Cyclic Organophosphorus Compounds

XVII†—The Mass Spectra of Some 5,5-Dimethyl-perhydro-1,3,2-oxazaphosph(v)orines

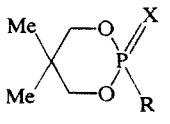
R. S. Edmundson
School of Chemistry, The University of Bradford, Bradford, BD7 1DP, UK

The electron impact mass spectra of six 5,5-dimethyl and eleven 3,5,5-trimethyl-perhydro-1,3,2-oxazaphosphorine 2-oxides and 2-sulphides are reported and compared with those of analogous 5,5-dimethyl-1,3,2-dioxaphosph(v) orinans. Compounds of the 3,5,5-trimethyl series produce an important ion at *m/z* 44 which clearly distinguishes them from the 5,5-dimethyl series. The 2-sulphides are characterized by loss of thiol radical rather than of sulphur; in the case of 2-cyclohexylamino-3,5,5-trimethyl-perhydro-1,3,2-oxazaphosphorine 2-sulphide at least, the thiol hydrogen is derived from the oxazaphosphorine ring NCH_2 group. Fission of the oxazaphosphorine ring occurs largely, but apparently not exclusively, at the P—O—C linkages.

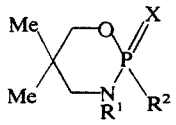
INTRODUCTION

5,5-Dimethyl-1,3,2-dioxaphosph(v)orinans **1** (X = O or S) have proved to be valuable model compounds for the study of reaction mechanisms in organophosphorus chemistry, as well as providing a fruitful area for structural investigations by both ^1H and ^{31}P nuclear magnetic resonance (NMR) spectroscopy, infrared spectroscopy and x-ray analysis. More recently, attention has turned to mass spectroscopic studies on these[1,2] and related[3] compounds.

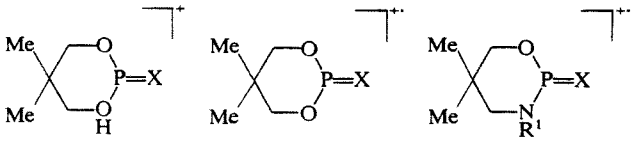
On the other hand, such studies have not been carried out to such an extent on perhydro-1,3,2-oxazaphosphorines,[4] a fact which is surprising in the light of the enormous interest in structural aspects of the chemistry of cyclophosphamide (2-bis-(2-chloroethyl)-amino-perhydro-1,3,2-oxazaphosphorine 2-oxide) and related compounds, and in the search for biologically active analogues of this important anti-tumour compound. Mass spectroscopy has been used to characterize other potential anti-cancer compounds possessing related structures,[5] and also metabolites of cyclophosphamide by determination of molecular weight,[6] but detailed analyses of fragmentation patterns have not been given. Chemical ionization mass spectrometry has been used, in conjunction with gas chromatography, to estimate cyclophosphamide.[7]



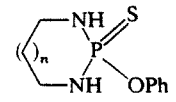
1



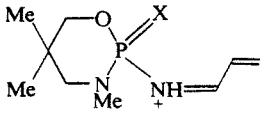
2



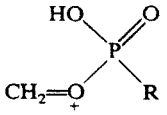
a *b* *c*



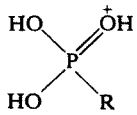
3 (*n* = 0, 1, or 2)



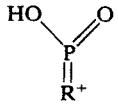
d



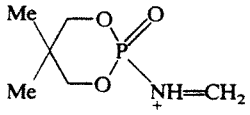
e



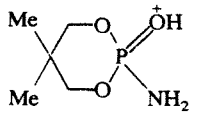
f



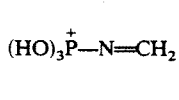
g



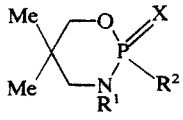
h



i



j



2

R^1 = H; X = O

R^2	**a** = C_6H_{11}-cyclo
	b = CH_2Ph
	c = *tert*-Bu
	d = Ph
	e = OPh

R^1 = H; X = S

R^2	**f** = OPh

R^1 = Me; X = O

R^2	**g** = Me
	h = *tert*-Bu
	i = Ph
	j = C_6H_{11}-cyclo
	k = CH_2Ph
	l = Cl
	m = OPh
	n = NHC_6H_{11}-cyclo

R^1 = Me; X = S

R^2	**o** = Cl
	p = OPh
	q = NHC_6H_{11}-cyclo

† For Part XVI, see Ref. 1.

CCC-0030–493X/82/0017–0558$03.50

RESULTS AND DISCUSSION

The relative intensities of the more important common ions obtained from 5,5-dimethyl-perhydro-1,3,2-oxazaphosphorine 2-oxides and 2-sulphides **2** ($R^1 = H$; X = O or S) and their 3-methyl derivatives **2** ($R^1 = Me$; X = O or S) under electron impact conditions have been determined. For both series of compounds **2** ($R^1 = H$ or Me), $[M]^{+\cdot}$ ions for the 2-sulphides (Table 2) are generally more intense than those from the 2-oxides (Table 1), a tendency which has also been found for the 1,3,2-dioxaphosphorinans **1** (X = O or S).

Fragmentation of substituents attached to the oxazaphosphorine ring

Pronounced loss of methyl radicals from 5,5-dimethyl-1,3,2-dioxaphosph(*v*)orinans occurs only through fission of a P—Me bond, or by fragmentation of an appropriate exocyclic substituent, e.g., iso-Pr or *tert*-Bu, attached to phosphorus either directly or indirectly through O or N; loss of a methyl group from the 5-position is very weak. Generally, $[M-15]^+$ ions are also weak for the 2-oxides of both the 5,5-dimethyl and the 3,5,5-trimethyl series of oxazaphosphorines, and they are barely detectable for the 2-sulphides. Intense $[M-15]^+$ ions do result from cleavage of a *tert*-butyl group in **2c** and **2h**, and by fission of the P—Me bond in **2g**; the marked loss of methyl from the 2-phenoxy compound **2e** is unusual, and a similar observation has been made by Francis *et al.* for the corresponding 1,3,2-dioxaphosph(**v**)orinan. Otherwise, the *N*-methyl compounds show no propensity to lose methyl from either a ring carbon atom or the ring nitrogen atom. The *N*-trideuteriomethyl analogues of **2m** and **2p** lose only 15, and not 18 u, indicating the preferential loss of a methyl group from a ring carbon atom.

For the 1,3,2-dioxaphosph(**v**)orinans, the ion *a* (X = O) is formed (relative intensities 2–23%) by direct fission of the P—R bond in **1** with hydrogen transfer, and it is accompanied by the much weaker ion *b* (X = O) produced without hydrogen transfer; both ions are formed more extensively from those compounds having amino substituents attached to phosphorus than from those with other substituents. The corresponding ion from the perhydro-oxazaphosphorines, *c* (X = O), is more important when R^1 is Me (*m/z* 162; relative intensity up to 29%) than when R^1 is H (*m/z* 148). In addition, the relative intensities of the two sulphide ions *c* (X = S, R^1 = H or Me), at *m/z* 164 and 178 respectively, are greater than is that of the corresponding ion, *b* (X = S) at *m/z* 165, for the dioxaphosphorinan series.

Table 1. Fragmentation data for 5,5-dimethyl and 3,5,5-trimethyl-perhydro-1,3,2-oxazaphosphorine 2-oxides *m/z* (% relative abundance)

Compound	$[M]^{+\cdot}$	$[M-15]^+$	$[M-54]^{+\cdot}$	$[M-55]^+$	$[M-56]^{+\cdot}$	$[M-85]^+$	41	44	55	56	67	68	69	84/98	106	162
a	231 (8)	216 (a)	177 (8)	176(100)	—	—	—	—	(15)	(17)	—	—	—	—	—	—
b	239(17)	224 (a)	185(11)	184(100)	—	—	(17)	—	—	(15)	—	—	(10)	—	—	—
c	205 (7)	190 (4)	151 (9)	150(100)	149 (9)	—	(30)	—	(10)	(31)	—	—	(4)	—	—	—
d	225(23)	210 (2)	171(26)	170(100)	—	140(14)	(54)	—	(19)	(72)	—	(2)	(2)	—/(7)	(2)	—
e	241(66)	226(10)	187(37)	186(100)	185(39)	156(23)	(49)	—	(23)	(29)	—	—	(13)	(11)/—	(11)	(5)
g	177(49)	162(12)	123(42)	122 (98)	—	92(13)	(99)	(98)	(47)	(100)	—	(10)	(14)	(19)/(12)	(7)	(12)
h	219(46)	204(12)	165(49)	164 (98)	—	—	(93)	(98)	(33)	(66)	—	—	(13)	—/(23)	(11)	(29)
i	239 (6)	—	185(13)	184(100)	—	—	(13)	(100)	(7)	(12)	—	—	—	(3)/(2)	—	—
j	244 (9)	—	191(14)	190(100)	—	—	(20)	(100)	(14)	(10)	(3)	(3)	—	—/(4)	(3)	(4)
k	253 (3)	—	—	198(100)	—	—	(19)	(75)	(9)	(13)	—	—	(6)	—/(7)	(7)	(7)
l	197(14) 199(3)	182(a) 184(a)	143(11) —	142(100) 144(100)	—	—	(34)	(56)	—	—	—	(2)	(3)	(4)/—	(25)	(17)
m	255(57)	240 (7)	201(22)	200(100)	199(20)	170 (8)	(27)	(59)	(9)	(9)	(1)	(2)	(3)	—/(19)	(22)	(1)
n	260(18)	245 (a)	206(21)	205(100)	—		(41)	(96)	(27)	(38)	—	—	(11)	(9)/(95)	(14)	(20)

[a] Trace only.

Table 2. Fragmentation data for 5,5-dimethyl- and 3,5,5-trimethyl-perhydro-1,3,2-oxazaphosphorine 2-sulphides *m/z* (% relative abundance)

Compound	$[M]^{+\cdot}$	$[M-32]^{+\cdot}$	$[M-33]^+$	$[M-54]^{+\cdot}$	$[M-55]^+$	$[M-56]^{+\cdot}$	41	44	55	56	69	84/98	146	164/178
f[a]	257(100)	—	224(10)	203 (9)	202 (70)	201(46)	(30)	—	(14)	(11)	(45)	(100)/—	—	(18)/—
o	213 (65) 215 (23)	— —	180(94) 182(29)	159(27) —	158 (98) 160 (75)	157(67) 159(27)	(59)	(98)	(24)	(35)	(20)	—/(50)	(9)	—/(27)
p[b]	271 (52)	229(3)	228(18)	217(15)	216(100)	215(89)	(35)	(48)	(15)	(9)	(25)	—/(95)	(23)	—/(48)
q[c]	276 (37)	244(2)	243(16)	—	251 (d)	—	(43)	(60)	(29)	(14)	(22)	—/(100)	(100)	—/(22)

[a] *m/z* 132 (12%); *m/z* 148 (67%).
[b] *m/z* 106 (26%); *m/z* 162 (57%).
[c] *m/z* 67 (5%); *m/z* 68 (5%).
[d] Trace only.

The four 2-phenoxy compounds (**2e**, **2f**, **2m** and **2p**) do not afford $[M-PhOH]^{+\cdot}$ or, as appropriate, $[M-PhSH]^{+\cdot}$ ions, nor do the two oxides yield $[M-PhO]^+$ ions. On the other hand, the sulphides **2f** and **2p** do give $[M-PhO]^+$ ions (18 and 48% respectively) as well as $[M-PhS]^+$ ions (67 and 57% respectively); for compound **2f**, the relative intensities of the $[M-PhO]^+$ and $[M-PhS]^+$ ions formed at 145 °C are 11 and 50%.

Like the 1,3,2-dioxaphosphorinan 2-sulphides, the perhydro-1,3,2-oxazaphosphorine 2-sulphides do not lose sulphur directly on electron impact. However, direct formation of the $[M-SH]^+$ ion (metastables) is more important for the compounds **2f**, **2o** and **2p** than for the corresponding dioxaphosphorinans, but the reverse is true for the cyclohexylamide **2q**. Deuterium labelling in selected compounds in the 5,5-dimethyldioxaphosphorinan series has demonstrated that the thiol hydrogen (deuterium) is derived from a *C*-methyl group (**1**: X = S, R = NHC_6H_{11}-cyclo) or from a ring methylene group (**1**: X = S; R = Cl or Ph).[1] In the light of evidence described elsewhere,[1,8] and in the ability of the N—Me group to survive hydrogen transfer processes in compounds which lack sulphur, it seems unlikely that N—H and N—Me groups in the oxazaphosphorine ring act as sources of the thiol hydrogen. For the trideuteriomethyl analogue of compound **2p**, the $[M-32]^{+\cdot}/[M]^{+\cdot}$, $[M-33]^+/[M]^{+\cdot}$ and $[M-34]^+/[M]^{+\cdot}$ ratios are 0.020, 0.124 and 0.015 respectively, compared with 0.000, 0.100 and 0.000 for the triprotomethyl compound; the implication is that the thiol hydrogen is derived from a site other than the ring N—Me group. At 145 °C, the [4,4-$^2H_2$] analogue of compound **2f** gives $[M-34]^+/[M]^{+\cdot}$ and $[M-33]^+/[M]^{+\cdot}$ ratios of 0.026 and 0.005, with no formation of the $[M-32]^{+\cdot}$ ion; for compound **2f** itself, $[M-34]^+$ ions are not observed, and the $[M-33]^+/[M]^{+\cdot}$ and $[M-32]^{+\cdot}/[M]^{+\cdot}$ ratios are 0.051 and 0.010 respectively. Thus, at least for compound **2f**, the thiol hydrogen appears to be derived from the perhydro-oxazaphosphorine ring N—CH_2 group, although the experience gained elsewhere[1] suggests that this situation need not necessarily occur with other compounds of the same series.

The behaviour of the perhydro-1,3,2-oxazaphosphorines possessing other substituents on phosphorus generally parallels that of the corresponding 1,3,2-dioxaphosphorinans and, with the exception of the *N*-cyclohexylamides, needs no further comment. The oxide **2n** yields an intense $[M-43]^+$ ion (42%), presumably *d* (X = O) (the corresponding ion *d* (X = S) is not formed from the sulphide **2q**), together with other more intense ions in which, evidently, the cyclohexane ring remains intact but the phosphorus-containing ring has undergone fragmentation.

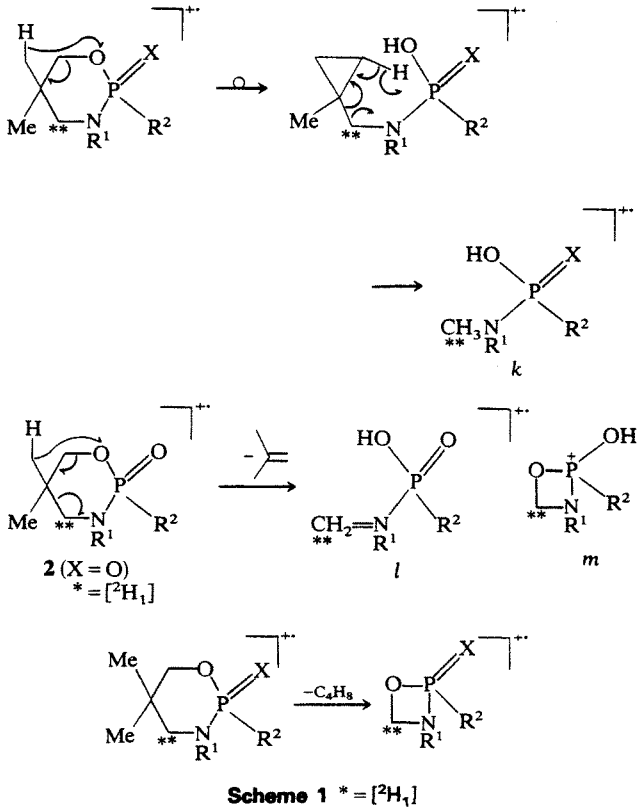
Fragmentation of the perhydro-oxazaphosphorine ring

Depending upon the substituent at phosphorus, compounds in the 5,5-dimethyl-1,3,2-dioxaphosph(**v**)orinan series may display very weak ions at $[M-28(C_2H_4)]^{+\cdot}$ resulting from either ring fragmentation or fission of substituents on phosphorus. Another ion at $[M-30(CH_2O)]^{+\cdot}$, is almost certainly associated with fission of the phosphorus-containing ring. More characteristic of the latter process are the generally intense ions at $[M-55(C_4H_7)]^+$ (*e*), $[M-67(C_5H_7)]^+$ (*f*) and $[M-85(C_4H_7+CH_2O)]^+$ (g), as well as the hydrocarbon ions at *m/z* 41 ($[C_3H_5]^+$), 56 ($[C_4H_8]^{+\cdot}$), 67($[C_5H_7]^+$), 68($[C_5H_8]^{+\cdot}$) and more particularly that at *m/z* 69.

The *m/z* 178 ion (*h*) is of such importance that it often forms the base peak for the 2-amino-dioxaphosph(**v**)orinans, and this, taken together with the occurrence of *m/z* 166 (*i*) and *m/z* 110 (*j*) ions, demonstrates the stability of the exocyclic P—N bond in such compounds under electron impact conditions.

This latter evidence would seem to suggest that fragmentation of the perhydro-oxazaphosphorine ring should occur preferentially through fission of the P—O—C bond system rather than through that of the P—N—C bonds. Scheme 1 represents a possible direct mode of formation of $[M-54]^{+\cdot}$ ions *k* via a rearranged molecular ion. Corroboration is provided by the presence of the appropriate metastables, and by the displacement of the ion by 2 u for the [4,4-$^2H_2$] analogues of compounds **2e** and **2f**. it should be noted that $[M-54]^{+\cdot}$ ions are not observed in the spectra of the 2-amino-1,3,2-dioxaphosph(**v**)orinans.

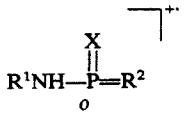
The same evidence lends support also to the proposed routes to the $[M-55]^+$ and $[M-56]^{+\cdot}$ ions, *l* and *n* respectively. $[M-55]^+$ ions, which might be formulated as *m*, are evidently formed directly from the molecular ion (metastables), and whilst they are of considerable importance for the sulphides of the oxazaphosphorine series, they form the base peak for many of the oxides **2** (R^1 = H or Me). The sulphides **2**



Scheme 1 * = [$^2H_1$]

(X = S; R^1 = H or Me) produce an intense $[M-56]^{+\cdot}$ ion *n*; this ion is obtained from the oxides **2** (X = O, R^1 = H) with only very weak intensities, and not at all from the oxides **2** (X = O: R^1 = Me), but once again, 2-phenoxy compounds **2e** and **2m**, exhibit exceptional behaviour. The intensities of the $[M-54]^{+\cdot}$, $[M-55]^{+}$ and $[M-56]^{+\cdot}$ ions for the *N*-trideuteriomethyl analogue of compound **2m** are 37, 100 and 50% (compared with 20, 100 and 22% for the triprotomethyl compound), and those for the analogue of the sulphide **2p** are 13, 84 and 88% (compared with 15, 100 and 89% for the triprotomethyl compound). Once again the presence of a phenoxy substituent produces unusual features; here, compound **2m** affords an $[M-57]^{+}$ ion (50%), also observed for the *N*-trideuteriomethyl analogue in approximately the same relative intensity.

The $[M-85]^{+}$ ion (*o*; X = O), actually observed for very few compounds, is evidently the result of loss of formaldehyde (or as appropriate, dideuterioformaldehyde) from ion *l* (or *m*).



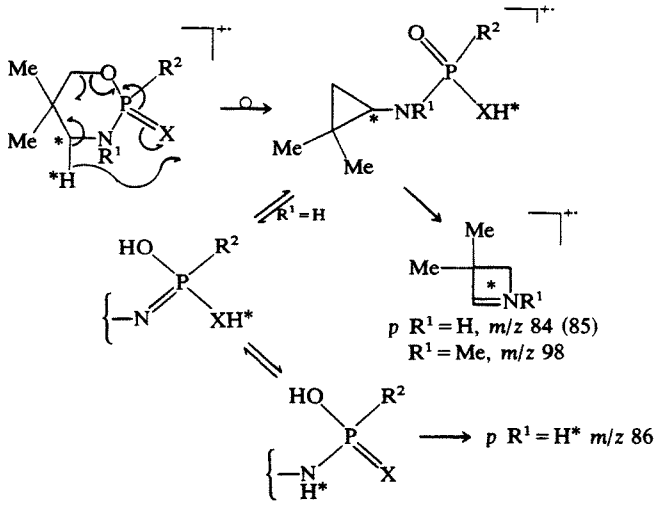
o

Metastables in the spectra of compounds **2j**, **2k** and **2n** suggest that for the series **2** (R^1 = Me) in general, the ion at *m/z* 98 (*p*, R^1 = Me) which is produced particularly strongly for the 2-sulphides, arises via a rearranged molecular ion as indicated in Scheme 2; an appropriate shift is observed when the trideuteriomethyl analogues are employed. The corresponding *m/z* 84 ion, *p* (R^1 = H) is probably formed in a similar fashion from the compounds **2** (R^1 = H). The 2-phenoxy compounds **2e** and **2f** also exhibit several very low intensity ions at around *m/z* 85 and the relative intensities of these produced at 145 °C, are indicated in Table 3. For the oxide **2e**, the ion at *m/z* 84 disappears on dideuteriation; at the same time, the very weak, but essentially equally intense, ions at *m/z* 85 and 86 appear, the former of which is found only in traces for **2e** itself. The formation of monodeuteriated ion *p* from dideuteriated **2e** is apparent; the subsequent formation of an ion of *m/z* 86 could be the result of the tautomeric transformations

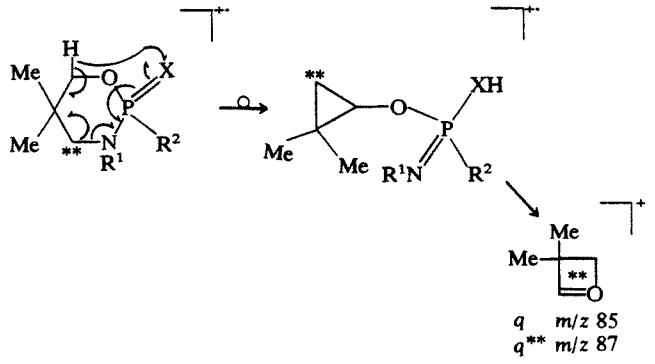
Table 3. Interrelationships of the *m/z* 84–87 ions for compounds 2e and 2f, and their $[^2H_2]$ derivatives

	m/z	% Relative abundance [4,4-$^1H_2$]	[4,4-$^2H_2$]
Compound **2e**	84	2.4	—
	85	0.1	1.1
	86	—	1.6
	87	—	—
Compound **2f**	84	100	3.1
	85	9.0	29.3[a]
	86	1.5	40.3[b]
	87	1.1	5.3

[a] Found *m/z* 85.085589; C_5H_9DN requires 85.087598, C_5H_9O requires 85.065336.
[b] Found *m/z* 86.091669; $C_5H_8D_2N$ requires 86.093875, C_5H_8DO requires 86.071613.



Scheme 2 * = $[^2H_1]$



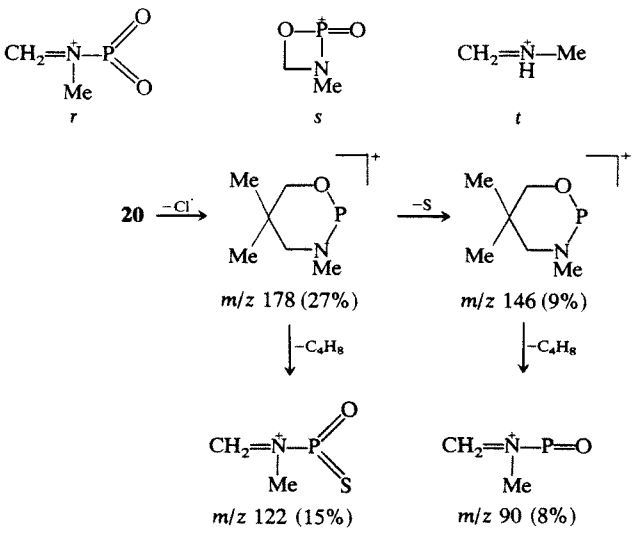
Scheme 3 * = $[^2H_1]$

indicated in Scheme 2. The alternative transformations indicated in Scheme 3 would yield only the ion *q* at *m/z* 85, or its dideuterio derivative at *m/z* 87 exhibited to only a very small extent by **2f** itself. Hence the major component of the *m/z* 86 ion from $[^2H_2]$-**2f** must be $[^2H_2]$-*p* (R^1 = H) rather than $[^2H_1]$-*q*. This argument is substantiated by accurate mass measurements on ions from compound **2f** (see Table 3). Thus, whilst the importance of the ion *q* for the oxide **2e** is slight, it is increased relative to that of the ion *p*, for the sulphide **2f**.

The ion at *m/z* 106 corresponds to $[M-R^2-56]^{+}$ and probably has the structure *r*, or alternatively *s*. This ion is of particular importance for the 3,5,5-trimethyl series, for which metastables suggest that it is formed by loss of R^2 from the $[M-56]^{+}$ ion rather than by further degradation of the $[M-R^2]^{+}$ ion.

For each of the two 2-chloro compounds **2l** and **2o**, two degradative pathways are of comparable significance. For the oxide **2l**, initial loss of 55 u is accompanied by initial loss of Cl· followed by loss of 56 u to give the *m/z* 106 ion *r*. In the case of the sulphide **2o**, pronounced initial loss of thiol radical is concurrent with initial loss of Cl· and subsequent further degradation in the manner depicted in Scheme 4.

The two groups of compounds **2a–2f** and **2g–2q** are clearly distinguishable by the presence or absence of the intense *m/z* 44 ion produced by the latter group;

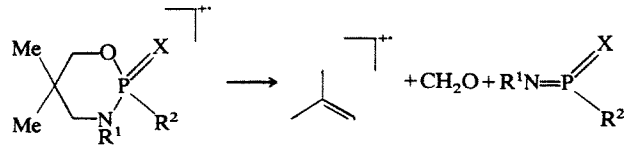


Scheme 4

this ion probably has structure *t*, and may be formed by fission of the ion *p* ($R^1 = Me$).

A mode of formation of the *m/z* 56 ion ($[C_4H_8]^{+\cdot}$), of widely varied intensity, by release of formaldehyde, is indicated in Scheme 5.

$[M-67]^+$ and $[M-68]^{+\cdot}$ ions, as well as the hydrocarbon ions at *m/z* 67 and 68, are even rarer and weaker in relative intensities than are the corresponding ions observed for the 1,3,2-dioxaphosphorinan series.



Scheme 5

EXPERIMENTAL

Light petroleum refers to the fraction b.p. 60–80 °C. Melting points and boiling points are uncorrected. Thin-layer chromatography and column chromatography used Merck Kieselgel. Infrared spectra were determined using a Perkin-Elmer Model 237 spectrometer, and ^1H NMR spectra with a JEOL JNM-MH-100 spectrometer.

3-Amino-2,2-dimethylpropanol

(a) Equimolar proportions of 3-hydroxy-2,2-dimethylpropanal, hydroxylamine hydrochloride and pyridine were heated in boiling 2-propanol for 8 h and the solvent then removed by evaporation *in vacuo*. Dissolution of the residue in water and extraction with ether afforded 2-cyano-2-methylpropanol, b.p. 62–63 °C/0.5 mm, ν_{CN}2240 cm^{-1}(s). The nitrile was reduced with lithium aluminium hydride in ether to give 3-amino-2,2-dimethylpropanol (30%), b.p. 135–140 °C/110 mm, m.p. 80 °C, (lit.[9] 105/35 mm, m.p. 98–100 °C; lit.[10] m.p. 78–80 °C). (Found: C, 58.3; H, 12.6. Calc. for $C_5H_{13}NO$: C, 58.05; H, 12.6%). *N-Benzoyl*; m.p. 108–109 °C, from benzene–light petroleum (Found: C, 69.6; H, 8.5. $C_{12}H_{17}NO_2$ requires C, 69.6; H, 8.2%).

(b) 3-Hydroxy-2,2-dimethylpropanal was converted (0.1 M scale) into its *O-methyl oxime*[11] in aq. ethanol–sodium acetate at room temperature. The dried, but otherwise unpurified, *O*-methyloxime in dry ether (100 cm^3) was reduced with lithium aluminium hydride (4.6 g) in diethyl ether (150 cm^3) and worked up in the usual way to give the aminoalcohol, b.p. 60–65 °C/1 mm, 50–60%.

Exposure of freshly distilled 3-amino-2,2-dimethylpropanol to air resulted in the rapid formation of the *carbamate* salt,

$$HOCH_2CMe_2CH_2NHCOO^-H_3\overset{+}{N}CH_2CMe_2CH_2OH,$$

m.p. 113–115 °C. (Found: C, 52.9; H, 10.2; N, 11.25. $C_{11}H_{26}N_2O_4$ requires C, 52.8; 10.4; N, 11.2%).

2,2-Dimethyl-3-methylaminopropanol

This, b.p. 80–85 °C/0.5 mm, m.p. 52–53 °C (from petroleum ether) (lit.[12] b.p. 68–90 °C/9–11 mm) was prepared by the reduction of 2,2-dimethyl-3-methylaminopropanal, b.p. 60–63 °C/25 mm, (lit.[12] 48–50.5 °C/12–13 mm) in 2-propanol with sodium borohydride.

Perhydro-1,3,2-oxazaphosph(v)orines

Generally, a solution (for reaction media see Table 4) of the appropriate phosphorus(v) dichloride was added to a stirred solution of the aminopropanol and redistilled triethylamine (2 equivalents). The mixture was allowed to stand 15–20 h at ambient temperature or heated under reflux. Triethylammonium hydrochloride was removed by filtration, either directly, or following addition of diethyl ether (2–3 volumes) to the reaction product solution. For compounds **2a–2d** and **2g–2k**, the filtrate was then evaporated to an oil which was chromatographed using chloroform containing methanol, 3–7%).

The *N*-cyclohexylamides **2n** and **2q** were obtained by treatment of the appropriate cyclic phosphoryl chloride with cyclohexylamine (1 equiv.) and triethylamine (1 equiv.). These and other compounds listed in Table 4 were purified by crystallization from the solvents indicated. Table 5 summarizes important infrared assignments.

Deuteriated compounds

[3,3-$^2H_2$]-3-Amino-2-dimethylpropanol was prepared by the reduction of 2-cyano-2-methylpropanol with [$^2H_4$]lithium aluminium hydride in diethyl ether.

[4,4-$^2H_2$]-5,5-Dimethyl-2-phenoxy-perhydro-1,3,2-oxazaphosphorine 2-oxide, m.p. 130–131 °C, and 2-sulphide, m.p. 90.5–91.5 °C, were obtained from [3,3-$^2H_2$]-3-amino-2,2-dimethylpropanol and the appropriate phosphorus(v) dichloride in the usual way.

The 2-phenoxy-5,5-dimethyl-3-[$^2H_3$]methylperhydro-1,3,2-oxazaphosphorine 2-oxide, m.p. 75 °C

Table 4. Preparative and analytical data for 2-substituted perhydro-5,5-dimethyl-1,3,2-oxazaphosph-(v)orines 2

Compound 2	Reaction medium[a]	Yield (%)	m.p. (°C)	Recryst-allized solvent[a]	Formula	Composition (%) Calc. C	Calc. H	Calc. P(N)	Found C	Found H	Found P(N)
a[e]	A	69	141–2	C	$C_{11}H_{22}NO_2P$	57.15	9.55	13.4	56.9	9.6	12.9
b[e]	A	38	126–7	C	$C_{12}H_{18}NO_2P$	60.3	7.5	13.0	60.4	7.3	12.6
c[e]	A	54	117–8	A–C	$C_9H_{20}NO_2P$	52.5	9.75	15.1	52.85	10.0	14.15
d[e]	A	55	132–3	B	$C_{11}H_{10}NO_2P$	58.7	7.1	13.8	58.75	7.15	12.95
e	B	60	130–130.5	B–D	$C_{11}H_{16}NO_3P$	54.8	6.7	(5.8)	54.95	6.8	(5.85)
f	B	77	90.5–91	C	$C_{11}H_{16}NO_2PS$	51.35	6.3	(5.45)	51.8	6.45	(5.55)
g[e]	A	100	96–7	C	$C_7H_{16}NO_2P$	47.5	9.05	17.5	47.6	9.0	17.25
h[e]	A	82	[b]	—	$C_{10}H_{22}NO_2P$	54.8	10.05	14.15	54.75	10.45	14.15
i[e]	A	96	77–8[c]	—	$C_{12}H_{18}NO_2P$	60.3	7.45	13.0	60.05	7.45	12.25
j[e]	A	92	80–1[d]	—	$C_{12}H_{24}NO_2P$	58.8	9.8	12.65	58.75	9.65	12.2
k[e]	A	99	117.5–118	C	$C_{13}H_{20}NO_2P$	61.7	7.9	12.25	61.3	7.95	12.0
l	B	71	69.5–70	C	$C_6H_{13}ClNO_2P$	36.45	6.6	15.65	36.76	6.8	15.55
m	B	60	77.5–80[f]	C	$C_{12}H_{18}NO_3P$	56.45	7.1	(5.5)	56.5	7.05	(5.6)
n	B	69	129.5–130	D	$C_{12}H_{24}N_2O_2P$	55.6	9.3	(10.8)	55.5	10.0	(10.8)
o	B	72	69	C–D	$C_6H_{13}ClNOPS$	33.7	6.1	(6.55)	34.05	6.4	(6.6)
p	B	78	47–9[g]	D	$C_{12}H_{18}NO_2PS$	53.1	6.9	(5.15)	53.5	6.8	(5.25)
q	B	46	94–4.5	D	$C_{12}H_{25}N_2OPS$	52.1	9.1	(10.1)	52.4	9.25	(9.9)

[a] A = benzene; B = ethyl acetate; C = cyclohexane; D = light petroleum.
[b] Oil, n_D^{25} 1.4711.
[c] By solidification of oil, n_D^{25} 1.5273.
[d] By solidification of oil, n_D^{25} 1.4922.
[e] Compounds prepared by Dr T. Moran.
[f] Lit.[13] m.p. 68°C.
[g] Lit.[13] m.p. 42°C.

Table 5. Infrared data for new compounds[a]

Compound	νNH	νP=O	νPOC
2a	3520, 3420	1232	1001
b	3420	1240	1082, 1035, 1002
c	3380, 3419	1237	1085, 1049, 1001
d	3204	1235	1089
e	3430	1268	1080, 1035, 1025, 1005
f	3435	—	1075sh, 1068, 1024
g[b]	—	1245	1052, 1008
h	—	1238	1050, 1003
i[b]	—	1255	1050
j[b]	—	1242	1052, 1001
k	—	1258	1052, 1008
l	—	1294	1048, 1030, 1010, 1000
m	—	1295, 1284	1052, 1028, 1000
n	3420	br	1050, 1025, 1008
o	—	—	1038, 1028, 1008sh
p	—	—	1070, 1044, 1028, 1005sh

[a] Determined for solutions in chloroform unless otherwise stated.
[b] Determined for KBr discs.

and 2-sulphide, m.p. 51–51.5°C, were obtained by alkylation of the anion formed from the appropriate *N*-proto compound and NaH with [$^2H_3$]iodomethane under benzene, and chromatography of the reaction mixture.

Mass spectra

These were obtained using an AEI MS 9 instrument operating at 70 eV with the ion source temperature 230–250°C unless otherwise stated. Samples of compounds were chromatographically homogeneous and of analytical purity. Satisfactory ^1H NMR spectra were obtained for all compounds.

Acknowledgements

Most of the spectra were obtained by Mr R. Nettleton, University of Bradford; spectra run at the lower temperature and also the high resolution spectra, were obtained by Dr B. Watson, University of Leeds. Both operators are thanked.

REFERENCES

1. Part XVI: R. S. Edmundson, *Phosphorus Sulfur* **9**, 307 (1981).
2. G. W. Francis, K. Tjessem, A. Dale and T. Gramstad, *Acta Chem. Scand. Ser. B* **30**, 31 (1976); A. Murai and M. Kainosho, *Org. Mass Spectrom* **11**, 175 (1976); P. Jakobsen, S. Treppendahl and J. Wieczorkowski, *Org. Mass Spectrom.* **6**, 1303 (1972); W. J. Stec, B. Zielińska and J. R. Van Wazer, *Org. Mass Spectrom* **10**, 485 (1975).
3. D. G. Hendricker, *J. Heterocycl. Chem* **4**, 385 (1967); D. Bouchu and J. Dreux, *Tetrahedron Lett.* 3151 (1976); B. Zieliński and W. J. Stec, *Org. Mass Spectrom.* **13**, 65 (1978); R. S. Edmundson and C. I. Forth, *Phosphorus Sulfur* **8**, 315 (1980); H. Kenttämaa and J. Enqvist, *Org. Mass Spectrom.* **15**, 520 (1980); H. Keck, W. Kuchen and H. F. Mahler, *Org. Mass Spectrom.* **15**, 591 (1980); K. J. Voorhees, F. D. Hilemann and D. L. Smith, *Org. Mass Spectrom.* **14**, 459 (1979).
4. R. Z. Musin, Yu Yu Efremov and M. A. Pudovik, *Khim. Geterosikl. Soedin.* 749 (1977), (*Chem. Abs.* **87**, 166993 (1977)).
5. See for example: J. A. Montgomery and R. F. Struck, *Cancer Treat. Repts.* **40**, 381 (1976).
6. T. A. Connors, P. J. Cox, P. B. Farmer, A. B. Foster and M. Jarman, in *Mass Spectrometry in Biochemistry and*

Medicine, ed. by A. Frigerio and N. Castagnoli, p. 19. Raven Press, New York (1974); J. Roboz, *Adv. Cancer Res.* **27**, 201 (1978).
7. I. Jardine, C. Fenselau, M. Appler, M. N. Kan, R. B. Brundrett and M. Colvin, in *Stable Isotopes, Proceedings of the International Symposium 1977*, ed. by T. A. Baillie, p. 97. Macmillan, London (1978).
8. J. M. Desmarchelier, D. A. Wustner and J. R. Fukuto, *Residue Rev.* **63**, 77 (1976); R. G. Cooks and A. F. Gerrard, *J. Chem. Soc. B* 1327 (1968).
9. J. R. Caldwell, US Pat. 2,618,658 (1952) (*Chem. Abs.* **47**, 9997 (1953)).
10. P. F. Alewood, M. Benn and R. Reinfried, *Can. J. Chem.* **52**, 4083 (1974).
11. H. Hjeds, *Acta Chem. Scand.* **19**, 1764 (1965).
12. K. Hayes and G. Drake, *J. Org. Chem.* **15**, 873 (1950).
13. J. Durrieu, R. Kraemer and J. Navech, *Org. Magn. Reson.* **4**, 709 (1972).

Received 16 April 1982; accepted 5 June 1982