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Synthesis of Fluorinated 2-Oxo-1,4,2-oxazaphosphol-4-ines and their Opening by Alcohols

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ABSTRACT

Trifluoromethyl-substituted 1,4,2λ⁵-oxazaphosphol-4-ines from phosphorus dichlorides and N-acylimines of hexafluoroacetone have been synthesized and characterized by ^1H, ^{19}F, and ^{31}P NMR. Alcohols open these oxazaphospholines at the P–O bond, forming the corresponding esters.

INTRODUCTION

In recent years, many chemists have directed their attention toward five-membered rings containing the P–C–N unit. Most syntheses of such rings involve cycloaddition reactions. *N*-Acylimines of hexafluoroacetone (AHFA) (**1**) are important partners in [1 + 4]-cycloaddition reactions with phosphorus(III) esters. Burger et al. have obtained oxazaphospholes with pentacoordinated phosphorus atoms [1–3] by this method (see also Ref. [4]). Recently there was also reported the synthesis of 1,4,2λ³-oxazaphospholes from trifluoromethyl-substituted methylamides and ethyl dichlorophosphite [5]. Data about the preparation of the same ring system by use of reagents containing a tetracoordinated phosphorus atom are not available, excluding our preliminary communication on the synthesis of **3d** [6].

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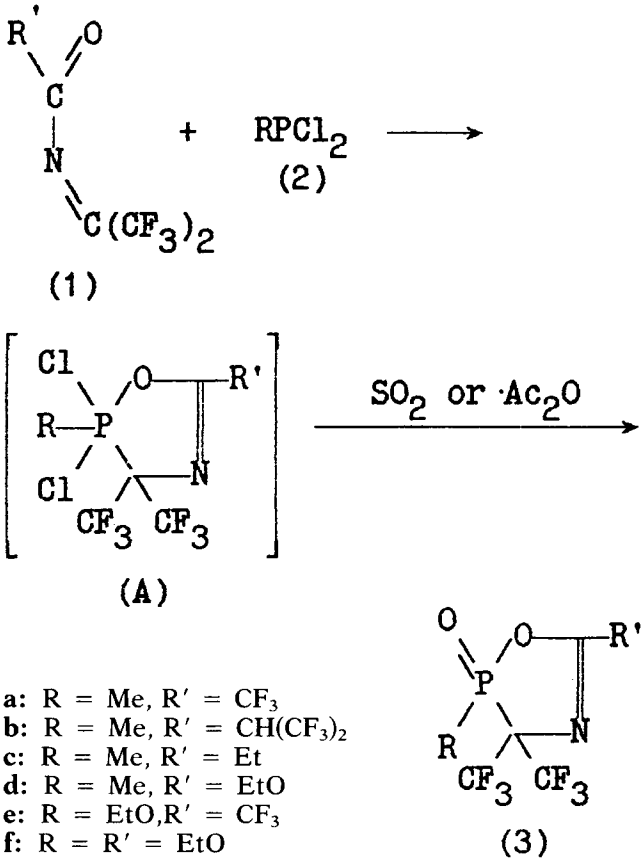
RESULTS AND DISCUSSION

We report here a synthesis of 2-oxo-1,4,2-oxazaphosphol-4-ines (**3**) from phosphorus dichloridites and AHFA (**1**) in the presence of sulfur dioxide or acetic anhydride (Table 1, Reaction 1).



a: R = Me, R′ = CF_3
b: R = Me, R′ = $CH(CF_3)_2$
c: R = Me, R′ = Et
d: R = Me, R′ = EtO
e: R = EtO, R′ = CF_3
f: R = R′ = EtO

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TABLE 1 Physical Properties of Compounds **3** and **4**

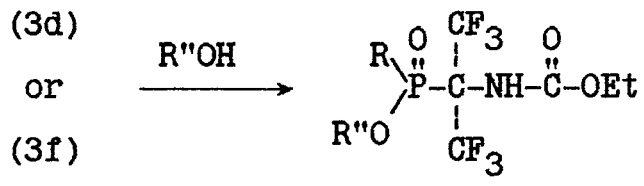
	Yield (%)	bp °C (mm)	n_D^{20}	Molecular Formula	Found (Calcd.) (%) C	H	P
3a	64	73–74 (10)	1.3474	$C_6H_3F_6NO_2P$	22.6 (22.3)	1.0 (0.9)	9.6 (9.6)
3b[a]	90	94–96 (8)		$C_8H_4F_{12}NO_2P$	23.8 (23.7)	1.1 (1.0)	7.6 (7.6)
3c	52	103–105 (9)	1.4002	$C_7H_8F_6NO_2P$	29.6 (29.7)	2.5 (2.8)	11.0 (10.9)
3e	55	75–80 (30)	1.3520	$C_7H_5F_9NO_3P$	23.7 (23.8)	1.4 (1.4)	8.6 (8.7)
3f	52	72 (1)	1.3827	$C_8H_{10}F_6NO_4P$	29.4 (29.2)	3.1 (3.1)	9.3 (9.4)
4a[b]	54	—	—	$C_{12}H_{16}F_6NO_4P$	31.8 (32.0)	4.2 (4.3)	8.3 (8.3)
4b	69	103 (0.05)	1.4050	$C_{10}H_{16}F_6NO_4P$	33.3 (33.4)	4.5 (4.5)	8.6 (8.6)
4c	62	106–108 (0.05)	1.4070	$C_{11}H_{18}F_6NO_4P$	35.5 (35.4)	4.8 (4.9)	8.2 (8.3)
4d	60	128 (0.05)	1.4112	$C_{12}H_{20}F_6NO_4P$	37.1 (37.2)	5.2 (5.3)	8.1 (8.0)
4e	56	116–118 (0.05)	1.4168	$C_{10}H_{12}F_6NO_4P$	33.6 (33.8)	3.5 (3.4)	8.8 (8.7)
4f	64	132 (0.05)	1.4130	$C_{11}H_{18}F_6NO_5P$	34.0 (33.9)	4.7 (4.7)	7.9 (8.0)
4g	50	141–142 (0.05)	1.4229	$C_9H_{13}ClF_6NO_4P$	28.7 (28.5)	3.4 (3.5)	8.2 (8.2)
4h	90	137–138 (0.05)	1.4126	$C_{14}H_{16}F_6NO_4P$	41.1 (41.3)	3.8 (4.0)	7.7 (7.6)

[a] mp 48–50°C
[b] mp 54–56°C

Compounds **3** are high boiling liquids (except for **3b**) that have been characterized by elemental analysis and NMR spectral data (Table 2).

Formation of oxazaphospholes (**3**) probably passes through an intermediate of structure (**A**), a dichlorophosphorane, that then reacts with SO_2 or Ac_2O to give the product.

Recently we have reported that the oxazaphospholine (**3d**) was smoothly opened by alkyl alcohols at the P–O bond, forming the correspondent phosphinates [7]. The same ring opening at the P–O bond of **3d, f** was observed by treatment with different alcohols. The mp and NMR spectral data of **4a** are the same as described in our paper [8] (Reaction 2).



(4)

4a: R = EtO R″ = Et
4b: R = Me, R″ = i-Pr
4c: R = Me, R″ = i-Bu
4d: R = Me, R″ = i-Am
4e: R = Me, R″ = $CH_2C{\equiv}CH$
4f: R = Me, R″ = $CH_2CH_2OCH_2CH_3$
4g: R = Me, R″ = CH_2CH_2Cl
4h: R = Me, R″ = CH_2Ph

The ^{19}F NMR spectra of compounds **3** and **4** showed magnetic nonequivalence for the two geminal trifluoromethyl groups at the prochiral endocyclic carbon atom. In some cases (**3e, f**) these signals overlap (see Tables 2 and 3).

The ^{31}P chemical shifts of **3a–c** and **3e, f** are in the ordinary region for phosphinates and phosphonates, respectively. The signals are split to a septet **3b, f** or to multiplets with $^3J_{PF} \simeq 3$ Hz. The ring opening of **3** by alcohols shifts the signals of the phosphorus atom of **4b–d** to high field.

It should be mentioned that the reactions of **3** with dialkylamines and aniline give indefinite results. Mixtures of products are observed and some of them are fluorinated at the phosphorus atom. A further investigation of this behavior is necessary.

TABLE 2 ^1H, ^{19}F and $^{31}P\{H\}$ NMR Spectral Data of Compounds **3**[a]

	δ^1H		$\delta^{19}F$		
	R	R′	3-CF_3	R′	$\delta^{31}P$[j]
a	2.3 (dq, 3H)[b,d]		10.3 (q, 3F)[c] 11.3 (q, 3F)[c]	4.4 (d, 3F)[d]	61.1
b	2.2 (d, 3H)[b]	4.5 (sept, 1H)[e]	9.7 (q, 3F)[c] 10.5 (q, 3F)[c]	12.2 (s, 6F)	59.1
c	2.1 (dq, 3H)[b,f]	1.3 (t, 2H)[g] 2.6 (q, 3H)[g]	9.3 (q, 3F)[c] 10.3 (q, 3F)[c]		56.3
e	1.5 (t, 3H)[g] 4.34–4.78 (m, 2H)		11.8 (m, 6F)[i]	6.2 (d, 3F)[h]	25.9
f	1.4–1.6 (m, 3H)[f,i] 4.3–4.6 (m, 2H)[i]		8.40 (m, 3F) 8.55 (m, 3F)		24.6

[a] ^1H, ^{19}F and ^{31}P NMR spectra of **3d** see [6].
[b] $^2J_{PH}$ 15 Hz.
[c] $^4J_{FF}$ 11 Hz.
[d] $^6J_{FH}$ 1.5 Hz.
[e] $^3J_{HF}$ 6 Hz.
[f] $^5J_{HF}$ 2 Hz.
[g] $^3J_{HH}$ 7 Hz.
[h] $^4J_{PF}$ 3 Hz.
[i] Overlapping of signals.
[j] For all **3**: m $^3J_{PF}$ 3 Hz.

TABLE 3 ^1H, ^{19}F and $^{31}P\{H\}$ NMR Spectral Data of Compounds **4**

	δ^1H[a]		NH[c]		
	R	R″	($^3J_{PH}$, Hz)	$\delta^{19}F$[d]	$\delta^{31}P$
a	1.54 (t, 6H) 4.28 (m, 4H)		5.81 (12)	10.92 10.96	10.5
b	1.78[b]	1.16 (d, 6H), 4.78 (m, 1H)	6.04 (10)	10.30 14.20	42.1
c	1.90 [b]	0.98 (d, 6H), 1.92 (m, 1H), 3.85 (m, 2H)	6.13 (8)	10.00 14.20	42.8
d	1.92 [b]	0.97 (d, 6H), 1.64 (m, 1H), 1.76 (m, 2H), 4.34 (m, 2H)	6.12 (9)	9.74 13.80	42.8
e	1.95 [b]	2.64 (t, 1H, J_{HH} 2), 4.65[e] (ddd, 1H), 4.90[e] (ddd, 1H)	6.02 (10)	10.00 13.60	45.5
f	1.89 [b]	1.19 (t, 3H), 3.50–3.70 (m, 2H, CH_2OEt), 4.15 (q + m, 2H + 1H), 4.45 (m, 1H, CH_2OP)	6.20 (10)	10.60 13.70	44.0
g	1.95[b]	3.71 (t, 2H), 4.19 (m, 1H), 4.55 (m, 1H)	6.03 (10)	10.06 13.56	43.5
h	1.83 [b]	5.04[f] (dd, 1H), 5.34[f] (dd, 1H), 7.32 (s, 5H)	6.15 (9)	10.40 14.48	45.2

[a] For all EtO of **4**: 1.21–1.30 (t, 3H); 4.06–4.18 (q or m, 2H).
[b] Doublet, 3H, $^2J_{PH}$ 16 Hz.
[c] Doublet, 1H.
[d] Two quartets, $^4J_{FF}$ 10 Hz.
[e] ABX spin system (X = P): J_{AB} 16, J_{AX} 10, J_{BX} 12.
[f] ABX spin system (X = P): J_{AB} 8.5, J_{AX} 11, J_{BX} 12.
[g] For all **4** singlet.

EXPERIMENTAL

^1H, ^{19}F, and $^{31}P\{H\}$ NMR spectra were recorded on the Bruker CXP 200 spectrometer. Chemical shifts are given from Me_4Si (internal standard), CF_3COOH, and 85% H_3PO_4 (external standards) in $CDCl_3$ solutions. All chemical shifts are downfield of standards. Melting points are uncorrected and were determined by use of a sealed capillary tube.

Synthesis of Fluorinated 2,5-Substituted 1,4,2λ^5-oxazaphosphol-4-ines (**3**)

General Procedure. A solution of 5 mmol of the phosphorodichloridite, 5 mmol of the AHFA, and 6–8 mmol of SO_2 or 5 mmol of Ac_2O in 30 mL of dry diethyl ether was heated in a sealed ampule at 60–80°C during 4–6 hours. After having been cooled, the ampule was opened, the solvent was removed, and the residue was distilled under reduced pressure. Physical data are reported in Table 1. The ^1H, ^{19}F, and $^{31}P\{H\}$ NMR spectral data of compounds **3** are reported in Table 2.

Ring Opening of Heterocycles (**3**) *by Alcohols*

General Procedure. To a solution of 4 mmol of **3** in 8 mL of diethyl ether a solution of 4.2 mmol of alcohol in 8 mL of diethyl ether was added dropwise under stirring at room temperature. After 3 h of stirring, the diethyl ether was evaporated, and the residue was distilled [9]. Physical data are reported in Table 1. The ^1H, ^{19}F, and $^{31}P\{H\}$ NMR spectral data of compounds **4** are reported in Table 3.

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[9] The phosphonate (**4a**) was purified by crystallization.