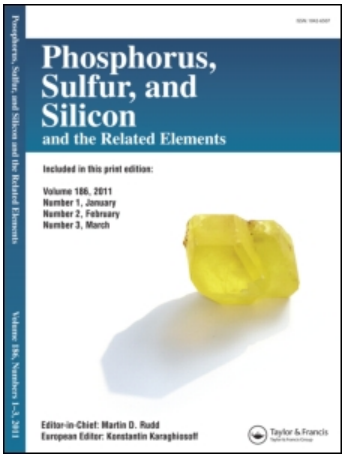


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

ORGANIC PHOSPHORUS COMPOUNDS 82. PREPARATION, PROPERTIES AND HERBICIDAL ACTIVITY OF 2-SUBSTITUTED 5-PHENOXY- AND 5-PYRIDYLOXY PHENYL PHOSPHONIC AND PHOSPHINIC ACID DERIVATIVES

L. Maier[a]; D. Duerr[a]; H. Rempfler[a]
[a] Agricultural Division, Ciba-Geigy Ltd., Basel

To cite this Article Maier, L. , Duerr, D. and Rempfler, H.(1987) 'ORGANIC PHOSPHORUS COMPOUNDS 82. PREPARATION, PROPERTIES AND HERBICIDAL ACTIVITY OF 2-SUBSTITUTED 5-PHENOXY- AND 5-PYRIDYLOXY PHENYL PHOSPHONIC AND PHOSPHINIC ACID DERIVATIVES', Phosphorus, Sulfur, and Silicon and the Related Elements, 32: 1, 19 — 36
To link to this Article: DOI: 10.1080/03086648708080649
URL: http://dx.doi.org/10.1080/03086648708080649

Phosphorus and Sulfur, 1987, Vol. 32, pp. 19–36
Photocopying permitted by license only

ORGANIC PHOSPHORUS COMPOUNDS 82. PREPARATION, PROPERTIES AND HERBICIDAL ACTIVITY OF 2-SUBSTITUTED 5-PHENOXY- AND 5-PYRIDYLOXY PHENYL PHOSPHONIC AND PHOSPHINIC ACID DERIVATIVES[1]

L. MAIER,† D. DUERR and H. REMPFLER
Ciba-Geigy Ltd., Agricultural Division, 4002 Basel

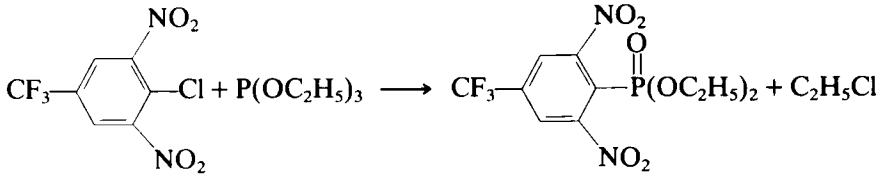
(Received September 19, 1986)

In the Cadogan reaction of 1,2-dinitro-4-chlorobenzene with phosphites and phosphonites the 2-nitro group is substituted but in 1,2-dinitro-4-alkoxycarbonylbenzenes the 1-nitro group is replaced exclusively (Table I and II).

Extension of the Cadogan reaction to 4-phenoxy and 4-pyridyloxy substituted 1,2-dinitrobenzenes produced mainly 5-phenoxy and 5-pyridyloxy substituted 2-nitrophenylphosphonates and -phosphinates some of which show high herbicidal and plant growth regulating activity (Table III to V and Figure 1 to 4). 4- and 6-phenoxy or pyridyloxy substituted 2-nitrophenylphosphonates are herbicidally inactive. The herbicidal activity decreases from the phenoxy-phenylphosphonates to -phosphinates to pyridyloxy-phenylphosphonates when the same substitution pattern is present. The methyl esters **3a**, **4a** and **5a** are the most active compounds in all three series.

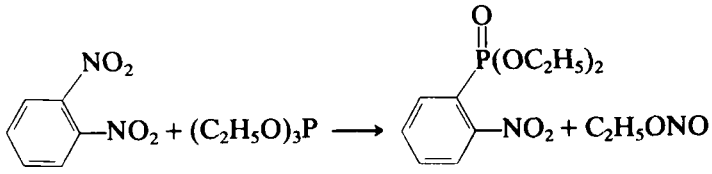
INTRODUCTION

Normally arylhalides do not give an uncatalyzed Michaelis Arbuzov reaction with trialkylphosphites. However, when the halogen atom is activated by electronegative substituents, Arbuzov products can be isolated in excellent yields,[2,3] e.g.



In general aromatic mononitro-compounds are deoxygenated by tervalent phosphorus compounds to give nitrene or nitrene-like intermediates[3] which can then react in a variety of ways. However, in the cases of *o*-dinitro- and 1,2,4-trinitro-benzene that reaction with certain tervalent organophosphorus reagents leads to displacement of an *o*-nitrogroup by tervalent phosphorus.[4] Thus, triethyl phosphite and *o*-dinitrobenzene react smoothly in boiling acetonitrile to give diethyl *o*-nitrophenylphosphonate and ethyl nitrite.[4]

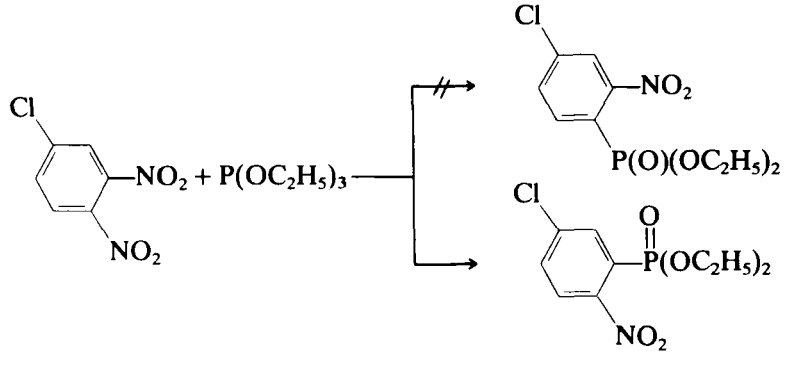
† Presented in part at the "Sixth International Congress of Pesticide Chemistry", August 10–15, 1986, Ottawa, Canada.



Only a trace of deoxygenation, as indicated by the formation of triethyl phosphate, occurs. Recently Cadogan's reaction[4] was used to prepare chlorocontaining 2-nitrophenylphosphonates and by hydrolysis the corresponding acid. These compounds were said to be plant growth regulators.[5]

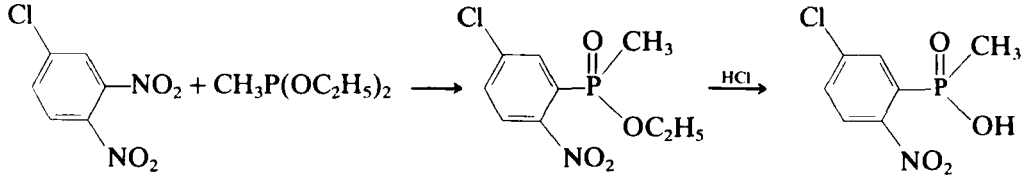
RESULTS AND DISCUSSION

By repeating this work[5] we observed that in the reaction of 1,2-dinitro-4-chlorobenzene with triethylphosphite only one isomer, e.i., 5-chloro-2-nitrophenylphosphonate is formed and not a mixture of 4-chloro- and 5-chloro-2-nitrophenylphosphonate as stated in the literature.[5] 0,0-Diethylmethyl-

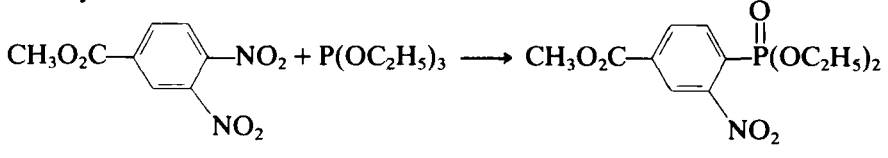


1k

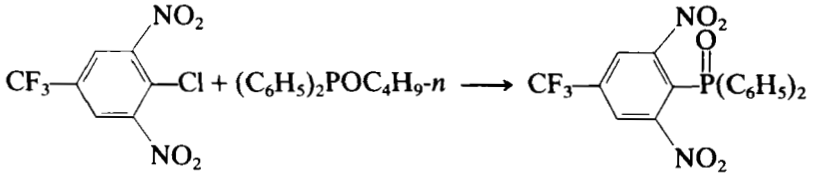
phosphonite reacted similarly and produced only one isomer e.i. 0-ethyl-5-chloro-2-nitrophenyl methylphosphinate.



However, 1,2-dinitro-4-methoxycarbonylbenzene interacted with triethylphosphite and gave diethyl 2-nitro-4-methoxycarbonyl benzene phosphonate exclusively:

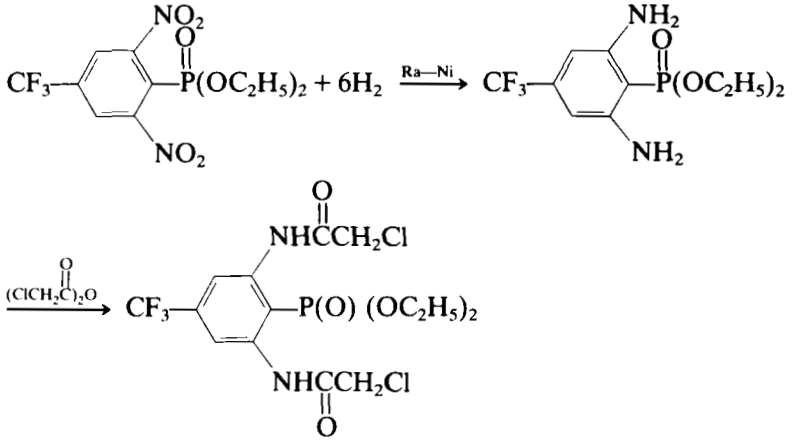


Phosphinites also give this reaction and produce substituted phosphine oxides:



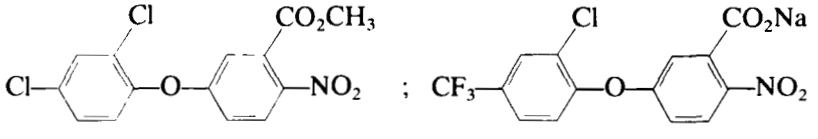
6

The nitro groups can be reduced readily with hydrogen in the presence of Raney-nickel as a catalyst.[6] The substituted aniline produced may be acylated by conventional procedure, e.g.



The physical and spectroscopical properties of the arylphosphonates prepared are summarized in Table I, and those of arylphosphinates in Table II. All of these compounds show only weak herbicidal and plant growth regulating properties.

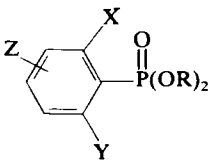
During the past ten years several herbicides of the diphenylether type appeared on the market which contain a nitro-group in the 2-position to a carboxygroup such as e.g. Bifenox[7] and Acifluorfen.[8]



Bifenox ; Acifluorfen

These compounds are selective post emergent herbicides against broad-leaved weeds in groundnuts, rice, soyabeans and wheat. It seemed of interest to us to prepare compounds in which phosphonic- and phosphinic acid groups have replaced the carboxylic acid part and to compare their herbicidal activity with that of the carboxylic acid analogs. A simple way leading to these compounds would be the reaction of phosphites and phosphonites with properly substituted 1,2-dinitrodiphenylethers.

TABLE I

Physical and spectroscopic properties of arylphosphonates  **1**

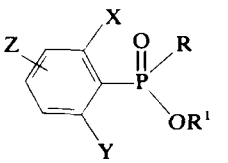
No.	R	X	Y	Z	Yield in %	m.p. (b.p. °C/Torr)	CH_3	^{1}H-NMR in $CDCl_3$ OCH_2, OCH_3, OCH, OH		Aromat. H	^{31}P-chem. shift 85%-H_3PO_4 ref.
a	CH_3	NO_2	NO_2	4-CF_3	65.1	57–62		3.63 (d, J12)		7.85 (d, J3)	
b	H	NO_2	NO_2	4-CF_3	51.4	220–1		4.9 (s)		8.53 (d, J3)	−2.6
c	C_2H_5	NO_2	NO_2	4-CF_3	82.4	55.5–6	1.4 (t)	4.37 (qui)		8.2 (d, J3.5)	2.79
d	i-C_3H_7	NO_2	NO_2	4-CF_3	67.2	76	1.4 (2d)	4.9 (m)		8.1 (d, J3.5)	0.0
e	C_2H_5	NO_2	NO_2	4-H_2NC(=O)	60.5	94–6	1.33 (t)	4.23 (qui)	2.2 (NH_2)	8.5 (d, J3.5)	
f	C_2H_5	H	NO_2	H	60.5	56.5–7.5[a]	1.33 (t)	4.23 (qui)		7.6–8.3 (m)	
g	H	H	NO_2	H	86.2	197–9		4.9 (s)		7.4 (m)	
h	C_2H_5	H	NO_2	5-Cl	60.3	61–2	1.4 (t)	4.2 (qui)		7.6–8.1 (s. exp.)	
i	H	H	NO_2	5-Cl	53.6	208–10		4.7 (s)		7.1–7.8 (m)	
k	C_2H_5	H	NH_2	5-Cl	52.6	72–5	1.4 (t)	4.2 (qui)	5.0 (NH_2)	6.7–7.5[b]	
l	C_2H_5	NO_2	NO_2	4-C≡N	84	109–112	1.33 (t)	4.27 (qui)		8.17 (d, J3.7)	
m	C_2H_5	H	NO_2	4-CO_2CH_3	70	(135/0.08)	1.4 (t)	4.03 (s), 4.3 (qui)		8–8.5 (m)	
n	C_2H_5	H	NO_2	4-$CO_2C_2H_5$	63	oil	1.35 (t)	4.2 (qui)		8.2–8.5 (s. exp.)	
							1.42 (t)	4.4 (qui)			

[a] Lit.[5] m.p. 49°C.

[b] ^{1}H-NMR of aromat. H at 250 MHz: 3-H 6.7 (2d, J_{PH} 7.5); 4-H 7.3 (2d); 6-H 7.5 (2d, J_{PH} 14.5) ^{13}C-NMR in $CDCl_3$ of aromat. C: 1-C 109.9 (J_{PC} 185); 2-C 149.8 (J_{PC} 7.5); 3-C 117.8 (J_{PC} 13.9) 4-C 133.8 (J_{PC} 2.4); 5-C 121.6 (J_{PC} 18.7); 6-C 132.3 (J_{PC} 8.1).

TABLE II

Physical and spectroscopic properties of arylphosphinates

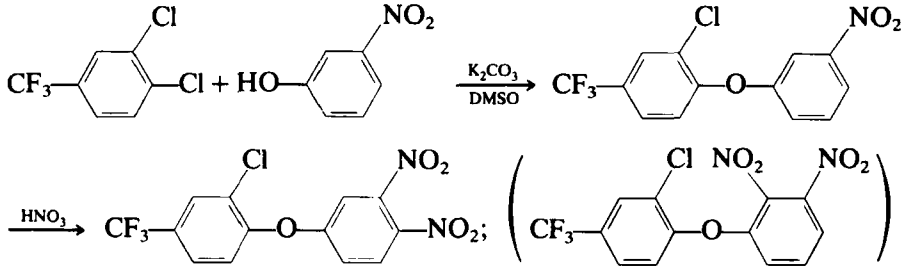


2

No.	R	R¹	X	Y	Z	Yield in %	m.p. (b.p. °C/Torr)	C_3H_7, CH_3	P-CH_3	^{1}H-NMR in $CDCl_3$ OCH_2, OH	Aromat. H	^{31}P-chem. shift 85% H_3PO_4 ref.
a	C_6H_5	C_4H_9	NO_2	NO_2	4-CF_3	77.5	89–90	0.7–1.9		4.07 (qui)	7.6 (Ph), 8.1 (d)	23.8
b	C_6H_5	H	NO_2	NO_2	4-CF_3	90	133–138				7.3–8.1 (br.)	
c	CH_3	C_2H_5	NO_2	NO_2	4-CF_3	47.7	130–2	1.3 (t)	2.17 (d, J16)	4.0 (qui)	8.2 (d)	36.4
d	CH_3	H	NO_2	NO_2	4-CF_3	25	223–5[a]	(in DMSO)	1.77 (d, J16)	4.73 (s)	8.63 (d)	
e	CH_3	C_2H_5	NO_2	H	H	63.8	(129/0.06)	1.23 (t)	1.83 (d, J16)		7.6–8.3 (m)	
f	CH_3	H	NO_2	H	H	75	152–3[b]		1.43 (d, J15)	4.63 (s)	7.4 (m)	
g	CH_3	C_2H_5	H	NO_2	5-Cl	56.5	(151–3/0.2)	1.3 (t)	1.9 (d, J15.5)	4.0 (qui)	7.7–8.15[c]	
h	CH_3	H	H	NO_2	5-Cl	57.2	132–3		1.2 (d, J14)	4.6 (s)	7.3 (br)	
i	CH_3	C_2H_5	NH_2	NH_2	4-CF_3	80	117–9	1.3 (t)	1.7 (d, J15)	4.1 (qui)	6.15 (d)	
k	CH_3	C_2H_5	$NHCCH_2Cl$ ‖ O	$NHCCH_2Cl$ ‖ O	4-CF_3	63	119–20	1.3 (t)	1.7 (d, J15)	4.1 (m, +CH_2Cl)	8.4 (d) 10.8 (s, NH)	

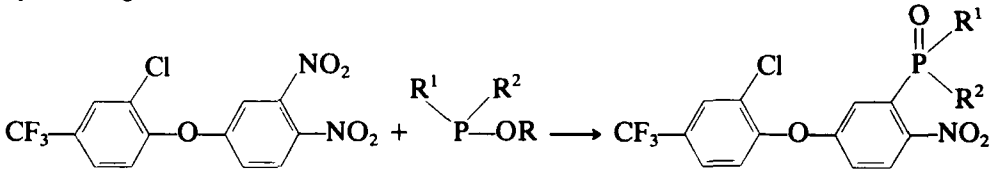
[a] Hydrolysis with 20% HCl effects partial cleavage of the P-aryl bond.
[b] Lit.[5] m.p. 154°C.
[c] 4-C 7.7 (2qu); 3-C 7.9 (2d, J_{PH} 4.5 Hz); 6-C 8.15 (2d, J_{PH} 13 Hz).

The 1,2-dinitrodiphenylethers were prepared according to a literature procedure,[9] e.g.



(A) (B)

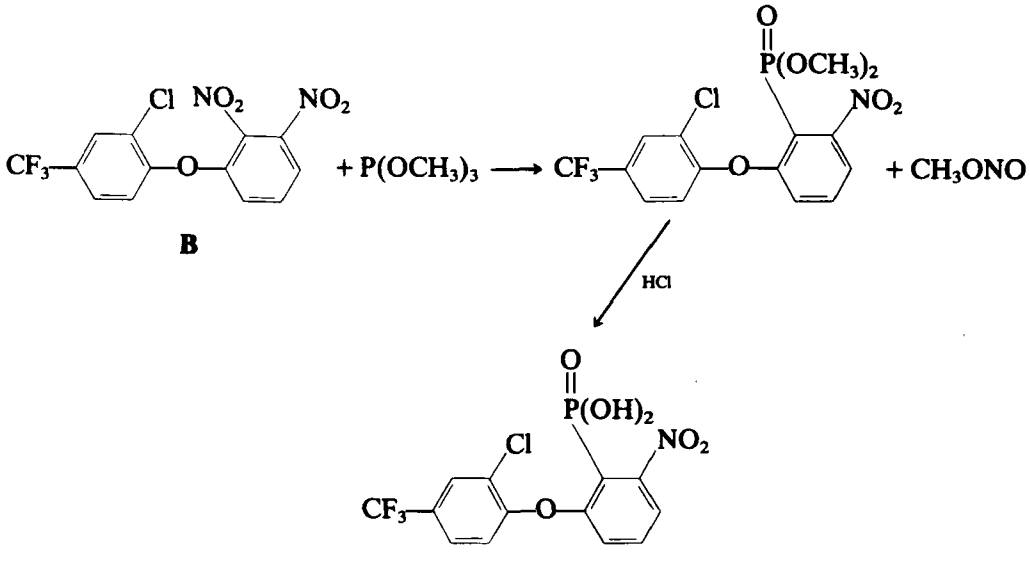
In addition to the 1,2-dinitro-4-(2'-chloro-4'-trifluoromethyl phenoxy)-benzene, **A**, we also isolated, by fractional crystallization, small amounts of 1,2-dinitro-3-(2'-chloro-4'-trifluoromethylphenoxy)-benzene, **B**. Both compounds undergo an Arbuzov reaction with phosphites,[10] phosphonites,[11] and phosphinites and yield the corresponding phosphonates, phosphinates and phosphine oxides in good yields, e.g.



A

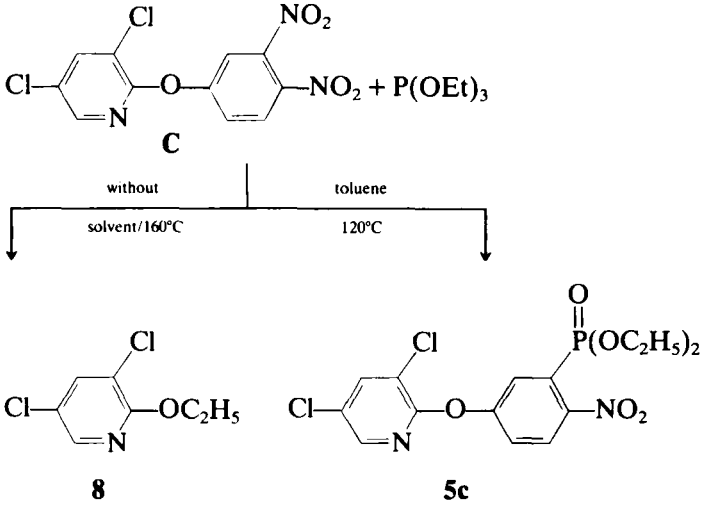
3, R^1, R^2 = OR
4, R^1 = Alkyl, R^2 = OR
7, R^1, R^2 = phenyl

and:



B

While with **A** a 5-phenoxysubstituted phenylphosphonate is produced, **B** gives a 6-phenoxysubstituted phenylphosphonate exclusively. The yield depends greatly on the conditions used. Thus interaction of **A** with $(CH_3O)_3P$ produced in refluxing acetonitrile 36.6% **3a** (R^1, $R^2 = OCH_3$); in refluxing toluene 64% **3a**, and in toluene at 80°C ~ 80% **3a**. And when the 3,5-dichloro-2-pyridyloxy-3,4-dinitrobenzene **C** was treated with excess triethylphosphite at reflux without a solvent, ether cleavage took place and 2-ethoxy-3,5-dichloropyridine was the only product isolated.



On the other hand, when the reaction was run in toluene at 120°C, the pyridyloxyphenylphosphonate, **5c**, was isolated in 82% yield.

The reaction is not completely regioselective. In addition to the 5-phenoxy-substituted phosphonates, small amounts of the 4-phenoxy-substituted phosphonates are also formed. Thus in the interaction of 1,2-dinitro-5-(5′-trifluoromethyl-pyridyl-2-oxy) benzene with trimethylphosphite the 5- and 4-pyridyloxy substituted phosphonates were obtained in a ratio of 5.4:1.

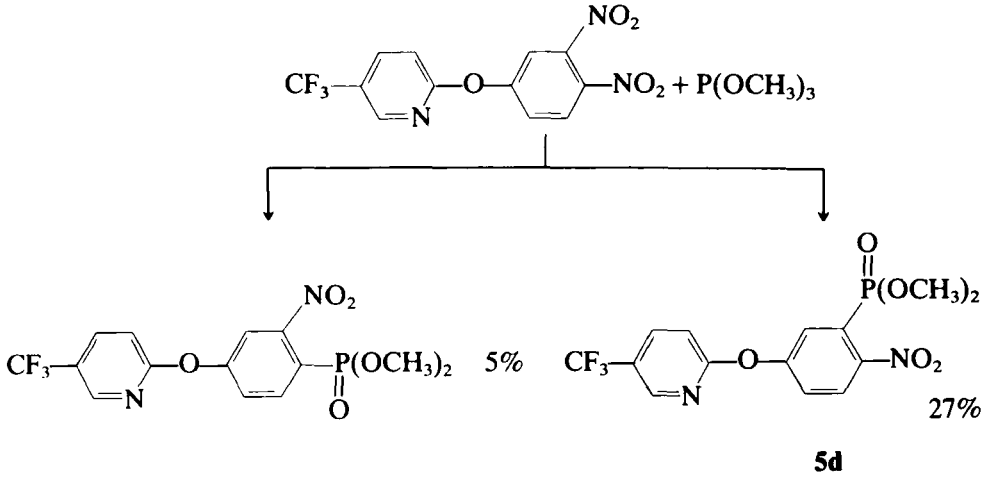
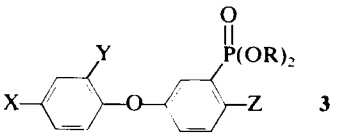
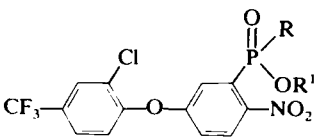


TABLE III

Physical and spectroscopic properties of phenoxy-phenylphosphonates  3

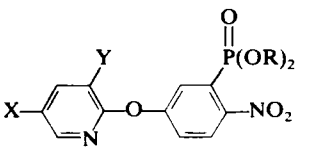
No.	R	X	Y	Z	Yield in %	m.p. (b.p. °C/Torr)	CH_3	^{1}H-NMR in $CDCl_3$ OCH_2, OCH, OH	Aromat. H	^{31}P-chem. shift 85% H_3PO_4 ref.
a	CH_3	CF_3	Cl	NO_2	80	83		3.9 (d, J12)	7.1–8.3 (m)	13.2
b	i-C_3H_7	CF_3	Cl	NO_2	63.7	53–6	1.2 (2d)	4.7 (sept.)	6.8–7.9 (m)	
c	C_2H_5	CF_3	Cl	NO_2	77	61–3	1.3 (t)	4.17 (qui)	7–8.3 (m)	10.23
d	CH_3	CF_3	Cl	Cl	32	(130/0.2)		3.77 (d, J11)	6.8–7.8 (m)	
e	$O{=}P(C_2H_5)(NEt_2)(OCH_3)$	CF_3	NO_2	NO_2	51.3	72–4	1.2 (t)	4.1 (qui)	7–8.3 (m)	9.76
f		CF_3	Cl	NO_2	85.8	oil	1.2 (t)	3.3 (NCH_2) 3.85 (d, J12)	7.1–8.2 (m)	
g	C_2H_5	CF_3	CN	NO_2	72.6	oil	1.33 (t)	4.2 (qui)	7.2–8.2 (m)	
h	i-C_3H_7	CF_3	NO_2	NO_2	62.1	93–102	1.23 (d)	4.67 (sept)	7–8.4 (m)	
i	H	CF_3	NO_2	NO_2	65	175–180	(in DMSO)	7.0 (OH)	7.3–8.6 (m)	
k	H	CF_3	Cl	NO_2	100	177–8		5.2	7–8.3 (m)	
l	C_2H_5	Cl	NO_2	NO_2	61	76–8	1.35 (t)	4.23 (qui)	7.1–8.3 (m)	10.04
m	CH_3	CF_3	Cl	NH_2	79.3	oil		3.77 (d, J11) 5.13 (s, NH_2)	6.6–7.8 (m)	
n	C_2H_5	NO_2	CF_3	NO_2	72.6	84–8	1.2 (t)	4.1	7–8.5 (m)	9.49
o	H	CF_3	CN	NO_2	82.1	227	(CD_3OD)	4.5 (OH)	6.6–7.7 (m)	
p	H	Cl	NO_2	NO_2	96	170–4	(in NaOD/D_2O)	4.9	6.3–7.6 (m)	
qu	C_2H_5	NO_2	$C(=O)NH_2$	NO_2	48.2	137–40	(DMSO) 1.07 (t)	3.9 3.1 (s, NH_2)	7–8.5 (m)	
r	H	NO_2	CF_3	NO_2	91	80	(CD_3OD)	4.45 (OH)	6.8–8.2 (m)	
s	CH_3	CF_3	Cl	$NHC(=O)CH_2Cl$	84.6	oil		4.03 ($ClCH_2$) 3.63 (d, J12)	6.8–8.4 (m) 10.6 (s, NH)	

TABLE IV

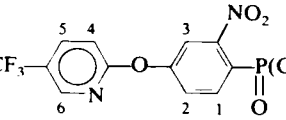
Physical and spectroscopic properties of phenoxy-phenylphosphinates  **4**

No.	R	R^1	Yield in %	m.p. (b.p. °C/Torr)	^{1}H-NMR in $CDCl_3$ CH_3, C_3H_7	P-CH_3, PC_2H_5	OCH_2, OCH_3, OH	Aromat. H	^{31}P-chem. shift 85% H_3PO_4 ref.
a	C_2H_5	CH_3	30.9	61–3		1.03 (2t, J21) 2.2 (2qu, J15)	3.55 (d, J11)	7.1–8.0 (m)	
b	CH_3	CH_3	50.1	123–4		2.03 (d, J16)	3.8 (d, J11.6)	7.1–8.3 (m)	40
c	CH_3	H	94.4	125–30	(CD_3OD)	1.53 (d, J15.5)	4.6 (s)	6.7–8.0 (m)	
d	CH_3	C_2H_5	51.6	106–70	1.2 (t)	1.93 (d, J16)	4.0 (qui)	7–8.2 (m)	37.86
e	CH_3	C_4H_9-*n*	23.9	45–6	0.8–1.8 (m)	2.0 (d, J15)	3.9 (2t)	6.9–8.2 (m)	
f	C_6H_5	CH_3	53.6	111–2			3.65 (d, J11)	7–8.2 (m)	

TABLE V

Physical and spectroscopic properties of pyridyloxy-phenylphosphonates  5

No.	R	X	Y	yield in %	m.p. (b.p. °C/Torr)		^{1}H-NMR in $CDCl_3$ CH_3	OCH_2, OCH_3, OH	Aromat. H	^{31}P-chem. shift 85% H_3PO_4 ref.
a	CH_3	CF_3	Cl	38.3	99–100			3.9 (d, J11.5)	7.5–8.4 (m)	
b	C_2H_5	CF_3	Cl	63.5	oil		1.3 (t)	4.2 (qui)	7.3–8.3 (m)	
c	C_2H_5	Cl	Cl	82	oil		1.4 (t)	4.3 (qui)	7.5–8.2 (m)	
d	CH_3	CF_3	H	27.1[a]	oil			3.9 (d, J11)	7.15–8.6 (m)	
e	CH_3	Cl	Cl	32.2	101–3			3.9 (d, J11)	7.3–8.3 (m)	
f	C_2H_5	CF_3	H	60.1	75–6		1.4 (t)	4.3 (qui)	7.1–8.5 (m)	10.5
g	H	CF_3	Cl	45.6	156–9	(D_2O/NaOD)		4.8 (s)	6.2–7.8 (m)	
h	H	CF_3	H	56.8	217–9	(CD_3OD)		5.2 (s)	7.3–8.7 (m)	6.6 (in CD_3OD)
i	H	Cl	Cl	46.8	229–32 (dec.)	(CD_3OD)		4.4 (s)	6.7–7.7 (m)	

[a] In addition 5.1%  was also isolated as an oil; ^{1}H-NMR (in $CDCl_3$) OCH_3 3.9 (d, J11); 1-C 8.1 (2d, J_{PC} 14); 2-C 7.45 (2m); 3-C 7.75 (2d, J_{PCC} 5); 4-C 7.17 (d); 5-C 8.0 (2d, J9 and 3); 6-C 8.5 (m).

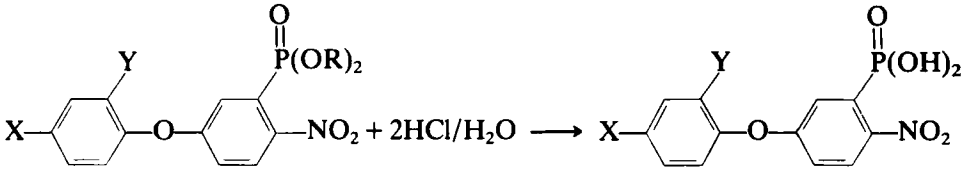
The physical and spectroscopic properties of the phenoxyphenylphosphonates, -phosphinates and pyridyloxy-phenylphosphonates are summarized in Tables III, IV, and V, respectively.

THERMAL STABILITY

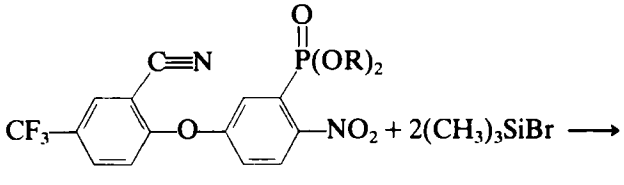
Thermal stability measurements of 2,6-dinitro-4-trifluoromethyl-0,0-diethylphosphonate, **1c**, showed that the compound is stable up to 160°C; at 190°C after 12 hours a rigorous reaction occurred and at 220°C the decomposition reaction started immediately. Therefore all the phenoxyphenylphosphonates were purified by chromatographic or crystallization procedures.

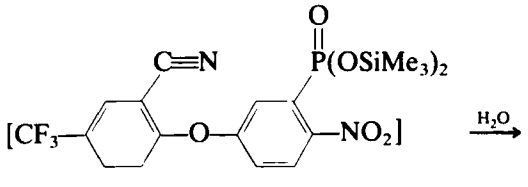
Reactions

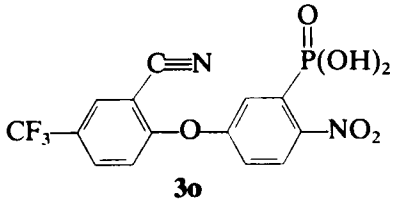
Hydrolysis with 20% HCl under reflux gave the free phosphonic acids. Compounds, which contained acid sensitive groups were dealkylated with trimethylbromosilane as described in the literature.[12]



and:

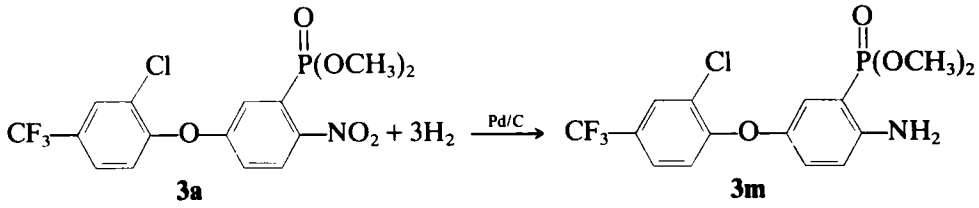


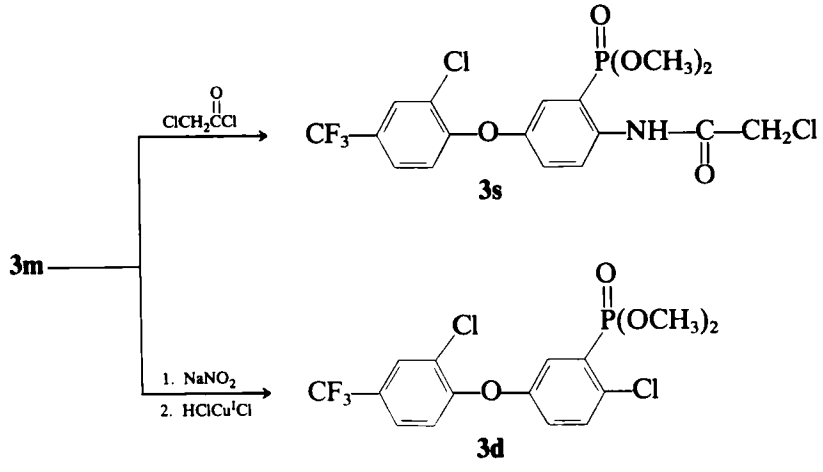




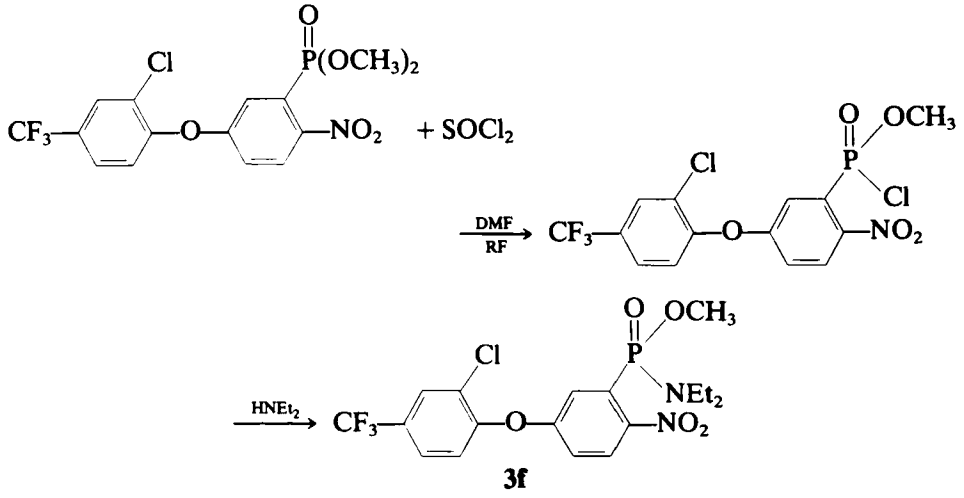
3o

The 2-nitrosubstituted phenoxyphenylphosphonates give the normal reactions of a nitro-group e.g.,





Chlorination with $SOCl_2$ at reflux in the presence of DMF as a catalyst[13] yields the halfester chloride which can be converted to the ester-amide:



Toxicology

The acute LD_{50} of the dimethylphosphonate analog of acifluorfen **3a**, when given orally to rat was approximately 2500 mg/kg.

HERBICIDAL ACTIVITY

In contrast to the substituted 2-nitroarylphosphonates and phosphinates (Table I and II) which show only weak herbicidal and plant growth regulating properties several of the substituted phenoxy- and pyridyloxy-phenylphosphonates and phosphinates (Table III, IV and V) exhibit high herbicidal and plant growth regulating properties (Figure 1 to 4). However only those compounds are

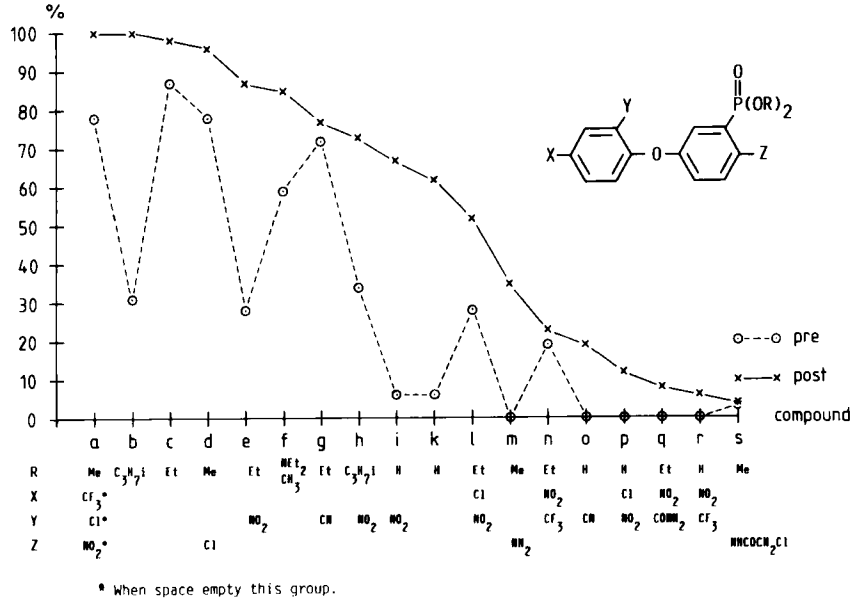


FIGURE 1 Herbicidal activity of phenoxy-phenylphosphonates at 4 kg/ha in the greenhouse.

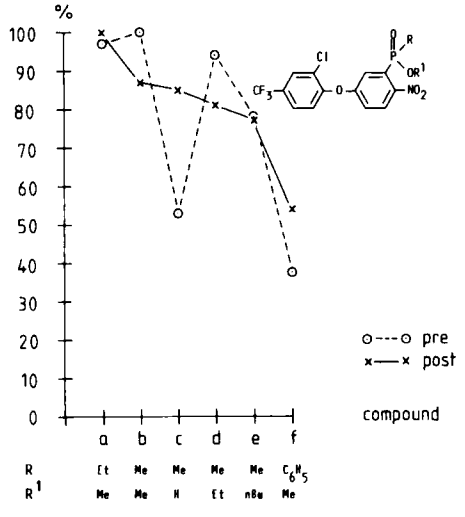


FIGURE 2 Herbicidal activity of phenoxy-phenylphosphinates at 4 kg/ha in the greenhouse.

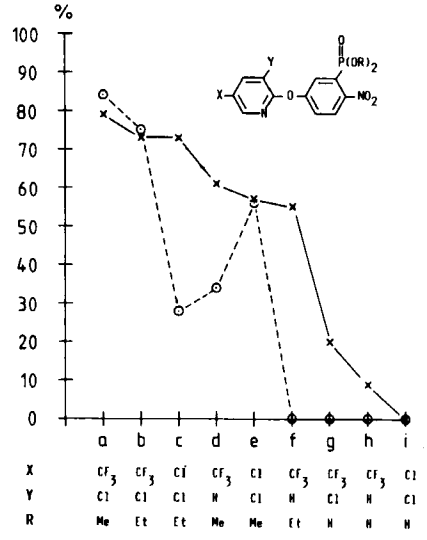


FIGURE 3 Herbicidal activity of pyridyloxy-phenylphosphonates at 4 kg/ha in the greenhouse.

herbicidally active which have a 5-phenoxy- or pyridyloxy substituent, whereas compounds with a 4- or 6-phenoxy- or pyridyloxysubstituent are inactive. In the Figures 1 to 3 are shown the average herbicidal activities of the compounds tested against 4 weeds in the preemergent test and 6 weeds (3 monocotyledonous and 3 dicotyledonous) in the postemergent test at 4 kg/ha. Inspection of the curves shows that the herbicidal activity decreases from the phenoxy-phenylphosphonates to phenoxyphenylphosphinates to pyridyloxy-phenylphosphonates when the same substitution pattern is present. In general the preemergent activity goes parallel with the postemergent activity with the exception of the acids which are preemergent much less active than postemergent. This is probably due to the adsorption of the acids in the soil. The methylesters with the same substitution

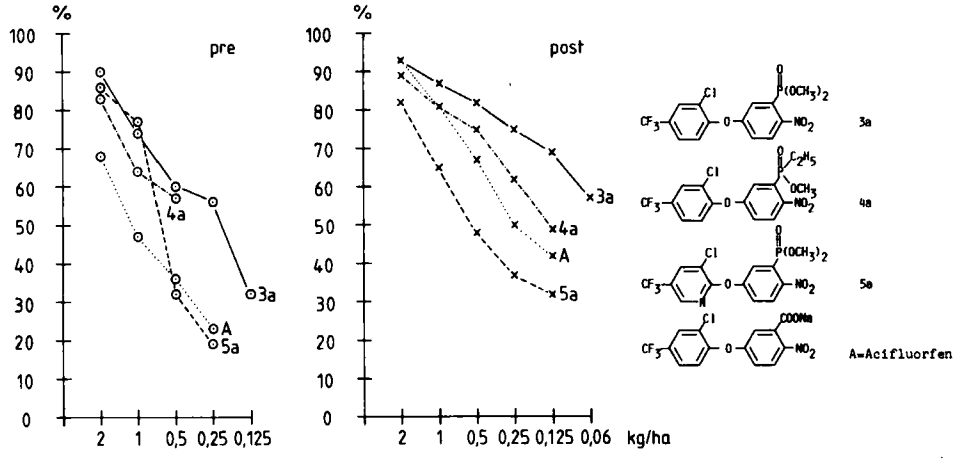


FIGURE 4 Dependence of the pre- and postemergent herbicidal activity of 3a, 4a and 5a from the concentration against four monocotyledonous and seven dicotyledonous weeds.

pattern are the most active compounds in all three series. Among the substituents a 2-chloro-4-trifluoromethyl group in the phenoxy- or a 3-chloro-5-trifluoromethyl group in the pyridyloxy part and a 2-nitro or 2-chloro group in the phenylphosphonate, or -phosphinate part give the highest activity, whereas a 2-amino group or substituted amino group causes a large drop in the activity. The dependence of the pre- and postemergent herbicidal activity of the most active compound in each series (**3a**, **4a**, **5a**) from the concentration against 4 monocotyledonous and 7 dicotyledonous weeds is shown in Fig. 4. At all concentrations post- and preemergent, the phenoxy-phenylphosphonate **3a** is the most active compound followed by **4a** and then **5a**. Also shown in Fig. 4 is a comparison with Acifluorfen. Against the 11 weeds tested, the phenoxyphenylphosphonate **3a** exhibits at all concentrations a higher activity than Acifluorfen, but the selectivity in wheat and soyabeans is not as good as with Acifluorfen.

EXPERIMENTAL

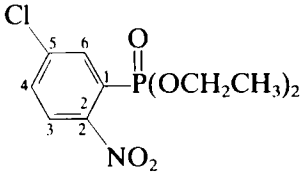
Phosphorus NMR-spectra were recorded using a Bruker WP 80 spectrometer at 32.28 MHz (ref. 85% H_3PO_4), and ^{1}H-NMR-spectra were recorded with a Varian EM 360 spectrometer at 60 MHz or a Bruker WM 250/250 MHz spectrometer (ref. $(CH_3)_4Si$). The chemical shifts are reported in ppm, with negative values being upfield of the standard, and positive downfield. The reactions with trivalent phosphorus compounds were run under argon.

The phosphonates and phosphinates listed in Table I and II were prepared according to the literature.[2,4,5]

1. 0,0-Diethyl-5-chloro-2-nitrophenylphosphonate, **1k**

To a refluxing solution of 202.7 g (1 Mol) of 3,4-dinitrochlorobenzene in 1000 ml of toluene is added with stirring in one hour 344 ml (2 Mol) of triethylphosphite. The mixture is refluxed for 6 h, then the volatile material is removed on a rotavap and the residue chromatographed over silica gel and eluded with ethyl acetate. The eluate is evaporated and the residue recrystallized from di-isopropyl ether. There is obtained 177.1 g (=60.3%) **1k**, beige crystals, m.p. 61–62°C (Lit.[5] m.p. 56°C).

$C_{10}H_{13}ClNO_5P$ (293.6) calc'd: C 40.90 H 4.46 N 4.77% found: C 41.0 H 4.50 N 4.8%



^{1}H-NMR (in $CDCl_3$): δ 1.4 (t, CH_3, 6H); 4.2 (qui, OCH_2, 4H); aromat. H: 4-H 7.6 (m, 1H); 3-H 7.8 (2d, J_{PCCCH} 6 Hz, J_{HH} 9 Hz, 1H); 6-H 8.1 (2d, J_{PCCH} 14.5 Hz, J_{HH} 2 Hz, 1H).

^{13}C-NMR (in $CDCl_3$): 1-C 126.0 (J_{PC} 188.7 Hz); 2-C 150.3; 3-C 125.8 (J_{PCCC} 9 Hz); 4-C 135.3 (J_{PCCCC} 6.4 Hz); 5-C 139.0 (J_{PCCC} 17.5 Hz); 6-C 133.0 (J_{PCC} 2.2 Hz).

2. 0.0-Diethyl-2-nitro-4-methoxycarbonylphenylphosphonate, **1o**

To 22.61 g (0.1 Mol) of 3,4-dinitrobenzoic acid methyl ester in 50 ml toluene is dropwise added under reflux 20.77 g (0.125 Mol) of triethylphosphite. After 4 h reflux the mixture is evaporated on a rotavap and the residue purified by short way distillation. There is obtained 22.2 g (=70%) **1o**, b.p. 135°C/0.08 Torr, a yellow oil.

$C_{12}H_{16}NO_7P$ (317.23) calc'd: C 45.44 H 5.09 N 4.42 P 9.77%
found: C 45.0 H 5.3 N 4.4 P 10.2%

^{1}H-NMR (in $CDCl_3$: δ CH_3 1.4 (t, 6H); OCH_3 4.03 (s, 3H); OCH_2 4.3 (qui, 4H); C_6H_3 8–8.5 (m, 3H).

^{31}P (in $CDCl_3$): 10.14 ppm.

3. 0,0-Diethyl-2-nitro-4-ethoxycarbonylphenylphosphonate, **1p**

Analog to **1o** there was obtained 63% **1p**, purified by flashchromatography.

^{1}H-NMR (in $CDCl_3$ at 250 Mz): δ 1.35 (t, CH_3) and 1.42 (t, CH_3), (9H); 4.2 (qui, $POCH_2$, 4H); 4.4 (qu, $COCH_2$, 2H); aromat. H: 6-H 8.2 (2d, J_{PCCH} 13, J_{HH} 9, 1H) 5-H 8.3 (2m, 1H); 3-H 8.5 (2d, J_{PCCCH} 5Hz, 1H).

$C_{13}H_{18}NO_7P$ (331.26) calc'd: C 47.14 H 5.48 N 4.23 P 9.35%
found: C 47.5 H 5.6 N 4.5 P 9.0%

4. 2,6-Dinitro-4-trifluoromethylphenyl-diphenylphosphine oxide, **6**

A mixture of 27.1 g (0.1 Mol) of 2,6-dinitro-4-trifluoromethylchlorobenzene and 25.8 g (0.1 Mol) of 0-butyl-diphenyl-phosphinite in 100 ml of toluene is refluxed for 7 h, then evaporated on a rotavap and the residue recrystallized from di-isopropyl ether. There is obtained 32.0 g (=73.4%) **6**, m.p. 188–199°C.

$C_{19}H_{12}F_3N_2O_5P$ (436.28) calc'd: C 52.31 H 2.77 N 6.42 F 13.06%
found: C 52.5 H 3.0 N 6.4 F 12.7%

^{1}H-NMR (in $CDCl_3$): δ 7.5 (m, C_6H_5, 10H); 8.2 (d, C_6H_2, 2H)
^{31}P (in $CDCl_3$): 32.2 ppm.

5. 2-Nitro-5-(2'-chloro-4'-trifluoromethylphenoxy)-phenyl-diphenylphosphine oxide, **7**

A mixture of 36.26 g (0.1 Mol) of **A** and 43.2 g (0.2 Mol) of 0-methyl-diphenylphosphinite in 250 ml of toluene is refluxed for 4 h, then evaporated on a rotavap and the residue chromatographed on silica gel with ethyl acetate: hexane = 1:1. The eluate is evaporated and the residue recrystallized from di-isopropyl ether. There is obtained 31.4 g (=60.6%) **7**, m.p. 143°C.

$C_{25}H_{16}ClF_3NO_4P$ (517.83) calc'd: C 57.99 H 3.11 N 2.71 Cl 6.85 F 11.01%
found: C 58.03 H 3.24 N 2.72 Cl 6.89 F 10.91%

^{1}H-NMR in $CDCl_3$: δ 7.2–8.5 (m).

6. 2-Ethoxy-3,5-dichloropyridine, **8**

A mixture of 11 g (0.035 Mol) of 4-(3',5'-dichloropyridyl-2'-oxy)-1,2-dinitrobenzene and 20 ml (0.115 Mol) of triethylphosphite is refluxed for 30 h and then chromatographed on silica gel with ethyl acetate: hexane = 4:1. There is obtained 4 g (=59.5%) **8**, white crystals, m.p. 91–94°C.

$C_7H_7Cl_2NO$ (192.05) calc'd: C 43.78 H 3.67 N 7.29 Cl 36.92%
found: C 43.82 H 3.77 N 7.41 Cl 36.71%

^{1}H-NMR (in $CDCl_3$): δ 1.4 (t, CH_3, 3H); 4.05 (qu, OCH_2, 2H): pyrid. H 7.33 (d) and 7.51 (d) (2H).

7. 0,0-Diethyl-2-nitro-5-(3',5'-dichloro-pyridyl-2'-oxy)-phenylphosphonate, **5c**

A mixture of 27 g (0.082 Mol) of 4-(3',5'-dichloropyridyl-2-oxy)-1,2-dinitrobenzene, 16.2 g (0.098 Mol) of triethyl-phosphite and 100 ml of toluene is refluxed for 30 h, then evaporated on a rotavap and the residue chromatographed on silica gel with ethyl acetate. There is obtained 24.75 g (=81.2%) **5c**, a viscous oil.

$C_{15}H_{15}Cl_2N_2O_6P$ (421.17) calc'd: C 42.78 H 3.59 N 6.65 Cl 16.84%
found: C 42.7 H 3.6 N 7.2 Cl 16.8%

^{1}H-NMR (in $CDCl_3$): δ 1.33 (t, CH_3, 6H); 4.3 (qui, OCH_2, 4H); aromat. H 7.5–8.2 (m, 5H).

8. 2-Nitro-5-(2'-nitro-4'-trifluoromethylphenoxy)-phenylphosphonic acid diethyl ester, **3e**

A mixture of 9 g (24.1 mMol) of 1,2-dinitro-5-(2'-nitro-4'-trifluoromethylphenoxy)-benzene (m.p. 113–114°C), **A**,[9] and 4 g (24.1 mMol) of triethylphosphite, is heated to reflux in 50 ml of toluene under nitrogen for 19 hours, and then the solvent is removed by evaporation under reduced pressure. The residue (10.2 g) is purified by column chromatography on silica gel 60 with ethyl acetate/hexane (4:1). First the non-reacted starting material (3.45 g of dinitro derivative) and then the desired phosphonic acid diethyl ester (5.75 g = 51.3% of theory) is eluted. The final product is initially in the form of a viscous, reddish yellow oil and is obtained pure by evaporating off the solvent. After standing for some length of time, the oil crystallises to form yellow crystals, m.p. 72–74°C. As second fraction, 0.3 g of triethylphosphate is recovered.

$C_{17}H_{16}F_3N_2O_8P$ (464.29): calc'd: C 43.98 H 3.47 N 6.03 F 12.28%
found: C 43.6 H 3.6 N 6.1 F 12.0%

^{1}H-NMR ($CDCl_3$): δ 1.3 (t, 6H, CH_3); 4.1 (qui, 4H, OCH_2) 7.0–8.3 (m, 6H, C_6H_3) [ppm].

9. 2-Nitro-5-(2'-nitro-4'-chlorophenoxy)-phenylphosphonic acid diethyl ester, **3l**

A mixture of 7.5 g (22.08 mMol) of 3,4-dinitro-2'-nitro-4'-chlorodiphenyl ether[9] and 3.67 g (22.08 mMol) of triethylphosphite is refluxed in 50 ml of acetonitrile for 19 hours. After removing the solvent by evaporation, the oily black residue (9 g) is chromatographed on a column of silica gel with ethyl acetate/hexane (4:1), affording, in addition to 1.75 g of non-reacted trinitro derivative, 5.8 g (61.0% of theory) of **3l**, a honey-like reddish oil which crystallises on standing, m.p. 76–78°C.

$C_{16}H_{16}ClN_2O_8P$ (430.74) calc'd: C 44.62 H 3.75 N 6.51 Cl 8.23%
found: C 44.5 H 4.0 N 6.6 Cl 8.1%

^{1}H-NMR ($CDCl_3$): δ 1.35 (t, 6H, CH_3); 4.23 (qui, 4H, OCH_2) 7.1–8.3 (m, C_6H_3, 6H) [ppm].

10. 2-Nitro-5-(2'-nitro-4'-trifluoromethylphenoxy)-phenyl-phosphonic acid, **3i**

A mixture of 1.85 g of the 2-nitro-5-(2'-nitro-4'-trifluoromethylphenoxy)-phenylphosphonic acid diethyl ester, **3e**, obtained in Example 8, in 20 ml of ethanol, and 40 ml of 20% hydrochloric acid, is refluxed for 24 hours and then evaporated to dryness, affording as residue the monohydrate of the corresponding free phosphonic acid **3i** in the form of yellowish brown crystals in quantitative yield, m.p. 175–180°C.

$C_{13}H_8F_3N_2O_8P \cdot H_2O$ (426.18) calc'd: C 36.9 H 2.53 N 6.57 P 7.26%
found: C 37.9 H 2.5 N 6.7 P 7.5%

^{1}H-NMR (in DMSO): δ 7.0 (s, OH); 7.3–8.6 (m, aromat. H) [ppm].

11. 2-Nitro-5-(2'-cyano-4'-trifluoromethylphenoxy)-phenyl-phosphonic acid, **3o**

2-Nitro-5-(2'-cyano-4'-trifluoromethylphenoxy)-phenyl-phosphonic acid diethyl ester (yellowish red oil), **3g**, is prepared in accordance with the particulars of Example 8, starting from 3,4-dinitro-2'-cyano-4'-trifluoromethyldiphenyl ether (m.p. 108–110°C)[9] and triethylphosphite. Yield: 48%.

A mixture of 1.6 g of this ester and 1.5 ml of $(CH_3)_3$ SiBr is stirred overnight at room temperature and then concentrated. The residue is dissolved in acetone and, after the addition of water, the solution is concentrated, affording 1.2 g (82%) of **3o** monohydrate m.p. 227°C.

$C_{14}H_8F_3N_2O_6P \cdot H_2O$ (406.2) calc'd: C 41.4 H 2.48 N 6.9 P 7.62%
found: C 41.4 H 2.4 N 6.9 P 7.6%

^{1}H-NMR (in CD_3OD): δ 4.5 (s, OH); 6.6–7.7 (m, aromat. H) [ppm].

12. 2-Amino-5-(2'-chloro-4'-trifluoromethylphenoxy)-phenylphosphonic acid dimethyl ester, **3m**

2-Nitro-5-(2'-chloro-4'-trifluoromethylphenoxy)-phenyl-phosphonic acid dimethyl ester, **3a**, with a melting point of 83°C is obtained in accordance with the particulars of Example 8, starting from 3,4-di-nitro-2'-chloro-4'-trifluoromethyl diphenyl ether and trimethylphosphite. Yield: 80%.

10 g of this compound are then hydrogenated at room temperature in methanol in the presence of Pd on carbon as catalyst. After uptake of 109% of theory of hydrogen, the catalyst is removed by filtration and the filtrate is concentrated, affording 9.2 g (100% of theory) of **3m** in the form of a brown oil which, after chromatography on silica gel, becomes a slightly yellow oil.

^{1}H-NMR in $CDCl_3$: δ 3.77 (d, J_{POCH} 11.5; 6H; OCH_3); 5.13 (s, 2H, NH_2); 6.6–7.8 (m, 6H, C_6H_3) ppm.

The compounds listed in Tables III to V were prepared in a similar way.

ACKNOWLEDGEMENTS

We wish to thank Ciba-Geigy's Physical Science Center for the hydrogenation experiments, the combustion analyses and for the ^{31}P and ^{13}C NMR spectra, and Messieurs H. Spoerri, M. Walti and M. Hartmeyer for experimental help.

REFERENCES

1. Part 81: L. Maier and G. Rist, *Phosphorus and Sulfur*, **31**, 349 (1987).
2. Bayer AG, DOS 2 421 070 (1975); inv. H. Hübner and J. Blahak.
3. J. I. G. Cadogan, *Quart. Rev.*, **22**, 222 (1968).
4. J. I. G. Cadogan, D. J. Sears and D. M. Smith, *J. Chem. Soc*, (*C*) **1969**, 1314.
5. Bayer AG, DOS 2 619 841 (1977); inv. F. Maurer and K. Dörssen.

6. Bayer AG, DOS 2 459 491 (1976); inv. H. Hübner, J. Blahak and H. J. Memers.
7. Mobil Oil, DOS 2 408 432 (1974); "*Chemie der Pflanzenschutz -und Schädlingsbekämpfungsmittel*", ed. R. Wegler, Springer–Verlag Berlin Vol **5,** S. 76 (1977).
8. Mobil Oil, U.S. Pat 3 979 437 (1976); inv. R. J. Theissen; R. Wegler Vol **8,** 53 (1982).
9. Ciba-Geigy AG, E.P. Appl. 2 757 (1979); inv. D. Duerr, O. Rohr, G. Pissiotas and B. Böhner.
10. Ciba-Geigy AG, E.P. Appl. 14 684 (1980); inv. L. Maier and D. Duerr.
11. Ciba-Geigy AG, E.P. Appl. 43 801 (1982); inv. L. Maier.
12. C. E. McKenna, M. T. Higa, N. H. Cheung and M. C. McKenna; *Tetrahedron Letters* 155 (**1977**).
13. Ciba-Geigy AG, U.S. Pat 4 213 922 (1980); inv. L. Maier.