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N,N-DIHALOPHOSPHORAMIDES—VII[a]

DIETHOXYPHOSPHORYLNITRENE—A NEW REACTIVE INTERMEDIATE

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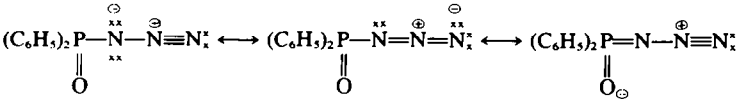
Abstract—The formation of diethyl phosphoroanilidate when solutions of diethyl N,N-dibromophosphoroamidate (DBPA) in benzene are refluxed over zinc, is considered to be diagnostic for a nitrene intermediate.

The intermediacy of various nitrene-type species, e.g., alkyl- and arylnitrenes, acylnitrenes, carbalkoxynitrenes, sulphonylnitrenes etc, in many reactions, is well documented. These species are usually generated by photolysis or thermolysis of the corresponding azides or by α-elimination from suitable systems. No reactions are known, however, in which the intermediate formation of either singlet or triplet phosphylnitrenes has been demonstrated.

In contrast to alkyl- and arylsulphonyl azides, which have been reported to undergo reaction at 105–120° with aromatic compounds to yield alkyl- and arylsulphonanilides,[1-4] diarylphosphinic azides were found to exhibit unusual thermal stability under similar conditions.[5] This unexpected behaviour of the phosphinic azides was rationalized in terms of considerable $p_\pi - d_\pi$ interaction, as represented by the canonical form (1c).[5]



1a 1b 1c

Transient formation of phosphylnitrenes during the addition of diphenylphosphinic azide or diethyl phosphoroazidate to norbornene was excluded by Berlin and Wilson,[6] who demonstrated the intervention of triazoline intermediates. No attempts to generate phosphylnitrenes by any α-elimination procedures have so far been reported.

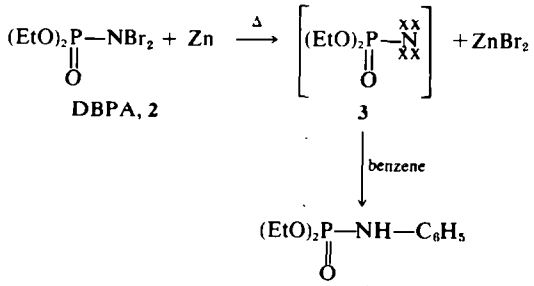
We have found evidence that refluxing a solution of diethyl N,N-dibromophosphoroamidate (DBPA, **2**) for 15 hr in benzene with an excess of freshly activated zinc dust yields diethoxyphosphorylnitrene (**3**), which inserts into a C—H bond of the solvent.

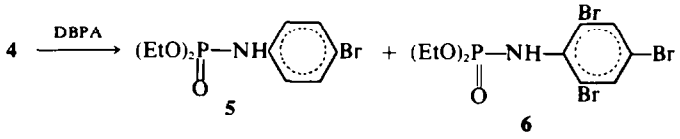
^{31}P NMR analysis of the crude reaction products, formed in low yield showed them to contain 20–40% of diethyl N-(2,4,6-tribromophenyl) phosphoroamidate (**6**). Gas chromatographic analysis also indicated the presence of minute amounts of diethyl phosphoroanilidate (**4**) and diethyl N-(4-bromophenyl) phosphoroamidate (**5**).

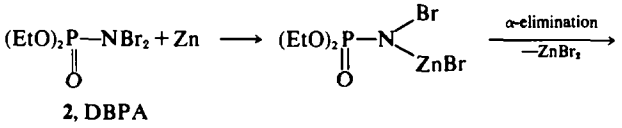
We believe that the formation of all three N-arylphosphoramidates is best rationalized in terms of the initial insertion of the nitrene (**3**) into one of the benzene C—H bonds to yield the N-phenylphosphoramidate (**4**). Subsequent bromination of **4** by the dibromo-amidate (**2**) would lead to the mono- and tribromo-compounds (**5** and **6**). This is supported by a separate experiment in which we refluxed diethyl N-phenylphosphoramidate, in benzene, with an excess of the N,N-dibromophosphoramidate (**2**). This afforded considerable amounts of the tribromoanilide (**6**) contaminated with the 4-bromoanilide (**5**) and unreacted starting material (**4**). An alternative explanation of the formation of **5** and **6**, assuming ring bromination prior to insertion, may be ruled out since electron-withdrawing substituents in the benzene ring evidently decrease the rate of insertion.[3,4]

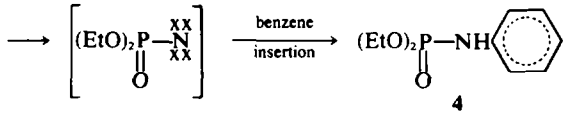
A plausible scheme to explain the formation of diethoxyphosphorylnitrene (**3**) from diethyl N,N-dibromophosphoroamidate (**2**) and zinc would be as follows:

[a]Part VI: S. Zawadzki and A. Zwierzak, *Tetrahedron* **29**, 315 (1973).

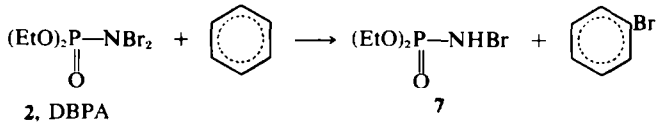


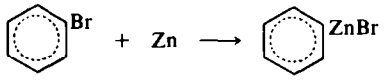


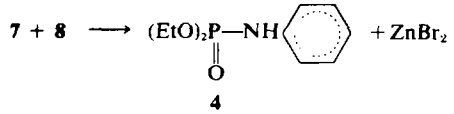




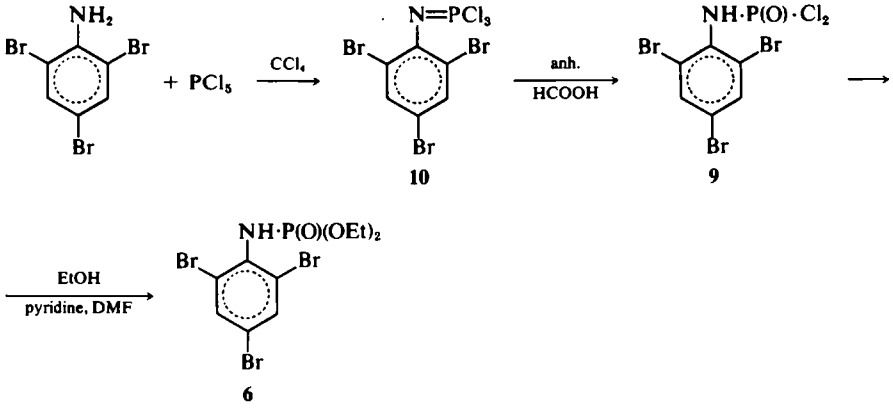
A similar explanation has been suggested by Breslow and Sloan[7] to account for the formation of N-cyclohexyl *p*-toluenesulphonamide in the reaction between Dichloramine T and zinc. The reaction of DBPA (**2**) with zinc, which failed when cyclohexane was used in place of benzene, may have been successful in this particular case because the intermediate bromozinc derivative would be expected to be soluble in benzene, whereas it is probably insoluble in cyclohexane. Furthermore, the rate of free radical bromination of cyclohexane by **2** is probably much higher than that of benzene and would preclude the slow insertion reaction. Although we consider insertion into a C—H bond of benzene to be diagnostic for a nitrene intermediate, there is still a possibility that this reaction followed a totally different course. However, in view of the acidity of **7** the last step appears very unlikely.







The structures of all compounds **4**, **5**, and **6**, obtained from the reaction between DBPA (**2**), zinc, and benzene, have been unequivocally proved by analytical and spectroscopic methods as well as by the direct comparison (in the case of compound **6**) with an authentic sample prepared by an independent method. It is notable that all direct phosphorylation procedures of 2,4,6-tribromoaniline failed, probably due to the extremely low nucleophilicity of this compound, whereas 4-bromoaniline could be phosphorylated easily by any conventional method. An authentic sample of diethyl N-(2,4,6-tribromophenyl) phosphoroamidate (**6**) was obtained by the action of ethanol on 2,4,6-tribromophenylamido phosphorodichloridate (**9**) in the presence of pyridine and dimethylformamide. Phosphorodichloridate (**9**) is readily available from the reaction between 2,4,6-tribromoaniline and phosphorus pentachloride, followed by formolysis of the resulting trichloroimidate (**10**):[8]



EXPERIMENTAL

Light petroleum refers to the fraction boiling at 40–60°. All extracts were dried over $MgSO_4$ and evaporated under reduced pressure. M.p.'s (taken in capillaries) are uncorrected. IR spectra were recorded in KBr discs using a Spectromom 2000 spectrophotometer (MOM, Budapest). ^1H NMR spectra were measured at 60 MHz with a Jeol JNM-C-60HL spectrometer with TMS as internal standard. ^{31}P NMR spectra were recorded at 24·3 MHz with the same spectrometer with 85% H_3PO_4 as external reference. A Heteronuclear Spin Decoupler, JNM-SD-HC, was used for precise ^{31}P chemical shift determinations. Gas chromatography (GLC) was performed on a 5 foot column, i.d. packed with 3% SE 30 on Chromosorb W (45–60 mesh) the Varian Aerograph 1520B, equipped with special flame-ionization detector adapted for organophosphorus compounds, was used. The column temperature was 160°, and the flow rate of the carrier gas (nitrogen) was 20 ml/min. Retention times are relative to diethyl phosphoroanilidate (internal standard). Abbreviations used: vs, very strong; s, strong; m, medium; w, weak; br, broad; s, singlet; d, doublet; t, triplet; q, quartet; qt, quintet.

Diethyl phosphoroanilidate[4] was prepared by the action of aniline (1 mole) on diethyl phosphorochloridate (1 mole) in the presence of triethylamine (1 mole) at room temp in benzene, yield–95%, m.p. 93–94° (lit.°: m.p. 96·5°). The IR spectrum showed characteristic bands at: 3180s (NH), 1605s, 1500s and 1410s (C═C arom.), 1230 vs (P═O), 1020 and 965vs, br (P—O—(C)) cm^{-1}. The ^1H NMR spectrum (CCl_4) showed signals at: $\delta = 1{\cdot}31$ (t, 6H, J_{HH} 7·8Hz, CH_3), 4·13 (qt, 4H, $J_{HH} \approx {}^3J_{PH}$ 7·8Hz, CH_2), 6·63–7·42 (m, 5H, arom. protons), 8·41 (d, 1H, J_{PH} 10·4Hz, NH). The ^{31}P NMR spectrum ($CHCl_3$) showed a signal at $\delta = -3{\cdot}00$ ppm.

Diethyl N-(4-bromophenyl)phosphoroamidate[5]. A mixture of diethyl phosphorochloridate (7.25g, 0·1 mole), 4-bromoaniline (17·2g, 0·1 mole), and triethylamine (10·1g, 0·1 mole) was refluxed in benzene (40 ml) for 1 hr. Triethylamine hydrochloride was filtered off and the solvent evaporated to give 29·2g (95%) of crude anilide. Recrystallization (light petroleum) gave 5 m.p. 79–80°. (Found: C, 38·75; H, 4·8; N, 4·7; P, 10·1; $C_{10}H_{15}O_3NPBr$ requires: C, 39·0; H, 4·9; N, 4·55; P, 10·0%). The IR spectrum showed characteristic bands at: 3125s (NH), 1580m and 1492vs (C═C arom), 1215vs (P═O), 1020vs, br and 975vs, br (P—O—(C)) 832s (arom. 1,4-disubst) cm^{-1}. The ^1H NMR spectrum (CCl_4) showed signals at: $\delta = 1{\cdot}30$ (t, 6H, J_{HH} 7·5Hz, CH_3), 4·10 (qt, 4H, $J_{HH} \approx {}^3J_{PH} =$ 7·5Hz), AA'BB' system (q, 4H, $\delta_A = 7{\cdot}30$, $\delta_B = 6{\cdot}96$, J_{AB} 9·0Hz, arom protons), 8·52 (d, 1H, J_{PH} 9·7Hz, NH). The ^{31}P NMR spectrum ($CHCl_3$) showed a signal at $\delta = -2{\cdot}30$ ppm.

(2,5,6-Tribromophenyl)-amido phosphorodichloridate (**9**) was prepared by the method of Zhmurova and Kirsanov.[8]

Diethyl N-(2,4,6-tribromophenyl)phosphoroamidate (**6**). A mixture of **9** (8·94g, 0·02 mole), EtOH (1·84g, 0·04 mole), pyridine (3·64g, 0·04 mole), and DMF (2·92g, 0·04 mole) was refluxed in benzene (80 ml) for 4 hr. The ppt was then filtered off and the soln washed with water (2× 30 ml), dried, and evaporated to give a partially crystalline oil (6·70g). Column chromatography of the crude anilide (Silica gel, 100–200 mesh, benzene-acetone-$CHCl_3$ (10:3:1)) afforded diethyl N-(2,4,6-tribromophenyl) phosphoroamidate (colourless needles from light petroleum) m.p. 156·5–157·5°. (Found: C, 25·8; H, 2·9; N, 3·3; P, 6·5; $C_{10}H_{13}O_3NPBr_3$ requires: C, 25·8; H, 2·8; N, 3·0: P, 6·7%). The IR spectrum showed characteristic bands at: 3100 m (NH), 1250vs (P═O), 1170w (Et—O—(P)), 1050vs, br. and 970s (P—O—(C)), 857 m (1,2,3,5-tetrasubst arom

ring) cm^{-1}. The ^1H NMR spectrum ($CDCl_3$) showed signals at: δ=1·35 (t, 6H, J_{HH} 7·5Hz, C$\underline{H}_3$) 4·28 (qt, 4H, $J_{HH} \approx {}^3J_{PH}$ 7·5H_2, C$\underline{H}_2$), 4·75–5·27 (brs, 1H, N$\underline{H}$) 7·80 (s, 2H, arom protons). The ^{31}P NMR spectrum ($CHCl_3$) showed a signal at δ=−1·60 ppm.

Diethyl N,N-*dibromophosphoramidate* was prepared by bromination of diethyl phosphoramidate.[10]

Generation and insertion of diethoxyphosphorylnitrene. A mixture of **2** 12·44g, 0·04 mole), freshly activated Zn dust (7·80g, 0·12 mole), and benzene (150 ml) was refluxed gently with stirring for 15 hr. The resulting soln was then filtered and the ppt washed with benzene (3×50 ml). The filtrate was then washed with water (2×40 ml), dried and evaporated to give a partially crystalline oil (1·30g). Colourless needles (0·15g) which could be isolated from this oil by filtration, m.p. 155–157°, were identified (m.mp., IR, NMR) as **6**. GLC analysis showed the crude product to contain a mixture of mono-, di-, and tribromobenzenes, compound **6** ($r_{t\,rel}$ = 11·0), small amounts of **4** ($r_{t\,rel}$ = 1·0), and **5** ($r_{t\,rel}$ = 4·2). As determined by ^{31}P NMR spectroscopy **6** amounted to 40% (by weight) of the crude product.

Bromination of diethyl phosphoroanilidate **4** *with diethyl N,N-dibromophosphoroamidate* (**2**). A mixture of **4** (2·29g, 0·01 mole), **2** (9·33g, 0·03 mole) and benzene (100 ml) was refluxed gently for 12 hr. The excess of unreacted **2** was removed with 20% $NaHSO_3$ aq (120 ml). The organic phase was washed with water (3×50 ml), dried, and evaporated to give a partially crystalline dark-red oil (4·5g). Colourless needles (0·45g), which could be isolated from this oil by successive washings with small amounts of CCl_4, melted at 144–148° and were identified (m.mp., IR, NMR) as **6**. The oily residue contained (GLC) small amounts of diethyl phosphoroanilidate and consisted mainly of **5** and **6**.

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