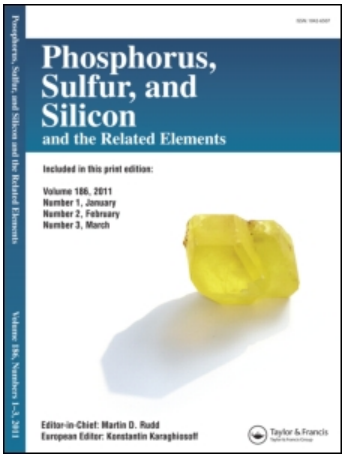

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ORGANOPHOSPHORUS COMPOUNDS AS POTENTIAL FUNGICIDES. PART V.[1] THE PREPARATION AND PROPERTIES OF SOME NOVEL N,N,N',N'-TETRAMETHYL-N''-(1-SUBSTITUTED-2,2,2-TRICHLOROETHYL) PHOSPHORIC TRIAMIDES

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ORGANOPHOSPHORUS COMPOUNDS AS POTENTIAL FUNGICIDES. PART V.[1] THE PREPARATION AND PROPERTIES OF SOME NOVEL N,N,N′,N′-TETRAMETHYL-N″-(1-SUBSTITUTED-2,2,2-TRICHLOROETHYL) PHOSPHORIC TRIAMIDES

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A series of N,N,N′,N′-tetramethyl-N″-(1-substituted-2,2,2-trichloroethyl)phosphoric triamides has been prepared in which the 1-substituent is an amido group, NHCOR (R = H, Me, CH_2Cl, CCl_3, 2,4-dichlorophenyl, 2-methylfuran-3-yl, 5,6-dihydro-2-methyl-1,4-oxathiin-3-yl), an alkoxy group (OMe, OEt, OBu, $OC_{12}H_{25}$), or a substituted acetamido group ($NHCOCH_2Y$), in which Y is triazolyl, N,N-dimethyldithiocarbamato, N,N-diethyldithiocarbamato, diethyl xanthato, diethoxythiophosphorylthio, or dodecylthio. The compounds in general showed low activity as fungicides when tested against a range of organisms at 300 ppm *in vitro*. However, certain compounds (the 1-formamido, 1-acetamido, and 1-chloroacetamido derivatives) showed 55–77% of the activity of the reference fungicide (guazatine) *in vivo*, when applied as seed-dressings at 400 ppm for the control of *Drechslera teres*. No adverse effect on seed germination was observed.

Key words: Organophosphorus, fungicides, N-substituted phosphoric triamides, 2,2,2-trichloroethyl derivatives.

INTRODUCTION

In a recent paper[1] we described the preparation and fungicidal activity of a series of diethyl N-(1-substituted-2,2,2-trichloroethyl)phosphoramidates (**1**), in which a range of substituent groups X (heterocyclic, carboxamido, phosphoramido, hydroxyethylthio, dithiocarbamato, and xanthato) was present. We also reported an increase in fungicidal activity *in vitro* against *Fusarium culmorum* and *Piricularia oryzae* in the case of the imidazole derivative in which one of the ethoxy groups attached to phosphorus was replaced by dimethylamino (**2**, X = imidazol-1-yl). It was therefore of interest to examine analogous compounds (**3**), in which two dimethylamino groups were attached to phosphorus. The preparations of the ethyl esters (**1**, **2**) were carried out (Scheme I) by condensation of diethyl phosphoramidate (**4**, $R^1 = R^2 = EtO$) or ethyl N,N-dimethylphosphorodiamidate (**4**, $R^1 = EtO$; $R^2 = Me_2N$) with chloral, followed by replacement of hydroxyl in the so-formed adduct (**5**) by chlorine, elimination of hydrogen chloride to give an imine (**6**), and subsequent addition of a nucleophile (X—H) containing active hydrogen.[1,2] An analogous method of preparation could not, however, be used for the preparation of derivatives (**3**) in which

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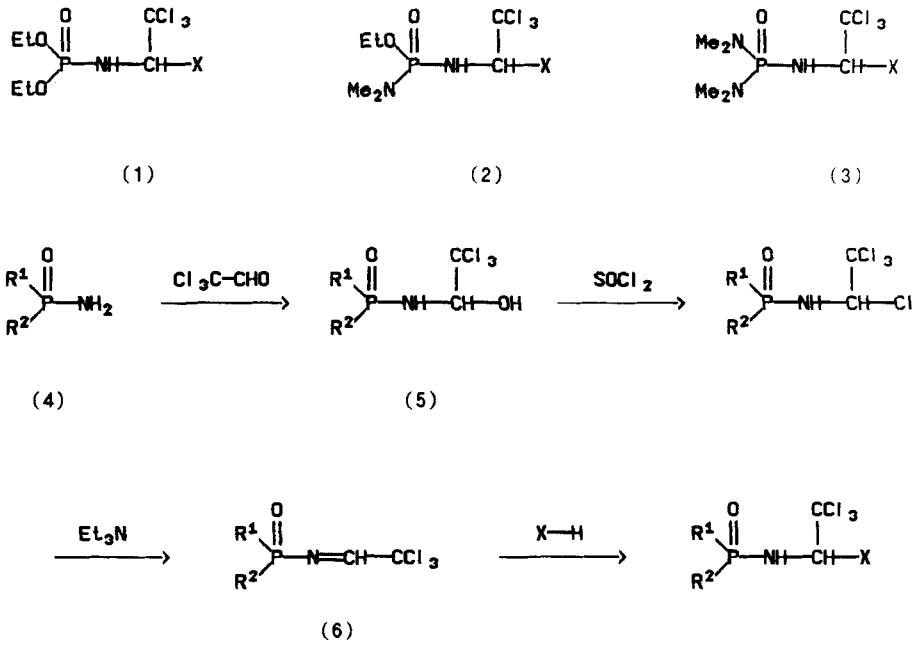


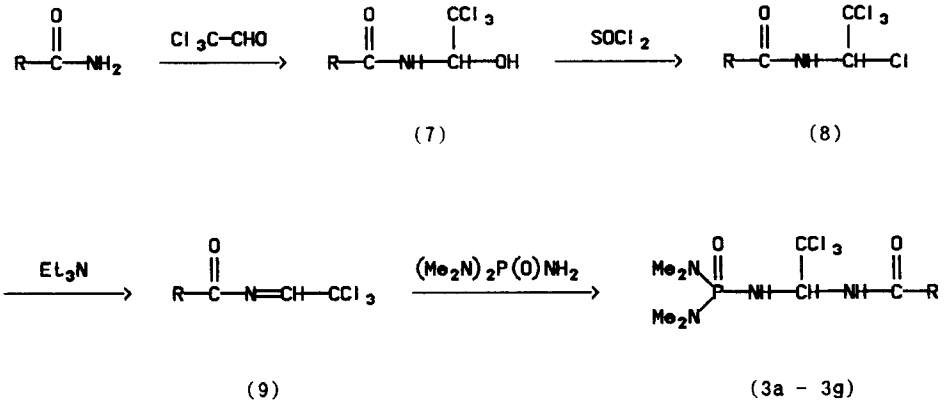
SCHEME I

two dimethylamino groups were attached to phosphorus, as the interaction of N,N,N′,N′-tetramethylphosphoric triamide (**4**, $R^1 = R^2 = Me_2N$) with chloral led to complex mixtures of products resulting from phosphorus-nitrogen fission.[3] The present paper describes methods for the preparation of N,N,N′,N′-tetramethyl-N″-(1-substituted-2,2,2-trichloroethyl)phosphoric triamides (**3**) in which X may be a carboxamido or alkyloxy group, or a substituted acetamido group ($NHCOCH_2Y$), in which Y is triazolyl, dithiocarbamato, xanthato, diethoxythiophosphorylthio, or alkylthio, and reports on their activity as fungicides.

RESULTS AND DISCUSSION

Preparations

The carboxamide derivatives (**3**, X = NHCOR) were found to be readily accessible (Scheme II) by a reverse sequence of reactions to that shown in Scheme I, i.e. by first forming the chloral adduct (**7**) of the carboxamide, followed by replacement of hydroxyl by halogen, elimination of hydrogen chloride from the tetrachloro compound (**8**) to form an imine (**9**),[4] and finally the addition of N,N,N′,N′-tetramethylphosphoric triamide. By this procedure a range of new compounds (**3a**–**3g**) was obtained in which X = formamido, acetamido, chloroacetamido, trichloroacetamido, 2,4-dichlorobenzamido, 2-methylfuran-3-carboxamido, and 5,6-dihydro-2-methyl-1,4-oxathiin-3-carboxamido, respectively. These carboxamide groups were chosen in order to obtain direct comparison with the analogous series of diethyl N-(1-substituted-2,2,2-trichloroethyl)phosphoramidates (**1**, X = NHCOR) prepared previously.[1]



(a) R = H; (b) R = Me; (c) R = CH_2Cl; (d) R = CCl_3; (e) R = 2,4-$Cl_2C_6H_3$;

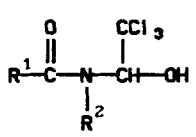
(f) R = -C:C(Me)OCH:CH; (g) R = -C:C(Me)OCH_2CH_2S

SCHEME II

Reactions were also attempted in which secondary amides (N-methylformamide and 2-piperidone) were used as starting materials. The chloral adducts of these amides (**10**) were treated with thionyl chloride to give the corresponding 1,2,2,2-tetrachloroethyl derivatives (**11**) in the hope that direct nucleophilic displacement of the 1-chloro substituent by N,N,N′,N′-tetramethylphosphoric triamide might be possible. In both cases, however, reaction in the presence of triethylamine was unsuccessful, the N,N,N′,N′-tetramethylphosphoric triamide being recovered unchanged, together with triethylammonium chloride. The latter is thought to result from the elimination of hydrogen chloride to give a trichlorovinyl derivative, $HCON(Me)CCl{:}CCl_2$.[5] It is clear, therefore, that replacement of the 1-chloro substituent in an N-(1,2,2,2-tetrachloroethyl)amide can occur only in those cases in which an elimination-addition sequence (Scheme II) is possible, i.e., in the case of primary amide derivatives. Direct nucleophilic displacement of chlorine from the 1-position of compounds of these types (**8**, **11**) is presumably inhibited by steric hindrance and by the strongly electron-withdrawing effect of the neighbouring trichloromethyl group.

Attempts to prepare an imidazole derivative (**3**, X = imidazol-1-yl) by an analogous procedure were also unsuccessful; although the chloral-imidazole adduct (**12**) was readily prepared,[6] attempts to replace the hydroxy group with chlorine by the use of thionyl chloride led to C—N fission and the formation of imidazole hydrochloride.

Further novel compounds (**3h–3m**) were obtained (Scheme III) by nucleophilic displacement of the terminal chlorine atom in N,N,N′,N′-tetramethyl-N″-(2,2,2-trichloro-1-chloroacetamidoethyl)phosphoric triamide (**3c**) by interaction in methanol or ethanol with sodium dimethyldithiocarbamate, sodium diethyldithiocarbamate, potassium ethyl xanthate, sodium *n*-dodecanethiolate, sodium O,O-diethyl dithiophosphate, and the sodium salt of 1,2,4-triazole, respectively. In the case of the triazolyl



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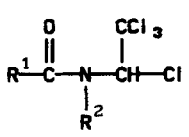

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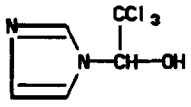

(12)

(a) R^1 = H, R^2 = Me

(b) R^1R^2 = $-(CH_2)_4-$

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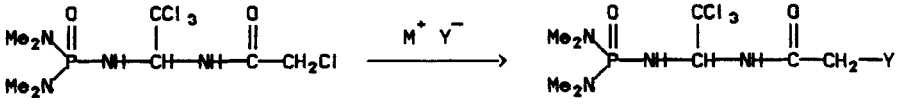


(3c) (3h - 3m)

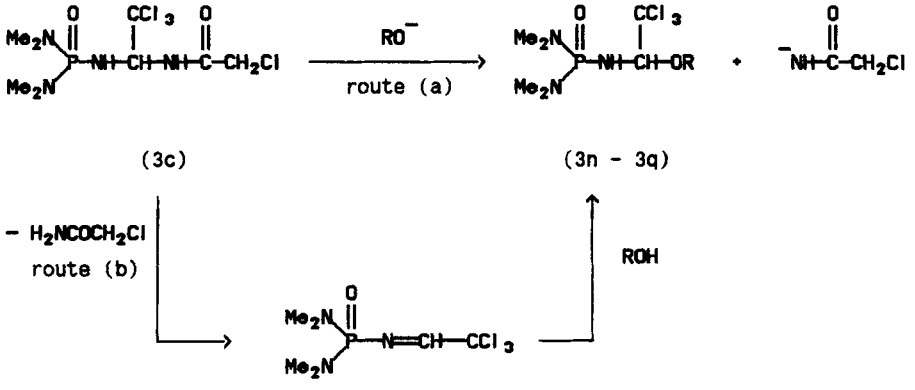
[M = Na (for 3h, 3i, 3m) or K (for 3j, 3k, 3l)]

(3h) Y = $-SC(S)NMe_2$; (3i) Y = $-SC(S)NEt_2$; (3j) Y = -SC(S)OEt;

(3k) Y = $-SC_{12}H_{25}$-n; (3l) Y = $-SP(S)(OEt)_2$;

(3m) Y = -NCH:NCH:N and -NCH:N.N:CH

SCHEME III



(3c) (3n - 3q)

(3n) R = Me; (3o) R = Et; (3p) R = n-Bu; (3q) R = n-$C_{12}H_{25}$

SCHEME IV

derivative (**3m**), both 1- and 4-substituted 1,2,4-triazoles were shown to be present by comparison of the ^1H and ^{13}C nmr spectra with those reported for 1- and 4-methyl-1,2,4-triazole (see Experimental). This mixture of products is presumably formed because of the mesomeric nature of the 1,2,4-triazole anion, which is an ambident nucleophile.

Attempts to prepare an imidazole derivative (**3**, X = $NHCOCH_2Y$, Y = imidazol-

1-yl) by reaction of the sodium salt of imidazole with the chloroacetamide derivative (**3c**) in methanol or ethanol failed, only the methoxy derivative (**3**, X = MeO) or ethoxy derivative (**3**, X = EtO) being isolated. The difference in behaviour between 1,2,4-triazole and imidazole in these reactions is probably due to the difference in their acidities. The acidity of imidazole (pK_a 14.52) is close to that of both methanol (pk_a 15.09) and ethanol (pk_a 15.93), whereas 1,2,4-triazole (pK_a 10) is significantly more acidic. A higher concentration of alkoxide ion will, therefore, be present in alcoholic solutions of sodium imidazole than in those of sodium 1,2,4-triazole. It is also interesting to note that the methoxide ion or ethoxide ion (generated in the methanolic or ethanolic solution of the sodium salt of imidazole, respectively) does not displace the terminal chlorine atom of the chloroacetamide derivative (**3c**) but displaces instead the carboxamide moiety from the 1-position of the 2,2,2-trichloroethyl group (Scheme IV) with the formation of the corresponding 1-alkoxy derivatives (**3n**, **3o**). Similar substitution reactions were observed with sodium butoxide and sodium dodecyloxide (giving **3p** and **3q**, respectively) and it is assumed that this type of displacement is general for alkoxides. Whether this displacement occurs through S_N2 attack on the methine carbon atom (Scheme IV, route a) or via an elimination-addition sequence involving an intermediate imine (Scheme IV, route b) is not known, although the latter appears to be more likely on steric grounds. The softer sulfur nucleophiles, in contrast, displace the terminal chlorine atom (giving **3h–3l**).

Products were characterized by elemental analysis, infrared and nmr spectroscopy (^1H, ^{13}C, and ^{31}P), and in certain cases by mass spectrometry.

Spectroscopy

The infrared spectra of the bisdimethylamino compounds (**3**), exhibited stretching frequencies associated with the phosphoryl (P═O) group in the range 1168–1200 cm^{-1}, i.e. at slightly lower frequency than for the analogous diethoxyphosphoryl compounds (1230–1295 cm^{-1}).[1] This observation is in accord with previous reports for related compounds[7] and corresponds with a shift to higher frequency as the electronegativity of the substituents on phosphorus is increased.[8–11] Other functional groups within the molecules gave rise to absorptions in the expected regions.[8] Carbonyl stretching frequencies occur in the region 1660–1710 cm^{-1}, with values nearer the lower limit when the carbonyl group is conjugated to an unsaturated system (**3e–3g**), or at the higher level when the highly electronegative trichloromethyl substituent group is attached to carbonyl (**3d**).[12]

Nmr spectra were normally recorded in DMSO-d_6, because the compounds (**3**) are only slightly soluble in less polar solvents. The ^1H nmr spectra were characterized by strong signals due to the dimethylamino groups which appeared as two overlapping doublets centred at 2.5–2.7 ppm (J_{PNCH} = 10.0–10.2 Hz), with a chemical shift difference ($\Delta\delta_H$) of ca. 0.05 ppm. The integration for these signals generally exceeded the expected value for 12 protons to some extent, because of overlap with the signal due to residual protons present in the DMSO-d_6 (δ_H 2.5 ppm). The splitting pattern was clear, however, showing the presence of anisochronous methyl protons in the dimethylamino groups attached to phosphorus. Further investigations will be necessary in order to establish the cause of this effect, although a possible explanation

lies in the presence of the chiral centre in the $NHCH(X)CCl_3$ group.[13] Surprisingly, however, the ^{13}C nmr spectra of these compounds revealed no corresponding difference in the chemical shifts of the dimethylamino carbon atoms, which gave rise to only one doublet, due to phosphorus-carbon coupling (δ_C ca. 36.2 ppm, J_{PNC} 3.4–4.4 Hz).

A further characteristic, although relatively weak feature of the ^1H spectra of the products, is the signal due to the methine proton of the $NHCH(X)CCl_3$ group. For those compounds (**3**) in which X = NHCOR this signal (δ_H 5.7–5.9 ppm) appeared as a multiplet, due to coupling to the phosphoramide proton, the carboxamide proton, and phosphorus. When X = OR, the methine proton appeared at slightly higher field (δ_H 4.8–5.0 ppm), as a doublet of doublets, due to coupling with the phosphoramide proton and phosphorus, and in all cases the signal collapsed to a simple doublet (J_{PNCH} 8–11 Hz) on exchange of the amido protons with D_2O or CD_3OD. The phosphoramide proton (PNH) generally appeared as an overlapping doublet of doublets (whose position varied according to the solvent) and the carboxamide proton as a broad doublet in the region of 8–9 ppm. Signals due to the phosphoramide and carboxamide protons were removed by exchange with D_2O or CD_3OD.

In the ^{13}C nmr spectra, signals for the dimethylamino carbon atoms and the trichloromethyl carbon atom appeared at 36.1–36.3 ($^2J_{PNC}$ 3.4–4.4 Hz) and 102–104 ppm ($^3J_{PNCC}$ 8.8–11.0 Hz), respectively, in all cases. The chemical shift of the methine proton, however, varied with the nature of the substituent group (X) to which it was attached, being in the range 68–71 ppm ($^2J_{PNC}$ 4.4–5.9 Hz) for compounds (**3**) in which X = NHCOR, or at lower field, δ_C 91–93 ppm ($^2J_{PNC}$ 5.4–6.1 Hz), when X = OR.

^{31}P nmr signals were consistently in the range 19.3–20.5 ppm, i.e. at significantly lower field than for the diethoxy analogues[1] for which δ_P is typically about 5–6 ppm.[14] It is of interest that oxygen, although more electronegative than nitrogen, provides a greater degree of screening of phosphorus than does nitrogen in these phosphoric acid derivatives.[15]

Biological Activity

The N,N,N′,N′-tetramethyl-N″-(1-substituted-2,2,2-trichloroethyl)phosphoric triamides (**3a–3q**) as a group showed little or no activity when tested *in vitro* at 300 ppm against *Piricularia oryzae*, *Rhizoctonia solani*, *Botrytis cinerea*, *Septoria nodorum*, *Fusarium avenaceum*, and *Drechslera sativa*. The highest recorded activity (ca. 30% of that for the reference fungicide, guazatine) was shown by the formamido (**3a**) and 2,4-dichlorobenzamido (**3e**) derivatives in tests against *P. oryzae*. Tested at 400 ppm *in vivo* as seed dressing agents, using seeds of spring barley (Tellus 374), three of the amide derivatives (**3a**, **3b**, **3c**) showed 55–77% of the activity of guazatine in the control of *Drechslera teres*. Little activity was, however, shown against *Septoria nodorum* in similar tests with winter wheat (Holme 3055). The compounds showed none of the adverse effects on seed germination which had been observed for certain of the diethoxy analogues.[1]

EXPERIMENTAL

Solvents and Reagents

Starting materials were obtained commercially and were generally used as supplied. Triethylamine was dried over potassium hydroxide pellets and redistilled, b.p. 89–90°C. Benzene, toluene, and diethyl ether were dried and stored over sodium wire. Methanol and ethanol were dried over a molecular sieve (Merck, 3 Å).

Analytical Methods

Elemental analysis for carbon, hydrogen, and nitrogen was carried out on a Perkin-Elmer 240 microanalytical instrument, and for chlorine by the oxygen flask method. Phosphorus was determined gravimetrically by digestion with concentrated sulphuric acid (15 cm^3) in the presence of a Kjeldahl selenium catalyst tablet until clear (1–4 h), further digestion (2–4 h) with concentrated nitric acid (15 cm^3), dilution with water, and precipitation as magnesium ammonium phosphate.[16]

Spectroscopy

Infrared spectra were obtained on Pye Unicam SP2000 and SP3-200 spectrophotometers; samples were prepared as KBr discs. Nmr spectra were recorded for solutions in DMSO-d_6, except for compounds (**3p**) ($CDCl_3$), (**4**, $R^1 = R^2 = Me_2N$) ($CDCl_3$), and (**3h**) (CD_3OD for ^{31}P only). ^1H nmr spectra were recorded at 60 MHz on a Perkin-Elmer R12B spectrometer, or at 80 MHz on a Bruker WP80 spectrometer. ^{13}C and ^{31}P nmr spectra were obtained on the Bruker instrument operating at 20.12 or 32.40 MHz, respectively. Chemical shifts are given downfield from TMS for ^1H and ^{13}C spectra and downfield from 85% phosphoric acid (external standard) for ^{31}P spectra. EI mass spectra (for exact mass measurements) and FAB mass spectra were obtained on a VG Micromass ZAB-1F instrument. FAB spectra were recorded for samples in a glycerol matrix, with a primary beam of xenon atoms produced by an ion gun (Ion Tech Ltd) operating at 1.0 mA at 8 kV.

Preparation of Intermediates

N,N,N′,N′-Tetramethylphosphoric triamide,[9] 2,4-dichlorobenzamide,[17] 2-methyl-furan-3-carboxamide,[18] 5,6-dihydro-2-methyl-1,4-oxathiin-3-carboxamide,[19] N-(1-hydroxy-2,2,2-trichloroethyl)formamide (**7a**),[20] N-(1-hydroxy-2,2,2-trichloroethyl)acetamide (**7b**),[21] N-(1-hydroxy-2,2,2-trichloroethyl)-chloroacetamide (**7c**),[22] N-(1-hydroxy-2,2,2-trichloroethyl)trichloroacetamide (**7d**),[23] N-(1-hydroxy-2,2,2-trichloroethyl) -2,4-dichlorobenzamide (**7e**),[24] N-(1-hydroxy-2,2,2-trichloroethyl)-5,6-dihydro-2-methyl-1,4-oxathiin-3-carboxamide (**7g**),[25] N-(1,2,2,2-tetrachloroethyl)formamide (**8a**),[22] N-(1,2,2,2,-tetrachloroethyl)acetamide (**8b**),[22] N-(1,2,2,2-tetrachloroethyl)chloroacetamide (**8c**),[22] N-(1-hydroxy-2,2,2-trichloro-ethyl)piperidone (**10b**),[26] N-methyl-N-(1,2,2,2-tetrachloroethyl)formamide (**11a**),[27] and 1-(1-hydroxy-2,2,2-trichloroethyl)-imidazole (**12**),[6] were prepared as described.

N-(1-Hydroxy-2,2,2-trichloroethyl)-2′-methyl-3′-furancarboxamide (**7f**). 2-Methylfuran-3-carboxamide (5.0 g, 0.04 mol) and anhydrous chloral (17.7 g, 0.12 mol), were heated (100°C) under reflux (3 h). The product was dissolved in hot anhydrous ether, petroleum (b.p. 40–60°C) was added, and the mixture was stored overnight at −18°C. Precipitated solids were removed, and the filtrate was evaporated to leave an orange oil which, on repeated recrystallization from diethyl ether/petroleum (b.p. 40–60°C), with charcoal treatment, gave the product (**7f**) (5.4 g, 50%) m.p. 122–123°C (decomp.) (Found: C, 35.5; H, 3.2; Cl, 39.0; N, 4.8. $C_8H_8Cl_3NO_3$ requires: C, 35.2; H, 2.9; Cl, 39.1; N, 5.1%).

N-(1,2,2,2-Tetrachloroethyl)trichloroacetamide (**8d**). The carboxamide-chloral adduct (**7d**) (8.3 g, 0.027 mol) and thionyl chloride in excess (31.2 g, 0.26 mol) were gently heated together under reflux, with stirring (3 h), after which the excess of thionyl chloride was removed under reduced pressure to leave a white solid. Extraction with hot petroleum (b.p. 60–80°C) gave a solution from which trichloroacetamide separated on storage overnight at 4°C. After filtration, evaporation of the filtrate gave a white solid residue which was recrystallized from petroleum (b.p. 60–80°C) to give the product (**8d**) (3.1 g, 35%) m.p. 97–99°C (Found: 14.4; H, 0.9; Cl, 76.4; N, 4.7. $C_4H_2Cl_7NO$ requires: C, 14.4; H, 0.6; Cl, 75.6; N, 4.3%).

N-(1,2,2,2-Tetrachloroethyl)-2,4-dichlorobenzamide (**8e**). By an analogous procedure to the above, the chloral adduct (**7e**) (10.0 g, 0.03 mol) and thionyl chloride (36.1 g, 0.30 mol) gave a product which was precipitated after removal of the excess of thionyl chloride and the addition of petroleum (b.p. 60–80°C). Recrystallization from petroleum (b.p. 60–80°C) gave the product (**8e**) (7.6 g, 72%) m.p. 124–125°C (Found: C, 31.8; H, 1.7; N, 4.2. $C_4H_5Cl_4NO$ requires: C, 30.3; H, 1.4; N, 3.9%).

N-(1,2,2,2-Tetrachloroethyl)-2'-methyl-3'-furancarboxamide (**8f**). The chloral adduct (**7f**) (5.4 g, 0.02 mol) and thionyl chloride (23.6 g, 0.20 mol) were heated at 40°C (1 h) and then under reflux (1 h). Removal of the excess of thionyl chloride gave the product as an orange oil, which could not be crystallized from either petroleum (b.p. 40–60°C) or diethyl ether, and was used without further purification.

N-(1,2,2,2-Tetrachloroethyl)-5,6-dihydro-2-methyl-1,4-oxathiin-3-carboxamide (**8g**). Thionyl chloride (15.6 g, 0.13 mol) was added dropwise to a stirred, boiling solution of the chloral adduct (**7g**) (4.0 g, 0.013 mol) in chloroform (30 cm^3) and the solution was then heated further under reflux (3 h). Removal of thionyl chloride and other volatiles under reduced pressure gave the product as a yellow oil which could not be crystallized from petroleum (b.p. 40–60°C) and was used without further purification.

General Method for the Preparation of N,N,N',N'-Tetramethyl-N''-(1-substituted-2,2,2-trichloroethyl)phosphoric Triamides (3, X = NHCOR) (Scheme II)

Triethylamine (1 mol. equiv.) was added to a solution of the N-(1,2,2,2-tetrachloroethyl)carboxamide (**8**) in benzene (ca. 6% w/v) with gentle mixing. After 15 min the triethylammonium chloride which precipitated was filtered off and washed with benzene (2 × 50 cm^3). N,N,N',N'-Tetramethylphosphoric triamide (**4**, $R^1 = R^2 = Me_2N$) (1 mol. equiv.) was added to the combined filtrate and washings and the mixture was allowed to stand overnight. The white solid which separated was filtered off and recrystallized from a mixture of chloroform and petroleum (b.p. 60–80°C) to give the following.

N,N,N',N'-Tetramethyl-N''-(2,2,2-trichloro-1-formamidoethyl)phosphoric triamide (**3a**): (5.7 g, 61%), m.p. 190–191°C (Found: C, 26.1; H, 4.9; Cl, 32.9; N, 17.4; P, 9.4; M^+ 324.0061. $C_7H_{16}Cl_3N_4O_2P$ requires: C, 25.8; H, 4.9; Cl, 32.7; N, 17.2; P, 9.5%; M^+ 324.0076); δ_H (DMSO-d_6) 2.49 and 2.54 [12H, 2 overlapping d, $^3J_{PNCH}$ 10.2 Hz, $(Me_2N)_2P$], 5.21 (1H, m, PNH), 5.81 (1H, m, d in CD_3OD, $^3J_{PNCH}$ 10.5 Hz, PNHCH), 8.15 (1H, d, $^3J_{HNCH}$ 1.2 Hz, becomes singlet in CD_3OD, NH—CHO), 8.65 (1H, br d, $^3J_{HCNH}$ 9.3, exchanges with CD_3OD, NH—CO); δ_C (DMSO-d_6) 36.2 [d, $^2J_{PNC}$ 3.7 Hz, $(Me_2N)_2P$], 67.6 (d, $^2J_{PNC}$ 5.1 Hz, CHNH), 103.4 (d, $^3J_{PNCC}$ 10.3 Hz, CCl_3), 160.4 (s, CO); δ_P (DMSO-d_6) 20.1; ν_{max}/cm^{-1} 1675 (C=O), 1185 (P=O).

N,N,N',N'-Tetramethyl-N''-(2,2,2-trichloro-1-acetamidoethyl)phosphoric triamide (**3b**): (1.9 g, 34%), m.p. 200–202°C (decomp.) (Found: C, 28.3; H, 5.3; Cl, 30.9; N, 16.2; P, 9.3; M^+ 338.0243. $C_8H_{18}Cl_3N_4O_2P$ requires: C, 28.3; H, 5.4; Cl, 31.3; N, 16.5; P, 9.1%; M^+ 338.0233); δ_H (DMSO-d_6) 1.92 (3H, s, CH_3CO), 2.49 and 2.54 [12H, 2 overlapping d, $^3J_{PNCH}$ 10.2 Hz, $(Me_2N)_2P$], 4.69 (1H, dd, exchanges with D_2O, PNH), 5.67 (1H, m, becomes d with D_2O, $^3J_{PNCH}$ 10.8 Hz, PNHCH), 8.36 (1H, d, $^3J_{HCNH}$ 9.1, exchanges with D_2O, NH—CO); δ_C (DMSO-d_6) 22.5 (s, CH_3CO), 36.2 [d, $^2J_{PNC}$ 3.7 Hz, $(Me_2N)_2P$], 68.9 (d, $^2J_{PNC}$ 5.1 Hz, CHNH), 103.7 (d, $^3J_{PNCC}$ 11.0 Hz, CCl_3), 168.5 (s, CO); δ_P (DMSO-d_6) 20.1; ν_{max}/cm^{-1} 1685 (C=O), 1200 (P=O).

N,N,N',N'-Tetramethyl-N''-(2,2,2-trichloro-1-chloroacetamidoethyl)phosphoric triamide (**3c**): (5.8 g, 45%), m.p. 187–188°C (decomp.) (Found. C, 25.4; H, 4.4; Cl, 38.3; N, 15.0; P, 8.1; M^+ 371.9836. $C_8H_{17}Cl_4N_4O_2P$ requires: C, 25.7; H, 4.5; Cl, 38.0; N, 15.0; P, 8.3%; M^+ 371.9842); δ_H (DMSO-d_6) 2.50 and 2.55 [12H, 2 overlapping d, $^3J_{PNCH}$ 10.2 Hz, $(Me_2N)_2P$], 4.24 (2H, s, CH_2Cl), 5.07 (1H, dd, exchanges with D_2O, PNH), 5.77 (1H, m, becomes d with D_2O, $^3J_{PNCH}$ 11.0 Hz, PNHCH), 8.70 (1H, d, $^3J_{HCNH}$ 9.0, exchanges with D_2O, NH—CO); δ_C (DMSO-d_6) 36.1 [d, $^2J_{PNC}$ 3.4 Hz, $(Me_2N)_2P$], 42.2 (s, CH_2Cl), 69.4 (d, $^2J_{PNC}$ 5.4 Hz, CHNH), 103.2 (d, $^3J_{PNCC}$ 10.2 Hz, CCl_3), 165.4 (s, CO); δ_P (DMSO-d_6) 20.1; ν_{max}/cm^{-1} 1680 (C=O), 1190 (P=O).

N,N,N',N'-Tetramethyl-N''-(2,2,2-trichloro-1-trichloroacetamidoethyl)phosphoric triamide (**3d**): (0.9 g, 43%), m.p. 180–181°C (decomp.) (Found. C, 21.7; H, 3.4; N, 12.4; P, 7.2; $[M + 1]^+$ 440.95. $C_8H_{15}Cl_6N_4O_2P$ requires: C, 21.7; H, 3.4; N, 12.6; P, 7.0%; $[M + 1]^+$ 440.91); δ_H (DMSO-d_6) 2.52 and 2.57 [12H, 2 overlapping d, $^3J_{PNCH}$ 10.2 Hz, $(Me_2N)_2P$], 4.98 (1H, dd, exchanges with D_2O, PNH), 5.71 (1H, m, becomes d with D_2O, $^3J_{PNCH}$ 11.5 Hz, PNHCH), 9.34 (1H, br, exchanges with D_2O, NH—CO); δ_C (DMSO-d_6) 36.1 [d, $^2J_{PNC}$ 3.4 Hz, $(Me_2N)_2P$], 71.3 (d, $^2J_{PNC}$ 5.4 Hz, CHNH), 92.2 (s, $CCCl_3$), 102.9 (d, $^3J_{PNCC}$ 8.8 Hz, $CHCCl_3$), 160.5 (s, CO) δ_P (DMSO-d_6) 20.2; ν_{max}/cm^{-1} 1710 (C=O), 1168 (P=O).

N,N,N',N'-Tetramethyl-N''-(2,2,2-trichloro-1-[2,4-dichlorobenzamido]ethyl)phosphoric triamide (**3e**): (3.3 g, 62%), m.p. 205–206°C (decomp.) (Found: C, 33.3; H, 4.0; Cl, 38.1; N, 11.9; P, 6.5; $[M + 1]^+$ 469.0. $C_{13}H_{18}Cl_5N_4O_2P$ requires: C, 33.2; H, 3.8; Cl, 37.7; N, 11.9; P, 6.6%; $[M + 1]^+$ 469.0); δ_H (DMSO-d_6) 2.53 and 2.58 [12H, 2 overlapping d, $^3J_{PNCH}$ 10.2 Hz, $(Me_2N)_2P$], 4.75 (1H, dd, exchanges with CD_3OD, PNH), 5.87 (1H, m, becomes d in CD_3OD, $^3J_{PNCH}$ 10.7 Hz, PNHCH), 7.55 (3H, Ar) 9.11 (1H, d, $^3J_{HCNH}$ 8.8, exchanges with CD_3OD, NH—CO); δ_C (DMSO-d_6) 36.2 [d, $^2J_{PNC}$ 4.0 Hz, $(Me_2N)_2P$], 69.4 (d, $^2J_{PNC}$ 5.1 Hz, CHNH), 103.4 (d, $^3J_{PNCC}$ 9.6 Hz, CCl_3), 129.5–135.2 (Ar), 164.4 (s, CO); δ_P (DMSO-d_6) 19.9; ν_{max}/cm^{-1} 1670 (C=O), 1200 (P=O).

N,N,N',N'-Tetramethyl-N''-(2,2,2-trichloro-1-[2'-methylfuran-3'-carboxamido]ethyl)phosphoric triamide (**3f**): (2.3 g, 28%), m.p. 185–186°C (decomp.) (Found: C, 35.2; H, 4.9; Cl, 26.3; N, 13.7; P, 7.5; M^+ 404.0332. $C_{12}H_{20}Cl_3N_4O_3P$ requires: C, 35.5; H, 4.9; Cl, 26.3; N, 13.8; P, 7.6%; M^+ 404.0338); δ_H (DMSO-d_6) 2.51 [15H, m, $(Me_2N)_2P$ and ring-Me], 4.73 (1H, dd, exchanges with D_2O, PNH), 5.86 (1H, m, becomes d with D_2O, $^3J_{PNCH}$ 11.2 Hz, PNHCH), 6.78 (1H, d, $^3J_{HCCH}$ 2.0 Hz, —O—CH=CH—), 7.59 (1H, d, $^3J_{HCCH}$ 2.0 Hz, —O—CH=CH—), 8.22 (1H, d, $^3J_{HCNH}$ 8.8, exchanges with D_2O, NH—CO); δ_C (DMSO-d_6) 13.1 (s, ring-Me), 36.1 [d, $^2J_{PNC}$ 3.7 Hz, $(Me_2N)_2P$], 69.0 (d, $^2J_{PNC}$ 4.4 Hz, PNHCH), 104.0 (d, $^3J_{PNCC}$ 10.3 Hz, CCl_3), 108.8 (s, —O—CH=CH—); 115.0 (s, —O—C=C—CONH), 141.3 (s, —O—CH=CH—), 156.7 (s, ring C—Me), 161.7 (s, CO); δ_P (DMSO-d_6) 20.5; ν_{max}/cm^{-1} 1667 (C=O), 1180 (P=O).

N,N,N',N'- Tetramethyl-N''- (2,2,2-trichloro-1- [5',6'-dihydro-2'-methyl-1',4'-oxathiin-3'-carboxamido]-ethyl)phosphorictriamide (**3g**): (3.2 g, 56%), m.p. 197–198°C (decomp.) (Found: C, 32.8; H, 5.0; N, 12.6; P, 6.8; M^+ 438.0205. $C_{12}H_{22}Cl_3N_4O_3PS$ requires: C, 32.8; H, 5.0; N, 12.7; P, 7.0%; M^+ 438.0215); δ_H (DMSO-d_6) 2.07 (3H, s, ring-Me), 2.49 and 2.54 [12H, 2 overlapping d, $^3J_{PNCH}$ 10.2 Hz, $(Me_2N)_2P$], 3.04 (2H, t, SCH_2), 4.29 (2H, q, CH_2O), 5.01 (1H, exchanges in CD_3OD, PNH), 5.78 (1H, m, becomes d with CD_3OD, $^3J_{PNCH}$ 11.0 Hz, PNHCH), 7.94 (1H, d, $^3J_{HCNH}$ 9.3, exchanges in CD_3OD, NH—CO); δ_C (DMSO-d_6) 20.3 (s, ring-Me), 23.8 (s, SCH_2), 36.1 [d, $^2J_{PNC}$ 3.4 Hz, $(Me_2N)_2P$], 66.1 (s, CH_2O), 69.2 (d, $^2J_{PNC}$ 4.7 Hz, PNHCH), 97.7 (s, S—CH=CH), 103.9 (d, $^3J_{PNCC}$ 9.5 Hz, CCl_3), 153.1 (s, CH=CH—O), 164.5 (s, CO); δ_P (DMSO-d_6) 20.3; ν_{max}/cm^{-1} 1665 (C=O), 1180 (P=O).

General Method for the Preparation of N,N,N',N'-Tetramethyl-N''-(1-substituted-2,2,2-trichloro-ethyl)phosphoric Triamides (3, X = NHCOCH$_2$Y) (Scheme III)

The sodium or potassium salt M^+ Y^- [M = Na (for 3h, 3i, 3m) or K (for **3j**, **3k**, **3l**)] (Scheme III) was dissolved in methanol and added dropwise to a well stirred methanolic solution of an equimolar quantity of N,N,N',N'-tetramethyl-N''-(2,2,2-trichloro-1-chloroacetamidoethyl)phosphoric triamide (**3c**), under reflux. Heating was continued for a further 3 h, after which the solution was cooled, boiled again with activated charcoal, and filtered hot. The filtrate was evaporated to dryness under reduced pressure and the residual white solid was washed well with distilled water to remove sodium or potassium chloride. Recrystallization as specified gave the following products as white crystalline solids.

N,N,N',N'-Tetramethyl-N''-[2,2,2-trichloro-1-{1'-(dimethylaminothiocarbonylthio)acetamido}ethyl]phosphoric triamide (**3h**): (4.3 g, 87%) from chloroform/petroleum (b.p. 40–60°C), m.p. 191–192°C (decomp.) (Found: C, 28.6; H, 4.8; N, 15.4; P, 6.9; M^+ 457.0092. $C_{11}H_{23}Cl_3N_5O_2PS_2$ requires: C, 28.8; H, 5.0; N, 15.3; P, 6.8%; M^+ 457.0096); δ_H (DMSO-d_6) 2.49 and 2.53 [12H, 2 overlapping d, $^3J_{PNCH}$ 10.2 Hz, $(Me_2N)_2P$], 3.40 (s) and 3.46 (s) (6H, Me_2NCS), 4.15 (2H, s, $COCH_2$) 4.99 (1H, dd, exchanges in CD_3OD, PNH), 5.75 (1H, m, becomes d in CD_3OD, $^3J_{PNCH}$ 10.7 Hz, PNHCHNH), 8.57 (1H, d, $^3J_{HCNH}$ 8.8 Hz, exchanges in CD_3OD, NHCO); ^{13}C (DMSO-d_6) 36.2 [d, $^2J_{PC}$ 3.7 Hz, $(Me_2N)_2P$], 40.6 (s, $COCH_2$), 41.3 (s, CH_3NCS), 45.3 (s, CH_3NCS), 69.4 (d, $^2J_{PC}$ 5.1 Hz, NHCHNH), 103.5 (d, $^3J_{PC}$ 10.3 Hz, CCl_3), 166.1 (s, C=O), 194.2 (s, C=S); ^{31}P (CD_3OD) 19.3; ν_{max}/cm^{-1} 1668 (C=O), 1175 (P=O).

N,N,N',N'- Tetramethyl-N''- [2,2,2-trichloro-1- {1'- (diethylaminothiocarbonylthio)acetamido}ethyl]phosphoric triamide (**3i**): (3.4 g, 66%) from chloroform/diethyl ether, m.p. 171–172°C (decomp.) (Found: C, 31.9; H, 5.6; N, 14.4; P, 6.3; M^+ 485.0397. $C_{13}H_{27}Cl_3N_5O_2PS_2$ requires: C, 32.1; H, 5.5; N, 14.4; P, 6.4%; M^+ 485.0409); δ_H (DMSO-d_6) 1.21 (6H, m, CH_3CH_2), 2.49 and 2.53 [12H, 2 overlapping d, $^3J_{PNCH}$ 10.2 Hz, $(Me_2N)_2P$], 3.94 (4H, m, CH_3CH_2), 4.15 (2H, s, $COCH_2$), 5.01 (1H, dd, exchanges with D_2O, PNH), 5.75 (1H, m, becomes d with D_2O, $^3J_{PNCH}$ 10.7 Hz, PNHCHNH), 8.52 (1H, d, $^3J_{HCNH}$ 9.3 Hz, exchanges with D_2O, NHCO); ^{13}C (DMSO-d_6) 11.8 (d, CH_3CH_2), 36.2 [d, $^2J_{PC}$ 4.4 Hz, $(Me_2N)_2P$], 39.9 (s, $COCH_2$), 48.1 (d, CH_3CH_2), 69.4 (d, $^2J_{PC}$ 5.9 Hz, NHCHNH), 103.5 (d, $^3J_{PC}$ 9.6 Hz, CCl_3), 166.2 (s, C=O), 192.8 (s, C=S); ^{31}P (DMSO-d_6) 20.1; ν_{max}/cm^{-1} 1670 (C=O), 1188 (P=O).

N,N,N',N'- Tetramethyl-N''- [2,2,2-trichloro-1- {1'- (ethoxythiocarbonylthio)acetamido}ethyl]phosphoric triamide (**3j**): (3.6 g, 74%) from ethanol/water, m.p. 184–185°C (decomp.) (Found: C, 28.8; H, 4.7; N, 12.3; P, 6.8; M^+ 457.9933. $C_{11}H_{22}Cl_3N_4O_3PS_2$ requires: C, 28.7; H, 4.8; N, 12.2; P, 6.7%; M^+ 457.9936); δ_H (DMSO-d_6) 1.36 (3H, t, CH_3CH_2), 2.49 and 2.53 [12H, 2 overlapping d, $^3J_{PNCH}$ 10.2 Hz, $(Me_2N)_2P$], 4.03 (2H, s, $COCH_2$), 4.62 (2H, q, CH_3CH_2), 4.98 (1H, dd, exchanges in CD_3OD, PNH), 5.76 (1H, m, becomes d with CD_3OD, $^3J_{PNCH}$ 10.2 Hz, PNHCHNH), 8.71 (1H, d, $^3J_{HCNH}$ 8.8 Hz, exchanges in CD_3OD, NHCO); ^{13}C (DMSO-d_6) 13.4 (s, CH_3CH_2), 36.2 [d, $^{12}J_{PC}$ 3.7 Hz, $(Me_2N)_2P$], 38.7 (s, $COCH_2$), 69.5 (d, $^2J_{PC}$ 5.1 Hz, NHCHNH), 70.6 (s, CH_3CH_2), 103.3 (d, $^3J_{PC}$ 9.6 Hz, CCl_3), 165.5 (s, C=O), 212.8 (s, C=S); ^{31}P (DMSO-d_6) 20.0; ν_{max}/cm^{-1} 1675 (C=O), 1190 (P=O).

N,N,N',N'-Tetramethyl-N''-[2,2,2-trichloro-1-{1'-(dodecylthio)acetamido}ethyl]phosphoric triamide (**3k**): (2.4 g, 51%) from diethyl ether, m.p. 108–109°C (decomp.) (Found: C, 44.6; H, 7.6; Cl, 19.6; N, 10.5; P, 5.8; MH^+ 539.1. $C_{20}H_{42}Cl_3N_4O_4PS$ requires: C, 44.5; H, 7.8; Cl, 19.7; N, 10.4; P, 5.6%; MH^+ 539.2); δ_H (DMSO-d_6) 0.70 [3H, m, $CH_3(CH_2)_{11}$], 1.24 [22H, m, $S(CH_2)_{11}$], 2.50 and 2.54 [12H, 2 overlapping

d, $^3J_{PNCH}$ 10.2 Hz, $(Me_2N)_2P$], 3.25 (2H, s, $COCH_2$) 4.99 (1H, dd, exchanges with D_2O, PNH), 5.75 (1H, m, becomes d with D_2O, $^3J_{PNCH}$ 10.8 Hz, PNHCHNH), 8.45 (1H, d, $^3J_{HCNH}$ 9.3 Hz, exchanges with D_2O, NHCO); ^{13}C (DMSO-d_6) 13.4 [s, $CH_3(CH_2)_{11}$], 22.0, 28.2, 28.5, 28.6, 28.9, 31.2, 31.8 [singlets, $CH_3(CH_2)_{11}$], 34.7 (s, $COCH_2$), 36.2 (d, $^2J_{PC}$ 3.7 Hz, $Me_2N)_2P$], 69.4 (d, $^2J_{PC}$ 5.1 Hz, NHCHNH), 103.8 (d, $^3J_{PC}$ 9.6 Hz, CCl_3), 168.2 (s, C=O); ^{31}P (DMSO-d_6) 20.0; ν_{max}/cm^{-1} 1660 (C=O), 1185 (P=O).

N,N,N',N'- Tetramethyl-N"- [2,2,2-trichloro-1- {1'- (diethoxythiophosphonylthio)acetamido}ethyl]phosphoric triamide (**3l**): (3.8 g, 67%) from chloroform/diethyl ether, m.p. 125–127°C (resolidifies and melts again at 154–155°C) (Found: C, 27.5; H, 5.3; N, 10.7; P, 11.9; M^+ 522.0012. $C_{12}H_{27}Cl_3N_4O_4P_2S_2$ requires: C, 27.5; H, 5.2; N, 10.7; P, 11.8%; M^+ 522.0014); δ_H (DMSO-d_6) 1.29 (6H, t, CH_3CH_2), 2.50 and 2.54 [12H, 2 overlapping d, $^3J_{PNCH}$ 10.2 Hz, $(Me_2N)_2P$], 3.69 (2H, d, $^3J_{PSCH}$ 14.2 Hz, $COCH_2$), 4.13 (4H, m, CH_3CH_2), 4.96 (1H, dd, exchanges with D_2O, PNH), 5.76 (1H, m, becomes d with D_2O, $^3J_{PNCH}$ 10.2 Hz, PNHCHNH), 8.79 (1H, d, $^3J_{HCNH}$ 9.3 Hz, exchanges with D_2O, NHCO); ^{13}C (DMSO-d_6) 15.5 (d, $^3J_{PC}$ 7.9 Hz, CH_3CH_2), 35.5 (d, $^2J_{PSC}$ 3.4 Hz, $COCH_2$), 36.2 [d, $^2J_{PC}$ 3.4 Hz, $(Me_2N)_2P$], 63.8 (d, $^2J_{POC}$ 5.7 Hz, CH_3CH_2), 69.5 (d, $^2J_{PC}$ 5.1 Hz, NHCHNH), 103.2 (d, $^3J_{PC}$ 10.2 Hz, CCl_3), 166.0 (d, $^3J_{PSCC}$ 6.2 Hz, C=O); ^{31}P (DMSO-d_6) 20.0; ν_{max}/cm^{-1} 1668 (C=O), 1180 (P=O).

N,N,N',N'-Tetramethyl-N"-[2,2,2-trichloro-1-{1'-and 4'-(1', 2', 4'-triazolyl)acetamido}ethyl]phosphoric triamide (**3m**): (1.3 g, 30%) from chloroform/diethyl ether, m.p. 182–183°C (decomp.) (Found: C, 28.2; H, 4.7; Cl, 26.6; N, 24.3; P, 7.6; M^+ 405.0406. $C_{10}H_{19}Cl_3N_7O_2P$ requires: C, 29.5; H, 4.7; Cl, 26.2; N, 24.1; P, 7.6%; M^+ 405.0402); δ_H (DMSO-d_6) 2.49 and 2.53 [12H, 2 overlapping d, $^3J_{PNCH}$ 10.2 Hz, $(Me_2N)_2P$], 5.1 (3H, m, becomes 2H as two singlets with D_2O, PNH and $COCH_2$ of 1- and 4-isomers), 5.79 (1H, m, becomes d with D_2O, $^3J_{PNCH}$ 10.5 Hz, NHCHNH), 7.98 (s, triazole ring H, 1-isomer), 8.44 (s, triazole ring H, 4-isomer), 8.52 (s, triazole ring H, 1-isomer), 8.86 (1H, d, $^3J_{HCNH}$ 10.9 Hz, exchanges with D_2O, NHCO); ^{13}C (DMSO-d_6) 36.2 [d, $^2J_{PC}$ 3.4 Hz, $(Me_2N)_2P$], 46.4 (s, $COCH_2$, 4-isomer), 51.0 (s, $COCH_2$, 1-isomer), 69.3 (d, $^2J_{PC}$ 5.4 Hz, NHCHNH), 103.1 (d, $^3J_{PC}$ 10.9 Hz, CCl_3), 143.9 (s, C_1 and C_2 of 4-isomer), 145.5 (s, C_1 of 1-isomer), 151.5 (s, C_2 of 1-isomer), 165.4 (s, C=O); ^{31}P (DMSO-d_6) 20.0; ν_{max}/cm^{-1} 1670 (C=O), 1180 (P=O). (^1H and ^{13}C nmr assignments for the 1- and 4-triazole rings are based on comparison with literature data for 1- and 4-methyl-1,2,4-triazole).[28,29]

Reaction of the Sodium Salt of Imidazole with N,N,N',N'-Tetramethyl-N"-(2,2,2-trichloro-1-chloroacetamidoethyl)phosphoric Triamide (**3c**) *in Methanol or Ethanol (Scheme IV)*

(a) In Methanol

Under similar conditions to those given in the previous section, the sodium salt of imidazole (0.96 g, 0.11 mol) in methanol (30 cm^3) and the phosphoramide (**3c**) (4.0 g, 0.11 mol) in methanol (100 cm^3) gave an orange oil after removal of the solvent *in vacuo*. Crystallization from chloroform/petroleum (b.p. 40–60°C) gave an off-white solid which was shown by ^1H nmr to be unreacted starting material (**3c**) (0.6 g, 15%). Evaporation of the mother liquor to dryness and further recrystallization from diethyl ether gave N,N,N',N'-tetramethyl-N"-(2,2,2-trichloro-1-methoxyethyl)phosphoric triamide (**3n**) (0.35 g, 10%), m.p. 157–158°C (decomp.) (Found: C, 26.3; H, 5.5; N, 13.8. $C_7H_{17}Cl_3N_3O_2P$ requires: C, 26.9; H, 5.4; N, 13.4%); δ_H (DMSO-d_6) 2.53 and 2.59 [12H, 2 overlapping d, $^3J_{PNCH}$ 10.2, $(Me_2N)_2P$], 3.35 (3H, s, OCH_3), 4.75 (1H, dd, becomes d with D_2O, $^3J_{PNCH}$ 7.8 Hz, $CHCCl_3$), 5.44 (1H, dd, exchanges with D_2O, PNH); ^{13}C (DMSO-d_6) 36.3 [d, $^2J_{PC}$ 4.1 Hz, $(Me_2N)_2P$], 56.5 (s, CH_3O), 92.7 (d, $^2J_{PC}$ 6.1 Hz, $CHCCl_3$), 101.8 (d, $^3J_{PC}$ 9.5 Hz, $CHCCl_3$); ^{31}P (DMSO-d_6) 19.6; FAB MS: m/z (%) 312 (MH^+, 7), 280 ($[MH - MeOH]^+$, 21), 246 ($[MH - MeOCl]^+$, 37), 135 ($[Me_2N)_2PO]^+$, 100).

(b) In Ethanol

Similarly, a solution prepared by adding sodium (0.21 g, 0.01 g atom) to imidazole (0.65 g, 0.01 mol) in ethanol (30 cm^3) was allowed to react with the phosphoramide (**3c**) (3.23 g, 0.01 mol) in ethanol (75 cm^3) as above. After removal of the solvent the product was extracted with diethyl ether, insoluble material was removed by filtration, petroleum (b.p. 40–60°C) was added to the hot filtrate, and the solution was stored overnight at −18°C to give crystals of chloroacetamide (0.3 g), δ_H (DMSO-d_6) 4.02 (s), 7.66 (br s), identical with an authentic specimen. Concentration of the mother liquor gave a further crop of crystals (1.39 g) which were dissolved in chloroform; the solution was washed with water (to remove imidazole), dried ($MgSO_4$), evaporated to dryness, and the residue was recrystallized from diethyl ether to give N,N,N',N'-tetramethyl-N"-(2,2,2-trichloro-1-ethoxyethyl)phosphoric triamide (**3o**) (0.54 g, 18%), m.p. 152–153°C (decomp.) (Found: C, 29.4; H, 5.9; N, 13.0. $C_8H_{19}Cl_3N_3O_2P$ requires: C, 29.4; H, 5.8; N, 12.7%) δ_H (DMSO-d_6) 1.18 (3H, t, OCH_2CH_3); 2.52 and 2.58 [12H, 2 overlapping d, $^3J_{PNCH}$ 9.8 Hz, $(Me_2N)_2P$], 3.72 (2H, m, OCH_2CH_3), 4.84 (1H, dd, $CHCCl_3$), 5.42 (1H, dd, exchanges with D_2O, PNH); ^{13}C (DMSO-d_6) 14.8 (s, OCH_2CH_3), 36.2 [d, $^2J_{PC}$ 4.1 Hz, $(Me_2N)_2P$], 64.3 (s, OCH_2CH_3), 90.9 (d, $^2J_{PC}$ 6.1 Hz, $CHCCl_3$), 102.1 (d, $^3J_{PC}$ 10.2 Hz, $CHCCl_3$); ^{31}P (DMSO-d_6) 19.6; FAB MS: m/z (%) 326 (MH^+, 3), 280 ($[MH - EtOH]^+$, 11), 246 ($[MH - EtOCl]^+$, 13), 135 ($[Me_2N)_2PO]^+$, 100).

Reactions of Alkoxides with N,N,N',N'-tetramethyl-N''-(2,2,2-trichloro-1-chloroacetamideoethyl)phosphoric Triamide (**3c**) *(Scheme IV)*

(a) Sodium n-butoxide

Sodium metal (0.25 g, 0.011 g atom) was dissolved in butan-1-ol (30 cm^3) (with heating) and the cooled solution was added dropwise to a well-stirred solution of the phosphoramide (**3c**) (4.0 g, 0.11 mol) in butanol under reflux. Heating was continued (1 h) after which the solution was cooled and filtered, the solvent was removed *in vacuo*, and the residual oil was extracted with hot diethyl ether (200 cm^3). The ethereal solution was concentrated and stored at −18°C for several days to give a precipitate which was recrystallized from diethyl ether to give N,N,N',N'-tetramethyl-N''-(2,2,2-trichloro-1-butoxyethyl)-phosphoric triamide (**3p**) (1.07 g, 28%), m.p. 115–116°C (decomp.) (Found: C, 33.4; H, 6.5; N, 11.8. $C_{10}H_{23}Cl_3N_3O_2P$ requires: C, 33.9; H, 6.5; N, 11.8%); δ_H ($CDCl_3$) 0.92 (3H, m, CH_3 of *n*-butyl), 1.49 (4H, m, $CH_3C\underline{H}_2C\underline{H}_2$), 2.65 and 2.71 [12H, 2 overlapping d, $^3J_{PNCH}$ 10.2, $(Me_2N)_2P$], 3.39 (1H, dd, PNH), 3.83 (2H, m, CH_2O), 4.99 (3H, dd, $CHCl_3$); δ_C ($CDCl_3$) 13.9, 19.2, 31.7 (singlets, $CH_3CH_2CH_2$), 36.7 [d, $^2J_{PC}$ 4.1 Hz, $(Me_2N)_2P$], 70.5 (s, CH_2O), 91.0 (d, $^2J_{PC}$ 5.4 Hz, $\underline{C}HCCl_3$), 101.9 (d, $^2J_{PC}$ 10.2 Hz, $CH\underline{C}Cl_3$); δ_P ($CDCl_3$) 19.2; FAB MS: m/z (%) 354 (MH^+, 2), 280 ([MH − BuOH]$^+$, 10), 246 ([MH − BuOCl]$^+$, 13), 135 ([$Me_2N)_2PO$]$^+$, 100).

(b) Sodium n-dodecyloxide

Sodium metal (0.32 g, 0.014 mol) was dissolved in dodecan-1-ol (10 cm^3) at 120°C (36 h), after which the solution was cooled, diluted with acetone (30 cm^3) and added dropwise to a well-stirred solution of the phosphoramide (**3c**) (4.0 g, 0.011 mol) in tetrahydrofuran (200 cm^3) under reflux. The mixture was heated for a further 3 h, filtered hot, and the volatiles were removed under reduced pressure to give a dark oil which was extracted with ether (450 cm^3). The ethereal solution, after charcoal treatment, concentration to ca. 100 cm^3, and cooling overnight (−18°C), deposited a white precipitate which was filtered off and recrystallized from benzene/petroleum (b.p. 40–60°C) to give a mixture (0.2 g) consisting of the phosphoramide (**3c**) and chloroacetamide in the ratio 1:3.4 (by nmr). Removal of ether from the mother liquor left an orange oil from which the excess of dodecanol was removed by distillation (b.p. 105–110°C). Extraction with petroleum (b.p. 60–80°C) gave a solution, which was stored overnight at −18°C to give an off-white solid (0.3 g). The latter was recrystallized from petroleum to give N,N,N',N'-tetramethyl-N''-(2,2,2-trichloro-1-dodecyloxyethyl)phosphoric triamide (**3q**) δ_H (DMSO-d_6) 0.85 (3H, m, CH_3 of dodecyl), 1.24 [20H, m, $CH_3(C\underline{H}_2)_{10}$], 2.52 and 2.58 [12H, 2 overlapping d, $^3J_{PNCH}$ 10.0 Hz, $(Me_2N)_2P$], 3.65 (2H, m, CH_2O), 4.83 (1H, dd, becomes d with D_2O, $^3J_{PNCH}$ 8.1 Hz, $C\underline{H}CCl_3$), 5.40 (1H, dd, exchanges with D_2O, PNH); δ_C (DMSO-d_6) 13.8, 22.0, 25.4, 28.7, 29.0, 31.2 (singlets, dodecyl chain), 36.3 [d, $^2J_{PC}$ 4.1 Hz, $(Me_2N)_2P$], 68.9 (s, CH_2O), 91.2 (d, $^2J_{PC}$ 6.1 Hz, $C\underline{H}CCl_3$), 102.2 (d, $^3J_{PC}$ 9.5 Hz, CCl_3), δ_P (DMSO-d_6) 19.5.

(c) Potassium n-dodecyloxide

Similarly, potassium metal (0.42 g, 0.011 g atom), dodecan-1-ol (50 cm^3), and the phosphoramide (**3c**) in diethyl ketone (200 cm^3) gave the dodecyloxy product (**3q**) (0.2 g), with identical nmr parameters to the above; FAB MS: m/z (%) 466 (MH^+), 1), 280 ([MH − $C_{12}H_{25}OH$]$^+$, 12), 246 ([MH − $C_{12}H_{25}OCl$]$^+$, 21), 135 ([$Me_2N)_2PO$]$^+$, 100).

Reactions of Chloral Derivatives of Secondary Amides

(a) N-Methylformamide Derivative

N,N,N',N'-Tetramethylphosphoric triamide (1.85 g, 0.012 mol) was added to a solution of N-methyl-N-(1,2,2,2-tetrachloroethyl)formamide (**11a**) (2.3 g, 0.01 mol) and triethylamine (1.26 g, 0.012 mol) in toluene (20 cm^3). The mixture was heated under reflux (3 h), cooled, and a white precipitate of triethylammonium chloride (1.21 g, 85%) was filtered off. On cooling the filtrate, unreacted N,N,N',N'-tetramethylphosphoric triamide (1.19 g, 64%) crystallized out and was identified by m.p. and ^1H nmr.

(b) Piperidone Derivative

N-(1-Hydroxy-2,2,2-trichloroethyl)-2-piperidone (**10b**) (4.9 g, 0.02 mol) was heated under reflux (1 h) with thionyl chloride (23.8 g, 0.2 mol) and the excess of thionyl chloride was then removed under reduced pressure to leave the tetrachloro derivative (**11b**) as a yellow oil. The latter was treated as in the above experiment with equimolar quantities of triethylamine and N,N,N',N'-tetramethylphosphoric triamide in benzene (25 cm^3), to give triethylammonium chloride (0.95 g, 35%) and unreacted N,N,N',N'-tetramethylphosphoric triamide (1.55 g, 51%).

Interaction of the Chloral-Imidazole Adduct (**12**) *with Thionyl Chloride*

Thionyl chloride (1.78 g, 0.15 mol) in chloroform (10 cm^3) was added dropwise to a solution of the

chloral adduct (**12**) (2.15 g, 0.01 mol), also in dry chloroform (20 cm^3), with cooling to maintain the temperature below 10°C. After 10 min the white precipitate which formed was filtered off and identified as imidazole hydrochloride (0.42 g, 40%), m.p. 145–147°C (lit.[30] 145°C), δ (DMSO-d_6) 7.7 (2H, d), 9.2 (1H, m), 12.9 (2H, br s, exchanges with D_2O).

Biological Screening

Fungicidal tests *in vitro* were carried out at 300 ppm in sterilized agar with incubation at 28°C (14 days) for *Piricularia oryzae*, *Rhizoctonia solani*, *Botrytis cinerea*, *Septoria nodorum*, *Fusarium avenaceum*, and *Drechslera sativa*. Laboratory tests for activity as seed dressings were carried out with seeds of spring barley (Tellus 374) infected with *Pyrenophora teres* (subdivision Ascomycotina) conidial stage *Drechslera teres*, and seeds of winter wheat (Holme 3055) infected with *Leptosphaeria nodorum* (subdivision Ascomycotina) conidial stage *Septoria nodorum*, as previously described.[1] In all cases, guazatine was used as the reference fungicide.

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REFERENCES AND NOTES

1. P. J. Eccles, H. R. Hudson, C. N. Mavrommatis and M. Pianka, *Phosphorus, Sulfur, and Silicon*, **105**, 33 (1995).
2. B. S. Drach and A. D. Sinitsa, *Zhur. Obshch. Khim.*, **38**, 2778 (1968); *Chem. Abstr.*, **70**, 77232e (1969); B. S. Drach, A. D. Sinitsa and A. V. Kirsanov, *Zhur. Obshchei Khim.*, **39**, 1940 (1969); *Chem. Abstr.*, **72**, 31337f (1970).
3. P. J. Eccles, H. R. Hudson, C. Mavrommatis, M. Pianka and A. R. Qureshi, Proc. Internat. Conf. Phosphorus Chem., Nice, France, September 1983, ed. J. G. Riess, F. Mathey, D. Robert and R. Wolf, *Phosphorus Sulfur*, **18**, 439 (1983).
4. B. S. Drach, A. D. Sinitsa and A. V. Kirsanov, *Zhur. Obshchei Khim.*, **39**, 2192 (1969); *Chem. Abstr.*, **72**, 42706b (1970).
5. N-Methyl-N-(1,2,2,2-tetrachloroethyl)formamide (**11a**) was shown to lose HCl on heating with triethylamine in toluene to give HCON(Me)CCl:CCl_2, identified by mass spectrometry and nmr. It was also shown (nmr) that chlorine was not displaced from N-(1,2,2,2-tetrachloroethyl)acetamide (**3b**) by interaction with N,N,N′,N′-tetramethylphosphoric triamide in the absence of triethylamine (C. N. Mavrommatis, PhD thesis, The Polytechnic of North London, 1983).
6. R. Bosshard and A. Hubele, Swiss Patent, 593,010 (1977); *Chem. Abstr.*, **88**, 46383x (1978).
7. "Atlas IK-Spektrov Fosfororganicheskikh Soedinenii," R. R. Shagidullin, F. S. Mukhametov, R. B. Nigmatullina, V. S. Vinogradova and A. V. M. Chernova, ed. A. N. Pudovik, Nauka, Moscow, 1977.
8. "The Infrared Spectra of Complex Molecules," 2nd Edition, L. J. Bellamy, Methuen, London, 1958.
9. R. Keat and R. A. Shaw, *J. Chem. Soc.*, 4802 (1965).
10. B. N. Laskorin, V. V. Yashkin and L. I. Sokal'skaya, *Dokl. Akad. Nauk SSSR*, **215**, 595 (1974); *Chem. Abstr.*, **80**, 145159v (1974).
11. R. B. Harvey and J. E. Mayhood, *Can. J. Chem.*, **33**, 1552 (1955).
12. J. Martens, K. Praefcke, H. Schwarz and H. Simon, *Phosphorus*, **6**, 247 (1976).
13. It is significant that only one doublet, δ_H ($CDCl_3$) 2.66, $^3J_{PNCH}$ 10.0 Hz was observed in the ^1H nmr spectrum of N,N,N′,N′-tetramethylphosphoric triamide (4, $R^1 = R^2 = Me_2N$), in which no chiral centre is present. A simple doublet is also exhibited by hexamethylphosphoric triamide [cf. G. Martin and G. Mavel, *Compt. Rendus*, **255**, 2095 (1962); G. Martin and A. Besnard, *Compt. Rendus*, **257**, 898 (1963)].
14. C. N. Mavrommatis, PhD thesis (CNAA), The Polytechnic of North London, 1983.
15. M. L. Nielsen and J. V. Pustinger, *J. Phys. Chem.*, **68**, 152 (1964); J. R. van Wazer, C. F. Cullis, J. N. Shoolery and R. C. Jones, *J. Am. Chem. Soc.*, **78**, 5717 (1956); R. A. Y. Jones and A. R. Katritzky, *Angew. Chem., Internat. Edn.*, **1**, 32 (1962).
16. A. I. Vogel, "Textbook of Quantitative Inorganic Analysis," 4th ed., Longman, London, pp. 498–499, 1978.
17. R. E. Lutz *et al.*, *J. Org. Chem.*, **12**, 678 (1947).
18. F. Garcia Gonzales, *Anales Soc. Espan. Fis. Quim*, **32**, 815 (1934).
19. A. E. Dukker, Neth. Appln. 6,605, 525; *Chem. Abstr.*, **66**, 95055 (1967).

20. F. Feist, *Ber.*, **45,** 945 (1912).
21. O. Jacobsen, *Annalen*, **157,** 245 (1871).
22. M. Pianka, J. D. Edwards and C. B. F. Smith, *J. Sci. Fd. Agric.*, **17,** 407 (1966).
23. H. Schubert, Ger. 949,946 (1956); *Chem. Abstr.*, **53**, 10039b (1959). We were unable to obtain this compound by the method given in the patent, but it was obtained, m.p. 127–129°C, by interaction of anhydrous chloral with trichloroacetamide under reflux (7 h), followed by treatment with diethyl ether, cooling to −18°C overnight, and recrystallization of the solid product from diethyl ether.
24. J. S. Eden, U.S. Patent 2,936,323 (1960).
25. D. Z. Barczynski and Z. Eckstein, *Przem. Chem.*, **57,** 176 (1978).
26. S. I. Shestakova, S. D. Volodkovich, S. S. Kukalenco, T. A. Ulanova and N. B. Polyakova, *Fiziol. Akt. Veshchestva*, **9,** 75 (1977); *Chem. Abstr.*, **81,** 120787f (1974).
27. H. G. Grant and L. A. Summers, *Aust. J. Chem.*, **33,** 613 (1980).
28. R. A. Olofson and R. V. Kendal, *J. Org. Chem.*, **35,** 2246 (1970).
29. J. Elguero, C. Marzin and J. D. Roberts, *J. Org. Chem.*, **39,** 357 (1974).
30. Pflatz and Bauer Inc., "Research Chemical Catalog," 8th Ed., 1979.