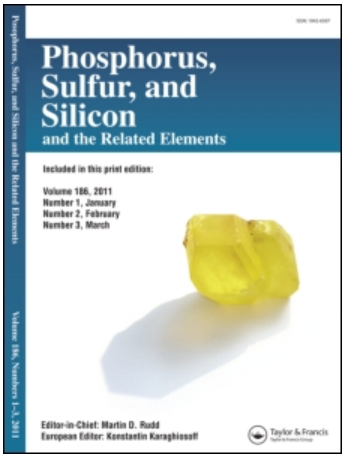

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ORGANOPHOSPHORUS COMPOUNDS AS POTENTIAL FUNGICIDES. PART VI.[1] PREPARATION, CHARACTERIZATION, AND BIOLOGICAL ACTIVITY OF ANALOGUES AND DERIVATIVES OF 1-AMINOPROPANEPHOSPHONIC ACID

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ORGANOPHOSPHORUS COMPOUNDS AS POTENTIAL FUNGICIDES. PART VI.[1] PREPARATION, CHARACTERIZATION, AND BIOLOGICAL ACTIVITY OF ANALOGUES AND DERIVATIVES OF 1-AMINOPROPANEPHOSPHONIC ACID

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α-Aminopropane-phosphonous, -methylphosphinic, and -phenylphosphinic acids do not exhibit comparable antifungal activity to that shown by α-aminopropanephosphonic acid (ampropylfos) against *Drechslera teres*, when applied as seed dressings. It is concluded that the phosphonic acid function is necessary for this type of activity. Moderate activity against several organisms was nevertheless shown by α-aminopropane- and α-aminoethane-phosphonous acids in foliar spray tests, although longer chain compounds were found to be inactive. α-Ureidopropanephosphonate (ammonium salt) also showed activity in foliar tests at 1000 ppm. A range of new ureylene- and thioureylene-bisphosphonates, prepared as potential profungicides of ampropylfos, proved to be inactive as seed dressings although tetrakis(2,2,2-trifluoroethyl) thioureylenebis(1-propylphosphonate) gave 75–100% control of *Puccinia recondita* as a foliar spray (1000 ppm). Characterization of the various compounds by nmr spectroscopy and mass spectrometry is discussed.

Keywords: Aminophosphonic; aminophosphinic; aminophosphonous; ureidophosphonate; ureylenebisphosphonate; thioureylenebisphosphonate; fungicide

INTRODUCTION

The potential of α-aminopropanephosphonic acid (ampropylfos) (**1**) as an agricultural seed dressing for use in the control of *Drechslera* spp. and other fungal pathogens of commercial importance[2–6] led us to investigate

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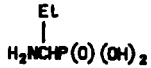
the possible use of analogues and derivatives. We have previously reported the activity of certain peptides incorporating α-aminopropanephosphonic acid in the *C*-terminal position[7] and we now report our studies on various phosphinic acids (**2**, **3**), ureidophosphonates (**4** – **6**), and ureylene- or thioureylene-bisphosphonates (**7**), which may be regarded as analogues, or potential profungicides, of α-aminopropanephosphonic acid.



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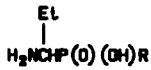
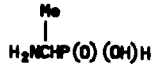


(2)

R = H (2a), Me (2b), Ph (2c)



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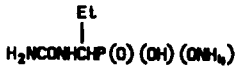

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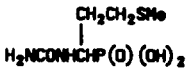

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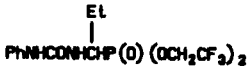

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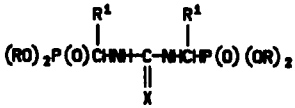


(7)

R = CF_3CH_2, R^1 = Et, X = O (7a); R = CF_3CH_2, R^1 = Et, X = S (7b);

R = CCl_3CH_2, R^1 = Et, X = O (7c); R = CCl_3CH_2, R^1 = Et, X = S (7d);

R = CF_3CH_2, R^1 = $MeSCH_2CH_2$, X = O (7e);

R = CF_3CH_2, R^1 = $MeS(O)CH_2CH_2$, X = O (7f); R = Ph, R^1 = Et, X = S (7g);

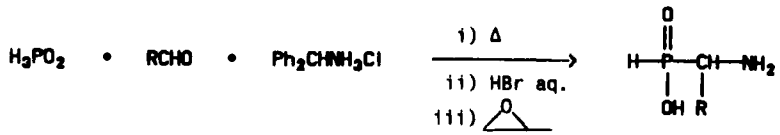
R = Ph, R^1 = $MeSCH_2CH_2$, X = S (7h)

RESULTS AND DISCUSSION

Preparative methods

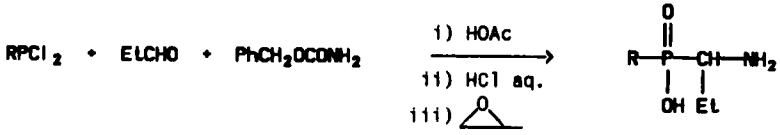
The α-aminophosphinic acids (**2**, **3**) are known compounds and were prepared by standard procedures. Those containing a P-H bond, otherwise

known as α-aminoalkylphosphonous acids (**2a**, **3**), were readily obtained by the interaction of hypophosphorous acid with diphenylmethylamine hydrochloride and propanal or ethanal, respectively (Scheme 1).[8] Compounds containing two P-C bonds are less easily accessible, although several preparative methods have been reported,[9] including the use of aryl or alkyl dichlorophosphines.[10] α-Aminopropyl(methyl)phosphinic acid (**2b**) has been mentioned only briefly in the literature, without characterization data,[11] but we found that a modest yield could be obtained by the dichlorophosphine procedure as described for other compounds of this type,[10] viz. by the interaction of methyldichlorophosphine, benzyl carbamate, and propanal in glacial acetic acid, followed by hydrolysis (Scheme 2, R = Me). An analogous procedure, using phenyldichlorophosphine (Scheme 2, R = Ph) has been described for the preparation of α-aminopropyl(phenyl)phosphinic acid (**2c**)[10] and we also found the use of diphenyl phenylphosphonite as a starting material to be suitable (Scheme 3).



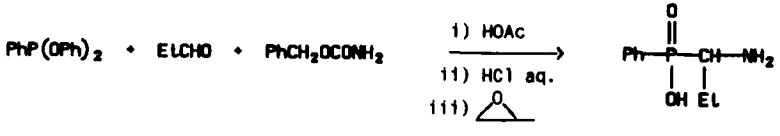
R = Me or Et

SCHEME 1



R = Me or Ph

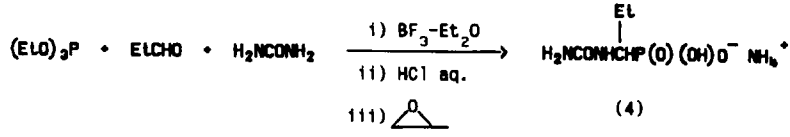
SCHEME 2



(2c)

SCHEME 3

The ureido-, ureylene-, and thioureylene derivatives (**4**, **5**, **6**, **7a-7h**) are new compounds, and were prepared by various modifications of the chemistry described by Birum,[12] in which trialkyl or triaryl phosphites interact with different combinations of aldehydes and ureas. In general it was reported[12] that mono- and di-substituted ureas gave monophosphonates whereas urea gave mixtures of monophosphonates and ureylene diphosphonates. In certain examples, acetic acid or boron trifluoride-etherate was shown to catalyze the reaction. In our present investigations the interaction of equimolar amounts of triethyl phosphite, propanal and urea, in the presence of boron trifluoride-etherate, gave the monophosphonate in the form of its ammonium salt, ammonium α-ureidopropanephosphonate (**4**) (Scheme 4).[13] The separation of product as the ammonium salt in this case is unusual, but probably occurred fortuitously because of the formation of ammonium chloride (and hence ultimately of ammonia) during the hydrolysis and work-up procedure using propylene oxide. Stoicheiometrically, it is clear that only a limited yield of the ammonium salt is obtainable. Further hydrolysis gave α-aminopropanephosphonic acid (**1**) only slowly, it being necessary to heat the ureido compound under reflux with concentrated hydrochloric acid for 72 h to complete the reaction. Other ureido monophosphonates (**5**, **6**) were obtained by the reaction sequences shown (Schemes 5 and 6), starting from urea or phenylurea, respectively.

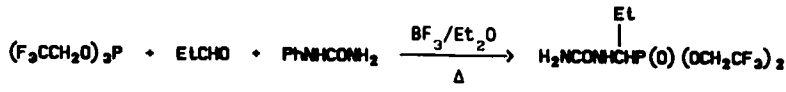


(4)

SCHEME 4

(5)

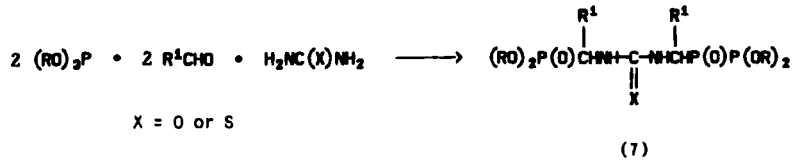
SCHEME 5



(6)

SCHEME 6

Ureylene- or thioureylene-bisphosphonates (**7a – 7h**) were prepared by the interaction of urea or thiourea with two molecular equivalents each of the corresponding phosphite and alkanal, in most cases by heating in anhydrous toluene in the region of 100 °C (Scheme 7). For preparation of the 3-methylsulfenyl compound (**7e**) boron trifluoride-etherate was used to catalyze the reaction and the product was subsequently oxidized to the 3-methylsulfinyl derivative (**7f**) using hydrogen peroxide in glacial acetic acid.[14] The tetrakis(2,2,2-trihaloethyl) and tetraphenyl bisphosphonates were all obtained as well-defined, white crystalline products, with characteristic spectroscopic data.



(7)

SCHEME 7

Nmr Spectroscopy

All the compounds under discussion exhibit complicated ^1H nmr spectra with numerous overlapping peaks resulting from the presence of a chiral α-carbon atom, diastereotopic protons in the β-CH_2 of the propyl or substituted propyl chain (except for compound **3**), diastereotopic methylene protons in the ester groups (which are themselves diastereotopic), phosphorus-proton coupling and (for compounds **6**, **7a**, **7b**, **7e**, and **7f**) fluorine-proton coupling.

The ^{13}C nmr spectra are superficially simpler and generally more useful for the characterization of these molecules. One bond phosphorus-carbon coupling is generally around 150–160 Hz for the phosphonic acids or phosphonates (**4**, **5**, **6**, **7a-7h**) but significantly less (93–96 Hz) for the phosphonous (**2a**, **3**) and phosphinic acids (**2b**, **2c**), which have fewer oxygen atoms attached to phosphorus. Two bond coupling as usual is small (2–3 Hz), or undetectable. Three-bond coupling in the propyl chain ($^3J_{PCCC}$) varies from *ca.* 9 Hz (for **2a**, **2c**) to between 12 and 18 Hz for all other compounds. In certain cases (**4**, **5**, **7c**, **7d**, **7g**, **7h**), three-bond coupling also gave rise to a doublet for the carbonyl or thiocarbonyl signal

($^3J_{PCNC}$ 6–9 Hz). Additionally, fluorine-carbon coupling in the trifluoroethyl esters (**6**, **7a**, **7b**, **7e**, and **7f**) gives rise to quartets for the CF_3 carbon atom ($^1J_{FC}$ 295 – 298 Hz) and for the adjacent methylene group ($^2J_{FCC}$ *ca.* 40 Hz). However, the diastereotopic nature of the ester groups, together with phosphorus-carbon coupling, produces a fine structure in the methylene quartet, each line of which consists of two overlapping doublets ($\Delta\delta_C$ = 0.5–0.8 ppm, $^2J_{POC}$ 6 – 7 Hz). Some indication of phosphorus coupling to the CF_3 carbon atom was also noted on expansion of the spectrum which revealed unresolved shoulders. In the case of trichloroethyl esters (**7c**, **7d**), the methylene carbon atoms appeared as two doublets ($^2J_{POC}$ 6 – 7 Hz), separated by 0.2–0.3 ppm, and the CCl_3 carbon atom as a doublet with similar phosphorus coupling.

^{31}P nmr chemical shifts are in the expected regions for phosphinic and phosphonic acid derivatives[15] and are summarized in Table I.

TABLE I ^{31}P nmr chemical shifts[a]

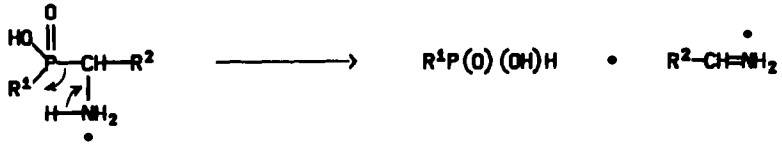
Compound type	*δ/ppm*	*Solvent*
aminophosphonic acid (**1**)	14.6	(D_2O)
aminophosphonous acids (**2a**, **3**)	20.5,[b] 21.4[c]	(D_2O)
aminophosphinic acid (P-methyl) (**2b**)	35.0	(MeOD)
aminophosphinic acid (P-phenyl) (**2c**)	24.1	(MeOD)
ureidophosphonate (NH_4^+ salt) (**4**)	23.3	(D_2O)
ureidophosphonic acid (**5**)	18.1	(D_2O)
bis(trifluoroethyl) phosphonate (**6**)	25.4	(MeOD)
tetrakis(trifluoroethyl) bisphosphonates (**7a**, **7b**)	27.0, 27.1	($CDCl_3$)
(**7e**, **7f**)	27.1, 27.8	(MeOD)
tetrakis(trichloroethyl) bisphosphonates (**7c**, **7d**)	23.9, 24.6	($CDCl_3$)
tetraphenyl bisphosphonates (**7g**, **7h**)	17.8, 18.9	($CDCl_3$)

a. Ref. 85% H_3PO_4. [b] J_{PH} 528 Hz. [c] J_{PH}531 Hz.

Mass Spectrometry

Fast atom bombardment mass spectrometry (FAB MS) provided additional characterization data for the non-volatile ionic compounds (**2a**, **2b**, **2c**, **3**,

4, **5**), all of which gave prominent pseudomolecular ions, $[MH]^+$, together with higher clusters such as $[2M+H]^+$, and fragment ions resulting from the elimination of hypophosphorous acid (from **2a** and **3**), or the corresponding methylphosphonous or phenylphosphonous acid (from **2b** and **2c**, respectively). In each case these eliminations give rise to the corresponding iminium ion $[RCH=NH_2]^+$ (R = Me or Et) which generally appears as the base peak (Scheme 8). Analogous fragmentations, by the loss of H_3PO_3, occur for α-aminoalkanephosphonic acids.[6] Ammonium α-ureidopropanephosphonate (**4**) similarly gave a distinctive MH^+ ion which appears to lose water or ammonia but does not generate an ion corresponding to the loss of H_3PO_3 only, as observed for the aminophosphonic acids.[6] The stable iminium ion $[EtCH=NH_2]^+$ was nevertheless responsible for the base peak in the spectrum and is presumably formed by the loss of HNCO from the ureido group, and of H_3PO_3. Evidence was also obtained for the elimination of a molecule of HNCO from the ureidophosphonic acid (**5**), which also gave the corresponding iminium ion, $[MeSCH_2CH_2CH=NH_2]^+$, and of ammonia from **2c** and **5**.



R^1 = H, Me, Ph; R^2 = Me, Et, $MeSCH_2CH_2$

SCHEME 8

Electron impact mass spectra of the non-ionic compounds (**6**, **7a-7h**) gave relatively weak but identifiable molecular ions and in certain cases (**7a** **7c**), protonated molecular ions were also present. The latter are presumably formed by a type of chemical ionization process in the ion source, by proton transfer from other fragment ions as reported elsewhere for certain carbonyl compounds and amides.[16] Spectra of the tetrakis(trichloroethyl) esters (**7c**, **7d**) revealed isotope ion clusters, the most abundant molecular ions being those which correspond to the presence of nine ^{35}Cl and three ^{37}Cl atoms.[17] Exact mass measurements confirmed the compositions of molecular ions derived from the tetrakis(trichloroethyl) and tet-

rakis(trifluoroethyl) esters (**7a-7d**) and for selected fragment ions derived from the fluoro compounds (Tables II – V). The assignment of putative structures to fragment ions in the spectra of tetrakis(trichloroethyl) esters (Tables IV and V) is based on analogy with the fluoro compounds and on the number of chlorine atoms present, as shown by the isotopic abundances.

TABLE II EMM's for molecular and fragment ions in the EI MS of $(CF_3CH_2O)_2P(O)CHEtNHC(O)NHCHEtP(O)(OCH_2CF_3)_2$ (**7a**)

Ion[a]	*Formula*	*Observed*	*Calc.*
MH^+	$C_{15}H_{23}F_{12}N_2O_7P_2$	633.0747	633.0788
$[MH-(RO)_2PHO]^+$	$C_{11}H_{18}F_6N_2O_4P_2$	389.0900	387.0908
$[(RO)_2P(O)CHEtNHCO]^+$	$C_8H_{11}F_6NO_4P_2$	330.0266	330.0330
$[(RO)_2P(O)CH(Et)NH]^+$	$C_7H_{11}F_6NO_3P_2$	302.0363	302.0380
$[(RO)_2P(O)CH=NH_2]^+$	$C_5H_7F_6NO_3P_2$	274.0041	274.0068
$[(RO)_2P(O)H]^{+\cdot}$	$C_4H_5F_6O_3P$	245.9915	245.9880
$[EtCH=NC(O)NH=CHEt]^+$	$C_7H_{13}N_2O$	141.1049	141.1028
$([EtCH=NH_2]^+$	C_3H_8N	58.0667	58.0657

a. $R = CF_3CH_2$.

TABLE III EMM's for molecular and fragment ions in the EI MS of $(CF_3CH_2O)_2P(O)CHEtNHC(S)NHCHEtP(O)(OCH_2CF_3)_2$ (**7b**)

Ion[a]	*Formula*	*Observed*	*Calc.*
MH^+	$C_{15}H_{23}F_{12}N_2O_6P_2S$	649.0532	649.0560
$M^{+\cdot}$	$C_{15}H_{22}F_{12}N_2O_6P_2S$	648.0473	648.0482
$[M-(RO)_2P(O)]^+$	$C_{11}H_{18}F_6N_2O_3PS$	403.0681	403.0680
$[M-(RO)_2P(O)H]^{+\cdot}$	$C_{11}H_{17}F_6N_2O_3PS$	402.0589	402.0602
$[M-(RO)_2P(O)-H_2S]^+$	$C_{11}H_{16}F_6N_2O_3P$	369.0807	369.0803
$[(RO)_2P(O)CHEt]^+$	$C_7H_{10}F_6O_3P$	287.0245	287.0272
$[(RO)_2P(O)CHMe]^+$	$C_6H_8F_6O_3P$	273.0114	273.0115
$[EtCH=NC(S)NH=CHEt]^+$	$C_7H_{13}N_2S$	157.0780	157.0799
$[EtCH=NC(S)N=CHEt]^{+\cdot}$	$C_7H_{12}N_2S$	156.0714	156.0721
$[157-H_2S]^+$	$C_7H_{11}N_2$	123.0914	123.0922
$[EtCH=NHC(S)NH_2]^+$	$C_4H_9N_2S$	117.0484	117.0486
$[EtC=NHC(S)NH]^+$	$C_4H_7N_2S$	115.0322	115.0330

Ion[a]	*Formula*	*Observed*	*Calc.*
$[C_4H_6NS]^+$	C_4H_6NS	100.0214	100.0221
$[EtCH{=}NH_2]^+$	C_3H_8N	58.0673	58.0657

a. $R = CF_3CH_2$.

TABLE IV Molecular and fragment ions in the EI MS of $(CCl_3CH_2O)_2P(O)CHEtNHC(O)NHCHEtP(O)(OCH_2CCl_3)_2$ (**7c**)

m/z	*(%)*[a]	*assignment*	*Cl isotopes present*
831	(7)	MH^+	$^{35}Cl_9{}^{37}Cl_3$
830	(3)[b]	$M^{+\cdot}$	$^{35}Cl_9{}^{37}Cl_3$
793	(4)	$[M\text{-}Cl]^+$	$^{35}Cl_9{}^{37}Cl_2$
711	(18)	$[M\text{-}CCl_3]^+$	$^{35}Cl_7{}^{37}Cl_2$
681	(58)	$[M\text{-}Cl_3CCH_2O]^+$	$^{35}Cl_7{}^{37}Cl_2$
531	(19)	$[681\text{-}Cl_3CCH_2OH]^+$	$^{35}Cl_7{}^{37}Cl_2$
485	(47)	$[M\text{-}(Cl_3CCH_2O)_2PO]^+$	$^{35}Cl_5{}^{37}Cl_1$
335	(52)	$[M\text{-}RO\text{-}(RO)_2PHO]^+$	^{35}Cl
225	(14)	$[Cl_3CCH_2OP(O)CH_2OH]^+$	$^{35}Cl_3$
141	(55)	$[EtCH{=}NC(O)NH{=}CHEt]^+$	–
58	(100)	$[EtCH{=}NH_2]^+$	–

a. Most intense peak in each isotope ion cluster listed.
b. EMM: 829.7129. Calc for $C_{15}H_{22}{}^{35}Cl_9{}^{37}Cl_3N_2O_7P_2$: 829.7077.

TABLE V Molecular and fragment ions in the EI MS of $(CCl_3CH_2O)_2P(O)CHEtNHC(S)NHCHEtP(O)(OCH_2CCl_3)_2$ (**7d**)

m/z	*(%)*[a]	*assignment*	*Cl isotopes present*
846	(3)[b]	$M^{+\cdot}$	$^{35}Cl_9{}^{37}Cl_3$
811	(25)	$[M\text{-}Cl]^+$	$^{35}Cl_8{}^{37}Cl_3$
775	(5)	$[M\text{-}Cl\text{-}HCl]^+$	$^{35}Cl_7{}^{37}Cl_3$
727	(8)	$[M\text{-}CCl_3]^+$	$^{35}Cl_7{}^{37}Cl_2$
697	(15)	$[M\text{-}Cl_3CCH_2O]^+$	$^{35}Cl_7{}^{37}Cl_2$
661	(13)	$[697\text{-}HCl]^+$	$^{35}Cl_6{}^{37}Cl_2$
547	(17)	$[697\text{-}Cl_3CCH_2OH]^+$	$^{35}Cl_5{}^{37}Cl_1$
501	(5)	$[M\text{-}(Cl_3CCH_2O)_2PO]^+$	$^{35}Cl_5{}^{37}Cl_1$
443	(21)	$[(RO)_2P(O)CHEtNCS]^+$	$^{35}Cl_5{}^{37}Cl_1$

m/z	*(%)*[a]	*assignment*	*Cl isotopes present*
225	(14)	$[Cl_3CCH_2OP(O)CH_2OH]^+$	$^{35}Cl_3$
100	(100)	$[EtCHNCS]^{+\cdot}$	–
58	(100)	$[EtCH{=}NH_2]^+$	–

a. Most intense peak in each isotope ion cluster listed.
b. EMM: 845.6858. Calc. for $C_{15}H_{22}{}^{35}Cl_9{}^{37}Cl_3N_2O_7P_2$: 845.6848.

Biological Activity

Previous reports of the biological activity of aminoalkylphosphinic acids in the agrochemical field have been concerned mainly with herbicidal or plant-growth regulatory activity,[18–21] although some fungicidally active derivatives are also known.[22]

In the present investigations it was found that the phosphinic (phosphonous) (**2a**), methylphosphinic (**2b**), and phenylphosphinic (**2c**) analogues of ampropylfos (**1**) were essentially inactive as seed dressing agents against *Drechslera teres* when applied at 400 ppm, whereas the phosphonic acid (ampropylfos) had shown good activity against this organism under similar conditions.[2–6] For this type of activity the phosphonic acid group appears to be essential. Nevertheless, the same analogues (**2a**, **2b**, **2c**), and also the ammonium salt of α-ureidopropanephosphonic acid (**4**), showed moderate activity against a number of fungal pathogens in foliar spray tests, but only at the relatively high concentration of 1000 ppm. Under these conditions, each of the compounds gave 50 – 75% control of *Puccinia recondita*. In addition, α-aminopropanephosphonous acid (**2a**) and α-aminoethanephosphonous acid (**3**) showed comparable levels of activity (50 – 100% control) against several organisms among *Erisyphe graminis, Puccinia recondita, Septoria nodorum* and *Fusarium culmorum*. The shorter chain molecule, α-aminoethanephosphonous acid (**3**) (previously reported to show strong herbicidal activity[23]), was found to be active at lower concentrations against *Plasmopara viticola* (100% control at 300 ppm) and *Pyricularia oryzae* (90% control at 100 ppm).[24] The longer chain aminophosphonous acids showed no significant fungicidal activity. It is of interest to note that a range of ring substituted *N*-benzyloxy derivatives of α-aminoethanephosphonous acid have been patented as agents for the control of *Plasmopara viticola*.[25]

None of the ureidophosphonates (**4 – 6**), or the ureylene- or thioureylene-bisphosphonates (**7**), showed any similar activity as seed dressings to

that of ampropylfos (**1**) against *Drechslera teres* and it is concluded that these compounds do not behave as profungicides by liberating α-aminopropanephosphonic acid *in vivo*. However, tetrakis(2,2,2-trifluoroethyl) thioureylenebis(1-propylphosphonate) (**7b**) gave 75 – 100% control of *Puccinia recondita* when applied as a foliar spray (1000 ppm).

EXPERIMENTAL

Staring Materials

Methyldichlorophosphine,[26] diphenyl phenylphosphonite,[27] tris(2,2,2-trifluoroethyl) phosphite,[28] and tris(2,2,2-trichloroethyl) phosphite[29] were prepared as described. Triphenyl phosphite, propanal, 3-(methylthio)propanal, and other general research chemicals were supplied by Aldrich. Toluene and ether were dried over sodium.

Analytical and Spectroscopic Methods

Analytical methods

Carbon, hydrogen, nitrogen and sulfur were determined on a Carlo Erba 1106 Elemental Analyser. Melting points were recorded on a Gallenkamp apparatus with mercury in glass thermometer and are uncorrected.

Spectroscopy

Nmr spectra were recorded on a Bruker WP-80 spectrometer operating at 80.018 MHz (^{1}H), 20.12 MHz (^{13}C), or 32.395 MHz (^{31}P). Samples were dissolved in D_2O, MeOD, or $CDCl_3$ (as indicated below) according to solubility. Chemical shifts (downfield positive) are quoted relative to TMS (internal standard for ^{1}H and ^{13}C spectra in organic solvents), sodium 3-trimethylsilylpropionate (internal standard for ^{1}H and ^{13}C spectra in D_2O), and 85% H_3PO_4 (external standard for ^{31}P spectra).

Low resolution EI mass spectra were obtained by direct injection using a Kratos Profile instrument operating at 70 eV. Positive ion FAB mass spectra and high resolution EI mass spectra were obtained on a VG Micromass ZAB-1F instrument. The FAB spectra were recorded using a glycerol matrix and with a primary beam of xenon atoms (8 kV).

Preparations

α-Aminopropanephosphonous acid (**2a**) and α-aminoethanephosphonous acid (**3**) were prepared from hypophosphorous acid, diphenylmethylamine, and the corresponding aldehydes, as described.[8]

α-Aminopropane(methyl)phosphinic acid (2b)

Compound **2b**, not previously reported, was prepared by a general procedure described for compounds of this type[10] using methyldichlorophosphine (2.90 g, 0.025 mol), benzyl carbamate (3.80 g, 0.025 mol), and propanal (2.17 g, 0.038 mol) in glacial acetic acid (5 ml), and was obtained as a fine white crystalline solid (1.1 g, 31%), m.p. 265 – 266°C (Found: C, 33.9; H, 7.8; N, 9.6. $C_4H_{12}NO_2P$ requires: C, 34.8; H, 8.7; N, 10.1%); δ_H (MeOD) 0.95–1.5 (d, 3H, CH_3P, $^3J_{PCH}$ 12 Hz), 1.25 (t, 3H, $C\underline{H}_3CH_2$, $^3J_{HCCH}$ 6 Hz), 1.6–2.0 (m, 2H, CH_2), 2.7–3.4 (m, 1H, CH); δ_C (MeOD) 13.1 (d, $\underline{C}H_3CH_2CH$, $^3J_{PC}$ 13 Hz), 15.5 (d, CH_3P, $^1J_{PC}$ 95 Hz), 24.1 (s, CH_2), 55.5 (d, $\underline{C}H$, $^1J_{PC}$ 94.3 Hz); δ_P (MeOD) 35.0; FAB MS: m/z (%) 313 (26), 274 ($2MH^+$, 23), 176 (35), 138 (MH^+), 131 (39), 128 (39), 58 ($MH^+ - MePO_2H_2$, 100).

α-Aminopropane(phenyl)phosphinic acid (2c)

Compound **2c**, was prepared from diphenyl phenylphosphonite (7.35 g, 0.025 mol), benzyl carbamate (3.8 g, 0.025 mol), and propanal (2.17 g, 0.038 mol) in glacial acetic acid (5 ml), by an analogous procedure to that described for reactions using triphenyl phosphite.[6,30] After isolation as described and oven drying (60 °C) the compound was obtained as a fine white crystalline solid (2.2 g, 43.5%), m.p. 255 °C (lit.[10] 256–258 °C) (Found: C, 53.1; H, 6.2; N, 6.2. Calc. for $C_9H_{14}NO_2P$: C, 54.0; H, 7.0; N, 7.0%); δ_H (MeOD) 1.35 (t, 3H, CH_3, $^3J_{HCCH}$ 6 Hz), 1.80–2.50 (m, 2H, CH_2), 3.88–4.31 (m, 1H, CH), 7.75–8.38 (m, 5H, Ar); δ_C (MeOD) 13.2 (d, CH_3, $^3J_{PC}$ 9 Hz), 24.0 (s, CH_2), 56.1 (d, $^1J_{PC}$ 96 Hz), 135.0 (s, *o*-ArC), 136.0 (s, *m*-ArC), 137.0 (s, *p*-ArC); δ_P (MeOD) 24.1; FAB MS: m/z (%) 399 ($2MH^+$, 18), 200 (MH^+, 49), 183 ($MH^+ - NH_3$, 28), 140 (23), 143 (18), 58 ($MH^+ - PhPO_2H_2$, 100).

Ammonium α-ureidopropanephosphonate (4)

A mixture of urea (1.92 g, 0.032 mol), triethyl phosphite (5.31 g, 0.032 mol) and propanal (1.85 g, 0.032 mol) in dry toluene (25 ml) was stirred

vigorously at room temperature. Boron trifluoride etherate (0.9 ml) in dry toluene (10 ml) was added dropwise (20 min), and the mixture was then heated under reflux (2 h). Voltile materials were removed under reduced pressure, and the residue was heated under reflux (8 h) with concentrated hydrochloric acid (100 ml). The aqueous layer was separated, washed with dichloromethane (2 × 10 ml), boiled with charcoal (1.1 g), filtered, and concentrated *in vacuo*. Methanol (10 ml) was added and the resultant solution was treated with propylene oxide to give maximum precipitation. The solid product was filtered off, washed with acetone (5 ml) and recrystallized (ethanol/water) to give *ammonium α-ureidopropanephosphonate* (**4**) as a white crystalline solid (1.97 g, 31.3%), m.p. 205 °C (Found: C, 23.9; H, 6.4; N, 20.8. $C_4H_{14}N_3O_4P$ requires: C, 24.1; H, 7.0; N, 21.1%); δ_H (D_2O) 1.15 (t, 3H, CH_3, $^3J_{HCCH}$ 7 Hz), 1.30–1.95 (br m, 2H, CH_2), 2.59–2.71 (d, 1H, NH, $^3J_{PCNH}$ 8 Hz, exchanged after 0.5 h), 3.38–4.15 (m, 1H, CH); δ_C(D_2O) 12.9 (d, CH_3, $^3J_{PC}$14 Hz), 25.7 (d, CH_2, $^2J_{PC}$ 3 Hz), 53.3 (d, CH, $^1J_{PC}$ 154.9 Hz), 159.1 (d, C=O, $^3J_{PCNC}$ 6.1 Hz); δ_P (D_2O) 23.3; FAB MS: m/z (%) 200 (MH^+, 48), 183 ($MH^+ - NH_3$, 18), 182 ($MH^+ - H_2O$, 68), 166 (19), 165 (23) 101 (50), 140 (59), 110 (50), 58 ($EtCH{=}NH_2^+$, 100).

(In an otherwise identical experiment, in which the period of heating with concentrated hydrochloric acid was extended to 72 h, the isolated product was α-aminopropanephosphonic acid (**1**) (1.19 g, 26.9%), m.p. 258–259 °C (lit.[31] m.p. 264–266 °C), with ^1H and ^{31}P nmr spectral data as reported[6]).

α-Ureido-3-(methylsulfenyl)propanephosphonic acid (5)

Freshly distilled 3-(methylsulfenyl)propanal (2.2 g, 0.02 mol) was added dropwise (1 h) to a stirred mixture of powdered urea (1.2 g, 0.02 mol) and tris(2,2,2-trichloroethyl) phosphite (10.0 g, 0.02 mol) at 95–100 °C. The mixture was heated further (0.5 h) and then concentrated under reduced pressure (13 mmHg at 60 °C) to give a gelatinous residue which was dissolved in a mixture of acetonitrile (3 ml) and water (0.7 ml). After heating gently under reflux (1 h) and concentration *in vacuo*, ethyl acetate (60 ml) was added to give a yellow mixture which was stored at 4 °C. The white precipitate which formed during several weeks was separated, washed with ether (2 × 4 ml) and dried to give *α-ureido-3-(methylsulfenyl)propanephosphonic acid* (**5**) as a fine white powder (0.76 g, 15.6%), m.p. 160 °C (Found: C, 25.9; H, 5.7; N, 12.6. $C_5H_{13}N_2O_4PS$ requires: C, 26.3; H,

5.7; N, 12.3%); δ_H (D_2O) 1.55–2.31 (m, 2H, $C\underline{H}_2CH$), 2.0 (s, 3H, CH_3), 2.60 (t, 2H, SCH_2, $^3J_{HCCH}$ 7.1 Hz), 3.90–4.35 (m, 1H, CH); δ_H ($CDCl_3$) 1.0–1.72 (m, 2H, $C\underline{H}_2CH$), 1.85 (s, 3H, CH_3), 2.55 (t, 2H, SCH_2, $^3J_{HCCH}$ 7.1 Hz), 3.70–4.10 (m, 1H, CH), 6.12 (br s, 1H, NH), 8.60 (br, 4H, OH and NH_2); δ_C (D_2O) 14.6 (s, CH_3S), 29.1 (d, $\underline{C}H_2CH$, $^2J_{PC}$ 1.6 Hz), 30.7 (d, SCH_2, $^3J_{PC}$ 15.8 Hz), 46.5 (d, CH, $^1J_{PC}$ 161.3 Hz), 158.6 (d, C=O, $^3J_{PCNC}$, 10.3 Hz); δ_P (D_2O) 18.1; FAB MS: m/z (%) 457 ($2MH^+$, 15), 267 (10), 251 (15), 229 (MH^+, 83), 212 ($MH^+ - NH_3$, 9), 187 (MH^+ – HCNO, 47), 114 (10), 104 ($MeSCH_2CH_2CH{=}NH_2^+$, 100). No further crystals could be obtained from the mother liquor on prolonged storage at 4 °C.

Bis(2,2,2-trifluoroethyl) α-(3-phenylureido)propanephosphonate (6)

Tris(2,2,2,-trifluoroethyl) phosphite (12.5 g, 0.038 mol), phenylurea (5.6 g, 0.038 mol) and propanal (2.32 g, 0.04 mol) were stirred in toluene (10 ml) at room temperature whilst boron trifluoride etherate (1.5 ml) in toluene (10 ml) was added dropwise (15 min). The mixture was heated under reflux at 95–105 °C (2.5 h), cooled, and the volatile components were removed by rotary evaporation. The brown residue (16.3 g) was dissolved in ethanol (15 ml), treated with petroleum (b.p. 30–40 °C), and stored at 4 °C for several weeks. The precipitate which formed was filtered off, washed with ethyl acetate (2 × 8 ml) and dried to give a pale pink solid (1.61 g). Repeated concentration of the mother liquor, followed by dissolving of the residue in ethyl acetate (12 ml), addition of light petroleum (35 ml), and storage at 4 °C, similarly gave further crops of precipitated solid (5.90 and 1.82 g). The total crude product (9.33 g) was recrystallized from water and ethanol to give *bis(2,2,2-trifluoroethyl) α-(3-phenylureido)propanephosphonate* (**6**) as a white crystalline solid (8.2 g, 48.6%), m.p. 154–155 °C (Found: C, 39.1; H, 4.0; N, 6.4. $C_{14}H_{17}F_6N_2O_4P$ requires: C, 39.8; H, 4.0; N, 6.6%); δ_H (MeOD) 0.98 (t, 3H, CH_3, $^3J_{HCCH}$ 6.1 Hz), 1.40–2.0 (br m, 2H, CH_2), 3.55–4.0 (m, 1H, CH), 3.85–4.30 (m, 4H, $POCH_2$), 6.95–7.05 (br d, NH, $^3J_{PCNH}$ 9.3 Hz, exchanged with D_2O), 7.50 (br s, 5H, Ar); δ_C (MeOD) 9.5 (d, CH_3, $^3J_{PC}$ 13.4 Hz), 23.1 (d, CH_2 $^2J_{PC}$ 3.0 Hz), 51.8 (d, CH, $^1J_{PC}$ 155 Hz), 62.2 (dq, $PO\underline{C}^AH_2CF_3$, $^2J_{FCC}$ 40.7 Hz, $^2J_{POC}$ 7.0 Hz), 62.9 (dq, $PO\underline{C}^BH_2CF_3$, $^2J_{FCC}$ 40.7 Hz, $^2J_{POC}$ 7.2 Hz), 124.1 9 (q, CF_3, $^1J_{FC}$ 295.5 Hz), 128.8 (s, *o*-ArC), 129 (s, *m*-ArC), 129.5 (s, *p*-ArC), 158.6 (t, C=O, $^3J_{PCNC}$ 8 Hz); δ_P (MeOD) 25.4; EI MS: m/z (%) 422 (M^+, 3), 314 (9), 268 (25), 240 (16), 177 (5), 135 (1), 93 (100).

Tetrakis(2,2,2-trifluoroethyl) ureylenebis(1-propylphosphonate) (7a)

Urea (2.3 g, 0.038 mol), tris(2,2,2-trifluoroethyl) phosphite (25.0 g, 0.076 mol), and propanal (4.4. g, 0.076 mol) were stirred in toluene (10 ml) at 80 °C and then heated at 90–96 °C (1 h) to give a clear colourless solution. Concentration under reduced pressure (13 mmHg at 90 °C) gave a yellow viscous oil (24.8 g) which solidified during several weeks at room temperature. Acetone (15 ml) was added, the resultant white solid (10.3 g) was filtered off, and the mother liquor was treated with toluene (15 ml) to give a second crop of crude product (9.0 g) during several days at room temperature. The total product was recrystallized twice from acetone to give *tetrakis(2,2,2-trifluoroethyl) ureylenebis(1-propylphosphonate)* (**7a**) as white needles (13.9 g, 57.9%), m.p. 156–158 °C (Found: C, 28.6; H, 3.4; N, 4.5. $C_{15}H_{22}F_{12}N_2O_7P_2$ requires: C, 28.4; H, 3.4; N, 4.5%); δ_H ($CDCl_3$) 1.05 (t, 3H, CH_3, $^3J_{HCCH}$ 7.1 Hz), 1.50–2.20 (br m, 2H, CH_2), 4.40–5.05 (m, 8H, $POCH_2$), 5.35–5.59 (m, 1H, CH). 7.49 (d, NH, $^3J_{PCNH}$ 10.2, exchanged with D_2O); δ_C ($CDCl_3$) 9.8 (d, CH_3, $^3J_{PC}$ 13.3 Hz), 22.9 (d, CH_2, $^2J_{PC}$ 3.1 Hz), 51.9 (d, CH, $^1J_{PC}$ 155.3 Hz), 62.2 (dq, $POC^AH_2CF_3$, $^2J_{FCC}$ 40.7 Hz, $^2J_{POC}$ 7.0 Hz), 62.9 (dq, $POC^BH_2CF_3$, $^2J_{FCC}$ 40.7 Hz, $^2J_{POC}$ 7.2 Hz), 124.1 (q, CF_3, $^1J_{FC}$ 295.5 Hz), 158.6 (s, C=O); δ_P ($CDCl_3$) 27.0; EI MS: m/z (%) 633 (MH^+, 2), 387 ($[MH-(RO)_2PHO]^+$, 26), 330 ($[(RO)_2P(O)CHEtNHCO]^+$, 3), 302 ($[(RO)_2P(O)CH(Et)NH]^+$, 2), 274 ($[(RO)_2P(O)CH=NH_2]^+$, 3), 246 ($[(RO)_2P(O)H]^{+\cdot}$, 3), 141 ($[EtCH=NC(O)NH=CHEt]^+$, 7), 99 (3), 84 (11), 58 ($[EtCH=NH_2]^+$, 100).

Tetrakis(2,2,2-trifluoroethyl) thioureylenebis(1-propylphosphonate) (7b)

A similar procedure to the above, using thiourea (2.8 g, 0.037 mol), tris(2,2,2-trifluoroethyl) phosphite (25.0 g, 0.076 mol), and propanal (4.4 g, 0.076 mol) gave *tetrakis(2,2,2-trifluoroethyl) thioureylenebis(1-propyl-phosphonate)* (**7b**) as white needles (14.7 g, 61.3%), m.p. 154–155 °C (Found: C, 28.5; H, 3.4; N, 4.2. $C_{15}H_{22}F_{12}N_2O_6P_2S$ requires: C, 27 8; H, 3.3; N, 4.4%); δ_H ($CDCl_3$) 1.0 (t, 3H, CH_3, $^3J_{HCCH}$ 7.1 Hz), 1.20–2.07 (br m, 2H, CH_2), 4.40–5.0 (m, 8H, $POCH_2$), 5.31–5.57 (m, 1H, CH), 7.45 (d, NH, $^3J_{PCNH}$ 10.3, exchanged with D_2O); δ_C ($CDCl_3$) 9.5 (d, CH_3, $^3J_{PC}$ 13.4 Hz), 23.1 (d, CH_2, $^2J_{PC}$ 3.0 Hz), 51.8 (d, CH, $^1J_{PC}$ 155 Hz), 62.1 (dq, $POC^AH_2CF_3$, $^2J_{FCC}$ 40.7 Hz, $^2J_{POC}$ 7.1 Hz), 62.9 (dq, $POC^BH_2CF_3$, $^2J_{FCC}$ 40.7 Hz, $^2J_{POC}$ 7.1 Hz), 124.1 (q, CF_3, $^1J_{FC}$ 296 Hz), 185.5 (s, C=S); δ_P ($CDCl_3$) 27.1, 27.3; EI MS; m/z (%) 649 (MH^+, 10),

648 ($M^{+\cdot}$, 29), 403 ($[M\text{-}(RO)_2P(O)]^+$, 32), 402 ($[M\text{-}(RO)_2P(O)H]^{+\cdot}$, 15), 387 (21), 369 ($[M\text{-}(CF_3CH_2O)_2P(O)\text{-}H_2S]^+$, 6), 287 ($[(RO)_2P(O)CHEt]^+$, 9), 273, ($[(RO)_2P(O)CHMe]^+$, 10), 157 ($[EtCH{=}NC(S)NH{=}CHEt]^+$, 11) 156 ($[EtCH{=}NC(S)N{=}CHEt]^{+\cdot}$, 11), 123 ($[157\text{-}H_2S]^+$, 8), 117 ($[EtCH{=}NHC(S)NH_2]^+$, 5), 115 ($[EtC{=}NHC(S)NH]^+$, 9), 100 ($C_4H_6NS^+$, 24), 58 ($EtCH{=}NH_2^+$, 100).

Tetrakis(2,2,2-trichloroethyl) ureylenebis(1-propylphosphonate) (7c)

Urea (0.9 g, 0.015 mol), tris(2,2,2-trichloroethyl) phosphite (14.3 g, 0.03 mol), and propanal (1.85. g, 0.032 mol) were stirred in toluene (10 ml) at 80 °C and then heated at 108–110 °C (1 h). Concentration under reduced pressure (13 mm Hg at 90 °C) then gave a viscous yellow oil (13.8 g) which solidified during several weeks at room temperature. The product was recrystallized twice from acetone, once from acetonitrile, and dried *in vacuo* at 60 °C to give *tetrakis(2,2,2-trichloroethyl) ureylenebis(1-propylphosphonate)* (**7c**) as a white crystalline solid (7.0 g, 56.2%), m.p. 204–205 °C (Found: C, 21.7; H, 2.8; N, 3.1. $C_{15}H_{22}Cl_{12}N_2O_7P_2$ requires: C, 21 6; H, 2.7; N, 3.3%); δ_H ($CDCl_3$) 1.03 (t, 3H, CH_3, $^3J_{HCCH}$ 6.9 Hz), 4.40 (br m, CH_2), 4.50–4.95 (m, 8H, $POCH_2$, 5.0–5.55 (m, 1H, CH), 7.65 (d, NH, $^3J_{PCNH}$ 10.0 Hz, exchanged with D_2O); δ_C ($CDCl_3$) 10.3 (d, CH_3, $^3J_{PC}$ 11.7 Hz), 23.8 (s, CH_2), 51.9 (d, CH, $^1J_{PC}$ 146.9 Hz), 76.3 (d, POC^AH_2, $^2J_{POC}$ 6.7 Hz), 76.5 (d, POC^BH_2, $^2J_{POC}$ 6.2 Hz), 93.9 (d, CCl_3, $^3J_{POCC}$ 6.0 Hz), 158.3 (t, C=O, $^3J_{PCNC}$ 9.3 Hz); δ_P ($CDCl_3$) 23.9: EI MS: m/z (%) 823.7164 ($M^{+\cdot}$, 0.6). Calc. for $C_{15}H_{22}{}^{35}Cl_{12}N_2O_7P_2$: 823.7164. (See also Table IV).

Tetrakis(2,2,2-trichloroethyl) thioureylenebis(1-propylphosphonate) (7d)

A similar procedure to the above, using thiourea (1.14 g, 0.015 mol), tris(2,2,2-trichloroethyl) phosphite (14.3 g, 0.03 mol), and propanal (1.85 g, 0.032 mol) gave *tetrakis(2,2,2-trichloroethyl) thioureylenebis(1-propyl-phosphonate)* (**7d**) as a white crystalline solid (4.9 g, 48.9%), m.p. 210–212 °C (Found: C, 20.7; H, 2.7; N, 3.2. $C_{15}H_{22}Cl_{12}N_2O_6P_2S$ requires: C, 21 2; H, 2.6; N, 3.3%); δ_H ($CDCl_3$) 1.06 (t, 3H, CH_3, $^3J_{HCCH}$ 7.1 Hz), 4.43 (br m, CH_2), 4.50–4.95 (m, 8H, $POCH_2$), 5.03–5.53 (m, 1H, CH), 7.73 (d, NH, $^3J_{PCNH}$ 9.8 Hz, exchanged with D_2O); δ_C ($CDCl_3$) 10.1 (d, CH_3, $^3J_{PC}$ 11.8 Hz), 23.4 (s, CH_2), 52.1 (d, CH, $^1J_{PC}$ 147.6 Hz), 76.2 (d, POC^AH_2, $^2J_{POC}$ 6.7 Hz), 76.5 (d, POC^BH_2, $^2J_{POC}$ 6.1 Hz), 94.9 (d, CCl_3, $^3J_{POCC}$ 6.5 Hz), 185.3 (t, C=S,

$^3J_{PCNC}$ 8.9 Hz); δ_P ($CDCl_3$) 24.6 Hz; EI MS: m/z (%) 839.6922 ($M^{+\cdot}$, 2). Calc. for $C_{15}H_{22}{}^{35}Cl_{12}N_2O_6P_2S$: 839.6937. (See also Table V).

Tetrakis(2,2,2-trifluoroethyl) ureylenebis(3-methylsulfenyl-1-propylphosphonate) (7e)

Urea (1.14 g, 0.019 mol), tris(2,2,2-trifluoroethyl) phosphite (12.5 g, 0.038 mol), and 3-(methylthio)propanal (3.9 g, 0.038 mol) were stirred in toluene (10 ml) at room temperature whilst boron trifluoride-etherate (1.5 ml) in toluene (10 ml) was added dropwise (15 min). The mixture was then heated under reflux at 95–105 °C (1.5 h), after which volatile materials were romoved under reduced pressure (13 mmHg at 70 °C). Ethanol (15 ml) was added to the residual brown oil (12.6 g) and the solution was stored at 4 °C for several months. White needles which separated were filtered off, washed with ether, and dried *in vacuo* at 50 °C to give a first crop of product (0.3 g), m.p. 119–120 °C. The mother liquor was concentrated and treated again with ethanol to give further crystals; and this procedure was repeated six times to give further crops of crystals which were combined and recrystallized from ethanol and water to give *tetrakis(2,2,2-trifluoroethyl) ureylenebis(3-methylsulfenyl-1-propylphosphonate)* (**7e**) as white needles (1.75 g, 12.7%), m.p. 122–123 °C (Found: C, 28.1; H, 3.4; N, 4.1. $C_{17}H_{26}F_{12}N_2O_7P_2S_2$ requires: C, 28.2; H, 3.5; N, 4.0%); δ_H (MeOD) 1.50–2.30 (m, 2H, $C\underline{H}_2CH$), 2.08 (s, 3H, CH_3S), 2.65 (t, 2H, CH_2S, $^3J_{HCCH}$ 7.1 Hz), 4.31–4.80 (m, $POCH_2$), 5.0–5.55 (m, 1H, CH), 6.49 (br d, NH, $^3J_{PCNH}$ 9.5 Hz, exchanged with D_2O); δ_C(MeOD) 15.0 (s, CH_3S), 29.9 (d, $\underline{C}H_2CH$, $^2J_{PC}$ 3.1 Hz), 30.9 (d, CH_2S, $^3J_{PC}$ 16.3 Hz), 46.8 (d, CH, $^1J_{PC}$ 160.8 Hz), 63.3 (dq, $PO\underline{C}^AH_2CF_3$, $^2J_{FCC}$ 41.0 Hz, $^2J_{POC}$ 7.0 Hz), 63.8 (dq, $PO\underline{C}^BH_2CF_3$, $^2J_{FCC}$ 41.0 Hz, $^2J_{POC}$ 7.2 Hz), 122.5 (q, CF_3, $^1J_{FC}$ 298 Hz), 158.6 (s, C=O); δ_P (MeOD) 27.1; EI MS: m/z (%) 724 (M^+, 10), 663 (8.8), 624 (M^+ – CF_3CH_2OH, 12), 479 [M^+ – $(CF_3CH_2O)_2P(O)CH(CH_2)_2SCH_3$, 4], 288 (10), 246 (12), 70 (100).

Tetrakis(2,2,2-trifluoroethyl) ureylenebis(3-methylsulfinyl-1-propylphosphonate) (7f)

Hydrogen peroxide (30%, 0.7 ml) was added to a stirred suspension of the sulfenyl derivative (7e) (0.9 g, 0.012 mol) in glacial acetic acid (9.1 ml) at 0 °C. After stirring (2 h) the solution was concentrated under reduced pressure. Water (5 ml) and methanol (4.5 ml) were then added to give a clear solution. Treatment with acetone (7.2 ml) generated cloudiness but no pre-

cipitate and the solution was therefore concentrated and treated again with water and methanol. Storage at 4 °C for several days gave a white precipitate which was dried *in vacuo* at 50 °C to give *tetrakis(2,2,2-trifluoroethyl) ureylenebis(3-methylsulfinyl-1-propylphosphonate)* (**7f**) as white needles (0.6 g, 63.0%), m.p. 150–151 °C (Found: C, 26.1; H, 3.3; N, 3.7. $C_{17}H_{26}F_{12}N_2O_9P_2S_2$ requires: C, 26.9; H, 3.4; N, 3.7%); δ_H(MeOD) 1.35–2.35 (m, 2H, $C\underline{H}_2CH$), 2.15 (s, 3H, CH_3), 2.85 (t, 2H, SCH_2, $^3J_{HCCH}$ 7.1 Hz), 4.31–4.80 (m, $POCH_2$), 5.0–5.55 (m, 1H, CH), 6.49 (br d, NH, $^3J_{PCNH}$ 9.5 Hz, exchanged with D_2O); δ_C (MeOD) 16.5 (s, CH_3S), 29.8 (d, $\underline{C}H_2CH$, $^2J_{PC}$ 3.1 Hz), 35.7 (d, CH_2S, $^3J_{PC}$ 16.1 Hz), 46.6 (d, CH, $^1J_{PC}$ 160.2 Hz), 63.4 (dq, $PO\underline{C}^AH_2CF_3$, $^2J_{FCC}$ 40.7 Hz, $^2J_{POC}$ 7.0 Hz), 63.9 (dq, $PO\underline{C}^BH_2CF_3$, $^2J_{FCC}$ 40.7 Hz, $^2J_{POC}$ 7.1 Hz), 122.7 (q, CF_3, $^1J_{FC}$ 296 Hz), 158.6 (s, C=O); δ_P (MeOD) 27.8; EI MS: m/z (%) 756 (M^+, 2), 548 (4), 392 (12), 360 (12), 328 (21), 292 (22), 278 (13), 247 (15), 246 (75), 229 (16), 82 (100).

Tetraphenyl thioureylenebis(1-propylphosphonate) (7g)

Thiourea (5.7 g, 0.075 mol), triphenyl phosphite (46.5 g, 0.15 mol) and propanal (8.7 g, 0.15 mol) were stirred in toluene (50 ml), when an exothermic reaction ensued. The mixture was then heated under reflux at 105–110 °C (1 h). Concentration under reduced pressure (13 mmHg at 90 °C) gave a viscous oil (44.3 g) which solidified during several weeks at room temperature. The product was recrystallized twice from acetone and once from dichloromethane to give *tetraphenyl thioureylenebis(1-propylphosphonate)* (**7g**) as a shiny white solid (24.7, 52.8%), m.p. 199–201 °C (Found: C, 58.3; H, 5.3; N, 4.3. $C_{31}H_{34}N_2O_6P_2S$ requires: C, 59.6; H, 5.4; N, 4.5%); $\delta_H(CDCl_3)$ 0.88 (t, 3H, CH_3, $^3J_{HCCH}$ 8.1 Hz), 1.31–1.50 (m, 1H, CH_2^A), 1.90–2.10 (m, 1H, CH_2^B), 5.62–5.80 (m, 1H, CH), 7.10–7.32 (m, 20H, Ar), 7.66–7.68 (d, NH, $^3J_{PCNH}$ 10.1 Hz); δ_C ($CDCl_3$) 10.9 (d, CH_3, $^3J_{PC}$ 12.8 Hz), 24.7 (s, CH_2), 50.0 (d, CH, $^1J_{PC}$ 152.6 Hz), 145.6 (m, Ar), 184.3 (t, C=S, $^3J_{PCNC}$ 8.6 Hz); δ_P ($CDCl_3$) 17.8; EI MS: m/z (%) 624 (M^+, 4), 531 (M^+ – PhO, 10), 437 (531 – PhOH, 14), 391 (14), 357 (19), 333 (23), 297 (10), 217 (18), 156 (24), 141 (15), 100 (66), 94 (100).

Tetraphenyl thioureylenebis(3-methylsulfenyl-1-propylphosphonate) (7h)

A similar procedure to the above, using thiourea (2.8 g, 0.038 mol), triphenyl phosphite (23.6 g, 0.076 mol) and 3-(methylthio)propanal (7.9 g,

0.076 mol) in toluene (25 ml) gave a viscous oily product (26.9 g). A solid mass which separated slowly (several months) at room temperature was filtered off and recrystallized twice from ethanol and water to give *tetraphenyl thioureylenebis(3-methylsulfenyl-1-propylphosphonate)* (**7h**) as a white solid (12.8 g 48.7%), m.p. 118–120 °C (Found: C, 53.9; H, 5.3; N, 3.9. $C_{33}H_{37}N_2O_6P_2S_3$ requires: C, 55.3; H, 5.3; N, 3.9%); $\delta_H(CDCl_3)$ 1.5–2.2 (m, 2H, $C\underline{H}_2CH$), 2.0 (s, 3H, CH_3S), 2.6 (t, 2H, CH_2S, $^3J_{HCCH}$ 7.0 Hz), 5.0–5.5 (m, 1H, CH), 7.1–7.3 (m, 20H, Ar), 7.6 (d, NH, $^3J_{PCNH}$ 10.1 Hz); δ_C ($CDCl_3$) 15.0 (s, CH_3), 27.9 (d, $\underline{C}H_2CH$, $^2J_{PC}$ 3.1 Hz), 28.9 (d, CH_2S, $^3J_{PC}$, 16.8 Hz), 51.1 (d, CH, $^1J_{PC}$ 151.5 Hz), 145.6 (m, Ar), 182.7 (t, C=S, $^3J_{PCNC}$ 7.9 Hz); δ_P ($CDCl_3$) 18.9; EI MS: m/z (%) 716 (M^+, 1), 622 (M^+ – PhOH, 0.6), 529 (6), 380 (11), 379 (4), 332 (11), 318 (17), 148 (37), 94 (100).

Biological screening

Activity against *Drechslera teres* in infected barley seeds (variety *Tellus*) was assessed at 400 ppm by the so-called "osmos' test as previously described.[2] Foliar sprays were applied as aqueous formulations containing test compounds at concentrations of 1000, 300, and 100 ppm, together with a similar quantity of wetting agent (ethoxylated fatty alcohol).

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