *NN*-diethyl*cyclo*hexylamine (13%), and *P*-ethyl-*NN'*-di*cyclo*hexylphosphonodiamidate (V) (4%). The last-named compound is presumed to have arisen by disproportionation of the original amidate. It will be noted that ethyl *P*-ethyl-*N*-*cyclo*hexylphosphonamidate (IV) has only one ester group available for nucleophilic attack. It follows therefore that the length of the reaction chain will be less than if the corresponding phosphoramidate were used, and a correspondingly larger amount of P–N bonds will remain intact. This is supported by the isolation of *cyclo*hexylamine (28%) after acid hydrolysis of the residue from the decomposition.

(IV)





(V)

The decompositions of diethyl *NN*-diethylphosphoramidate and ethyl *NNP*-triethylphosphonamidate were also studied. These compounds were the most stable encountered. The former was approximately half decomposed after 18 hr. at the boiling point, to give triethylamine and its salt with pyrophosphoric acid, while the latter, under the same conditions, gave triethylamine and a residuum of acids which could not be identified.

EXPERIMENTAL

All solids were recrystallised to constant m. p.

Diethyl NN-*diethylphosphoramidate*, a colourless oil (83%) obtained from diethyl phosphorochloridate (35 g.) and diethylamine (35 g.) in dry light petroleum (b. p. 40—60°; 250 ml.), had b. p. 106—108°/20 mm., n_D^{25} 1·4212 (Found : C, 46·2; H, 10·0. Calc. for $C_8H_{20}O_3NP$: C, 45·9; H, 9·6%).

Ethyl NNP-*triethylphosphonamidate*, b. p. 127—128°/25 mm., n_D^{25} 1·4368 (Found : C, 50·0; H, 10·2. $C_8H_{20}O_2NP$ requires C, 49·7; H, 10·4%), and *ethyl* P-*ethyl*-N-cyclo*hexylphosphonamidate*, m. p. 75°, colourless prisms from light petroleum (b. p. 40—60°) (Found : C, 54·9; H, 10·3. $C_{10}H_{22}O_2NP$ requires C, 54·8; H, 10·1%), were prepared in the same way from ethyl ethylphosphonochloridate and diethylamine and *cyclo*hexylamine respectively.

P-*Ethyl*-NN'-*di*cyclo*hexylphosphonodiamidate*, m. p. 160°, colourless needles from acetone (Found : C, 61·7; H, 11·1. $C_{14}H_{29}ON_2P$ requires C, 61·7; H, 10·7%), was prepared from ethylphosphonic dichloride and an excess (10%) of *cyclo*hexylamine in dry benzene as described above. Similarly were obtained *P*-ethyl-*NN'*-diphenylphosphonodiamidate (m. p. 147°) and *P*-methyl-*NN'*-diphenylphosphonodiamidate (m. p. 157°), with the exception that the reactions were effected in dry chloroform solution and the products were recrystallised from aqueous ethanol.

Diphenyl *N*-phenylphosphoramidate [4] had m. p. 129—130°, and diethyl *N*-phenylphosphoramidate [5] had m. p. 96°.

Decomposition of Diethyl N-*Phenylphosphoramidate*.—The amidate (18·5 g.) was heated in an

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[4] Foster, Overend, and Stacey, *J.*, 1951, 980.

[5] McCombie, Saunders, and Stacey, *J.*, 1945, 380.

oil-bath. At 260° a very vigorous reaction of about 30 sec. duration occurred, and two layers were formed. When cool they were separated. The top layer (6·7 g.) was distilled (b. p. 210—216°, n_D^{25} 1·5296), leaving no residue, and was shown to be a mixture of diethylaniline and ethylaniline (*ca.* 5% by infrared spectroscopy). A portion gave a good yield of *NN*-diethyl-*p*-nitrosoaniline, m. p. and mixed m. p. 84°. The bottom layer was a hard glass, insoluble in ether and soluble in water; its aqueous solution (pH 2) was extracted with ether to remove any soluble material but with a negative result; the aqueous layer was basified, giving an oil which was isolated by extraction. This gave a mixture (4·0 g.), b. p. 210—216°, n_D^{25} 1·5324, of diethyl- and ethyl-aniline of the same composition as that of the top layer. Thus were isolated diethyl- (85%) and ethyl-aniline (5%).

In a second experiment the bottom layer was dissolved in water and treated with silver nitrate solution to give a white precipitate. Its infrared spectrum indicated that it was a complex mixture of salts of oxyacids of phosphorus and was not identical with silver phosphate, metaphosphate, or pyrophosphate alone.

Decomposition of Ethyl P-*Ethyl*-N-cyclo*hexylphosphonamidate.*—The amidate (16 g.) was kept at 230—240° for 90 min. and then allowed to cool. The mixture, which consisted of a straw-yellow gummy solid with some supernatant liquid (1 ml.), was treated with water and extracted with ether. Evaporation of the ether layer left a residue (0·7 g.) which gave colourless needles (from acetone), m. p. 158°, not depressed on admixture with *P*-ethyl-*NN'*-di*cyclo*hexylphosphonodiamidate (m. p. 160°). The infrared spectra of the samples were identical.

The aqueous layer (pH *ca.* 2) from the above extraction was basified and extracted with ether. Working up of the extracts gave a colourless oil (4·0 g.), b. p. 170—180°, n_D^{25} 1·4501. Its infrared spectrum indicated the presence of both *NN*-diethyl*cyclo*hexylamine and a secondary amine (strong >NH band), and the absence of *cyclo*hexylamine. A portion of this distillate, gave a colourless methiodide (m. p. 238°, from acetone) which, from analyses, appeared to be N-*ethyl*-N-cyclo*hexyl*-NN-*dimethylammonium iodide* (Found: C, 42·1; H, 8·1. $C_{10}H_{22}NI$ requires C, 42·4; H, 7·8%). This suggested the presence in the original distillate of *N*-ethyl-*cyclo*hexylamine, which was confirmed by the formation of N-*ethyl*-N-cyclo*hexyl*-p-*toluenesulphonamide,* colourless plates, m. p. 104—105° (2·5 g. from 2·3 g. of distillate) (Found: C, 63·65; H, 8·4. $C_{15}H_{23}O_2NS$ requires C, 64·0; H, 8·2%). The water-insoluble oil (0·8 g.) also formed during the preparation of the sulphonamide was dissolved in chloroform and washed with alkali, then with water and dried. The product gave a methiodide, m. p. 224°, from acetone–light petroleum, undepressed on admixture with NN-*diethyl*-N-cyclo*hexyl*-N-*methylammonium iodide,* m. p. 224° (Found: C, 44·5; H, 8·4. $C_{11}H_{24}NI$ requires C, 44·5; H, 8·1%). The distillate therefore contained a mixture of *N*-ethyl- and *NN*-diethyl-*cyclo*hexylamine.

The aqueous fraction from the second ether-extraction described above was then examined. The solution was acidified and boiled for 15 min. When cool, it was basified and extracted with chloroform. Removal of the solvent left an oil, b. p. 137°, n_D^{25} 1·4561 (cf. *cyclo*hexylamine, n_D^{25} 1·4575). A portion of the base gave *N*-*cyclo*hexylphthalimide, m. p. and mixed m. p. 168—169° (Found: C, 73·4; H, 6·8. Calc. for $C_{14}H_{15}O_2N$: C, 73·3; H, 6·6%). In addition the infrared spectra of the free amine and *cyclo*hexylamine were identical.

Reactions between P-*Alkyl*-NN'-*diphenylphosphonodiamidates* (III) *and Trialkyl Phosphates.*—In each case the diamidate (1 mol.) with the trialkyl phosphate (2 mol.) was immersed in an oil-bath at 250°. A vigorous reaction soon ensued which subsided to gentle boiling after about 30 sec. The mixture, which then consisted of two liquid layers, was allowed to boil under reflux for a total of 10 min., and the layers were worked up separately. The top layer was pale yellow and was subjected first to infrared examination. In the experiments with triethyl phosphate this layer was shown to be diethylaniline, with no sign of the band at 2·95 μ (>NH). The top layer from the experiment with trimethyl phosphate was dimethylaniline, while that from the tri-*n*-butyl phosphate experiments consisted of di-*n*-butylaniline (90—95%) and *n*-butylaniline (5—10%). In another experiment involving tri-*n*-butyl phosphate, in which the time of boiling was increased to 1½ hr., no trace of *n*-butylaniline was detected spectroscopically in the products.

In each experiment the top layer was then dissolved in dilute acid and extracted with ether. The aqueous portion was basified, and the products were isolated by extraction with chloroform. They were distilled from zinc dust and their natures confirmed by the preparation of suitable derivatives, as described below.

The bottom layers of the reaction mixtures were all yellow gums. Their aqueous solutions were extracted with chloroform to remove any free base present, which was combined then with the top layer before it was distilled (see above). The aqueous part was basified to give further amounts of bases, which were distilled from zinc dust and subjected to infrared analysis for >NH content. The compositions of the mixtures from the bottom layers were identical with those from the top. The diethylaniline obtained from these experiments had b. p. 210—216°, n_D^{25} 1·5358—1·5394, and each sample gave *NN*-diethyl-*p*-nitrosoaniline, m. p. and mixed m. p. 84°. The dimethylaniline had b. p. 193°, n_D^{25} 1·5533, and gave *p*-bromo-*NN*-dimethylaniline, m. p. and mixed m. p. 53° (Found: N, 7·0. Calc. for $C_8H_{10}NBr$: N, 6·8%). The mixtures of di-*n*-butylaniline and *n*-butylaniline had b. p. 260—270°, n_D^{25} 1·5163—1·5170, and all gave di-*n*-butylaniline hydrochloride (from benzene–light petroleum), m. p. and mixed m. p. 156°, and di-*n*-butylaniline picrate, needles (from ether), m. p. and mixed m. p. 124—125° (Found: N, 12·7. Calc. for $C_{20}H_{26}O_7N_4$: N, 12·9%). The yields of amines produced in the reactions are given in the Table.

R in amidate (III)	R′ in (R′O)$_3$PO	Free amine (%)		Amine present as salt	
		Ph·NR′$_2$	Ph·NHR′	Ph·NR′$_2$	Ph·NHR′
Me	Et	39	0	59	0
Et	Et	32	0	64	0
Me	Bu^n	55	6	37	3
Et	Bu^n	41	4	24	*ca.* 1
Me	Me	46	0	25	0

Reaction of Diphenyl N-*Phenylphosphoramidate with Tri*-n-*butyl Phosphate*.—The amidate (4·3 g.) and the ester (7·0 g.) were kept at 250—260° for 1 hr. and then allowed to cool. The mixture was a homogeneous viscous liquid which was treated with an excess of aqueous alkali and extracted with ether. Working up of the extracts gave a mixture (2 g.) of di-*n*-butylaniline (90%) and *n*-butylaniline (10%), b. p. 260—270°, n_D^{25} 1·5170. The presence of the tertiary base was confirmed by the preparation of the picrate and the hydrochloride (constants given above).

Decomposition of Ethyl NNP-*Triethylphosphonamidate*.—The amidate (18 g.) was boiled under reflux for 18 hr. with moisture excluded, and then distilled to give triethylamine (6·2 g.) (methiodide, m. p. and mixed m. p. 293°), and leaving a brown water-soluble gum. This was dissolved in water and extracted with chloroform to remove any starting material. The aqueous layer was basified and extracted with chloroform. Evaporation of the extracts left a trace of a dark unidentified oil. The aqueous layer was evaporated to dryness and the mixture of sodium salts left was extracted with dry ethanol for 8 hr. Evaporation of the extracts left a white powder which appeared (infrared) to be a mixture of sodium salts of some oxyacids of phosphorus. The mixture could not be identified.

Decomposition of Diethyl NN-*Diethylphosphoramidate*.—The amidate (26 g.) was boiled under reflux with moisture excluded for 18 hr. The heterogeneous mixture was then separated, giving a dark liquid layer (10·7 g.) and a crystalline solid. The former gave triethylamine (1·4 g.; b. p. 89°; methiodide, m. p. and mixed m. p. 293°), starting material (8·8 g.; b. p. 115°/30 mm., n_D^{25} 1·4210), and a residue (0·4 g.) which could not be identified. The solid layer was insoluble in ether but dissolved readily in water to give an acid solution. A small portion (*ca.* 10%) of this solution gave a yellow precipitate with silver nitrate, which had an infrared spectrum identical with that of silver pyrophosphate. The main bulk was basified with sodium carbonate and extracted with chloroform. The extracts were dried and treated with methyl iodide. Evaporation left triethylmethylammonium iodide (3·5 g.), m. p. and mixed m. p. 293°.

In a second experiment, the solid component, in ethanol, was added to an ethanol solution of sodium ethoxide. The gelatinous precipitate was separated by use of the centrifuge, and the supernatant liquid was treated with methyl iodide to give triethylmethylammonium iodide. The gummy solid was triturated with a few drops of water to give a white solid, which had a spectrum identical with that of sodium pyrophosphate.

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