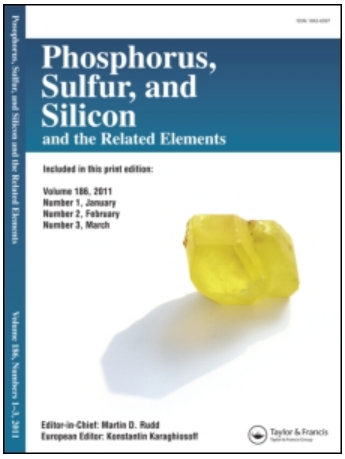

Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

A FACILE SYNTHESIS OF N-DIETHOXYPHOSPHORYLFORMAMIDINES

Stefan Zawadzki[a]; Andrzej Wijata[a]
[a] Institute of Organic Chemistry, Technical University (Politechnika), Lódź, Poland

To cite this Article Zawadzki, Stefan and Wijata, Andrzej(1990) 'A FACILE SYNTHESIS OF N-DIETHOXYPHOSPHORYLFORMAMIDINES', Phosphorus, Sulfur, and Silicon and the Related Elements, 53: 1, 307 — 311
To link to this Article: DOI: 10.1080/10426509008038040
URL: http://dx.doi.org/10.1080/10426509008038040

Phosphorus, Sulfur, and Silicon, 1990, Vol. 53, pp. 307–311
Reprints available directly from the publisher
Photocopying permitted by license only

A FACILE SYNTHESIS OF *N*-DIETHOXYPHOSPHORYLFORMAMIDINES

STEFAN ZAWADZKI† and ANDRZEJ WIJATA
Institute of Organic Chemistry, Technical University (Politechnika), Zwirki 36, 90-924 Łódź, Poland

(Received January 29, 1990)

The convenient synthesis of *N*-phosphorylated formamidines, **3** based on the reaction of diethyl(ethoxymethylene)phosphoramidate, **1** with primary and secondary amines is described.

Key words: *N*-Diethoxyphosphorylformamidines; ethyl [*N*-(diethoxyphosphoryl)]formimidate; amines; nucleophilic substitution.

INTRODUCTION

N-Phosphorylated amidines are useful compounds employed as potential herbicides[1] and antiblastic agents.[2] Several methods have been reported[3] for the preparation of this class of amidine derivatives. They can be obtained by: (i) phosphorylation of amidines and chloroamidines with phosphites[4,5] or phosphorochloridates,[4] (ii) the reaction of amines with *N*-phosphorylated imidates,[7,8] thioimidates[7] or imidoyl chlorides,[9–11] (iii) the reaction of phosphoryl azides with enamines,[2,12] (iv) reaction of phosphoramides with dimethylformamide acetals.[1] The recent report by Khayat and Al-Isa[13] recommends the synthesis of **3** by treating *N*-phosphorylated isobutyl formimidates with amines. The method suffers, however, several inconveniences. The starting imidates are obtained from highly toxic phosphoryl azides[14] reacting with a large excess of isobutyl vinyl ether and a long reaction time is required. Furthermore, the substrates are hygroscopic[15] and the procedure seems hazardous due to the evolution of diazomethane.

In connection with our investigations on the reactivity of ethyl[*N*-(diethoxyphosphoryl)]formimidate, **1** with nucleophiles[16] we wish to report now a simpler method for the preparation of the title compounds, **3**.

RESULTS AND DISCUSSION

We were able to demonstrate that *N*-diethoxyphosphorylformamidines, **3** can be conveniently obtained by condensation of easily available[16] ethyl[*N*-(diethoxyphosphoryl)]formimidate, **1** with primary or secondary amines (Equation 1). The general character of this procedure is exemplified below.

† Author to whom all correspondence should be addressed.

$$(C_2H_5O)_2\overset{\overset{O}{\|}}{P}N{=}CHOC_2H_5 + HNR^1R^2 \xrightarrow[\Delta,4h]{PhH} (C_2H_5O)_2\overset{\overset{O}{\|}}{P}N{=}CHNR^1R^2 + C_2H_5OH \quad (1)$$

1 2 3

2,3	R^1	R^2	2,3	R^1	R^2
a	H	$n\text{-}C_3H_7$	g	CH_3	CH_3
b	H	$i\text{-}C_3H_7$	h	C_2H_5	C_2H_5
c	H	$n\text{-}C_4H_9$	i	$n\text{-}C_3H_7$	$n\text{-}C_3H_7$
d	H	$c\text{-}C_6H_{11}$	j	$i\text{-}C_3H_7$	$i\text{-}C_3H_7$
e	H	C_6H_5	k	$-(CH_2)_4-$	
f	H	$C_6H_5CH_2$	l	$-CH{=}CH{-}N{=}CH-$	

In the case of secondary amines, (**2h–l**) the reaction is carried out by refluxing the formimidate **1** with a 4-fold excess of the appropriate amine **2** in benzene. Evaporation of solvent followed by distillation of the residue affords **3** in high yields (Table I). The analogues procedure applied to primary amines (**2a–f**) gives lower yields of **3**. The relatively low yields of **3a–f** can be explained by assuming an amine exchange reaction between the initially formed *N*-phosphorylformamidines and an excess of amine. Similar reaction occurs readily with acylamidines.[17]

In order to suppress this side reaction we have modified the synthetic procedure by adding dropwise one equivalent of primary amine to a benzene solution of **1**. All compounds prepared by this preparative variant are formed in high yields (example **3a–f**, Table I). Because of the high volatility of dimethyla-

TABLE I

N-Diethoxyphosphorylformamidines (**3a–f**)

Compound No.	Yield[a] (%)	Method, duration (h)	B.p. (°C/torr)	n_D^{20}	Molecular formula[d]
3a	78	B, 4	184–186/1.4	1.4560	$C_9H_{19}N_2O_3P$(222.2)
3b	78	B, 4	160–162/0.3	1.4570	$C_8H_{19}N_2O_3P$(222.2)
3c	72	B, 4	176–180/0.4	1.4566	$C_9H_{21}N_2O_3P$(236.3)
3d	78	B, 4	180–182/0.4	1.4810	$C_{11}H_{23}N_2O_3P$(262.3)
3e	74	B, 8	142–144/0.4	1.5324	$C_{11}H_{17}N_2O_3P$(256.2)
3f	56	B, 6	162–164/0.3	1.4918	$C_{12}H_{19}N_2O_3P$(270.3)
3g	88	B,[c]	160–161/2.2	1.4675[b]	$C_7H_{17}N_2O_3P$(208.2)
3h	86	A, 4	129–130/0.15	1.4610	$C_9H_{21}N_2O_3P$(236.3)
3i	76	A, 4	140–142/0.4	1.4592	$C_{11}H_{25}N_2O_3P$(264.3)
3j	66	A, 4	122–124/0.2	1.4556	$C_{11}H_{25}N_2O_3P$(264.3)
3k	70	A, 4	140–142/0.1	1.4668	$C_9H_{29}N_2O_3P$(234.2)
3l	78	A, 4	102–103/1.7	1.4557	$C_8H_{14}N_2O_3P$(231.2)

[a] Yield of distilled products;
[b] Lit.[1] n_D^{20} 1.4691
[c] The reaction was carried out for 4 days at room temperature.
[d] Satisfactory microanalysis obtained: C ± 0.34, H ± 0.22, N ± 0.30, P ± 0.21.

TABLE II

Spectroscopic data of *N*-diethoxyphosphorylformamidines **3**

ound o	IR(film)[a] $\nu(cm^{-1})$	^1H NMR ($CDCl_3$/TMS)[b] δ (ppm)J(Hz)	^{31}P NMI δ(ppm)(H
a	3250, 3064, 1656, 1220, 1060, 1036, 982	0.90, 0.94 (2t, 3H, J = 7.0) CH_3; 1.30, 1.31 (2t, 6H, J = 7.2) $2CH_3$; 1.58 (bsx, 2H, J = 7.0) CH_2; 3.13, 3.33 (2t, 2H, J = 7.0)CH_2N; 4.03 4.09 (2qt, 4H, J = 7.2)$2CH_2O$; 7.89, 8.10 (2d, 1H, J = 24.0, 21.5) CH═N	11.6, 11 (33:67
b	3240, 3075, 1640, 1620, 1222, 1075, 980	1.19 (d, 6H, J = 6.6) $2CH_3$; 1.30, 1.31 (2t, 6H, J = 7.0) $2CH_3$; 3.40, 3.80 (m, 1H) CNH; 4.03, 4.06 (2qt, 4H, J = 7.0) $2CH_2O$; 8.00, 8.06 (2d, 1H, J = 21.6, 21.9) CH═N	11.8, 10 (73:13
c	3270, 3065, 1640, 1630, 1218, 1050, 983	0.92 (bt, 3H, J = 6.0) CH_3; 1.30, 1.31 (2t, 6H, J = 7.0) $2CH_3$; 1.15–1.85 (m, 4H) CH_2CH_2; 3.10–3.55 (m, 2H) CH_2; 4.03, 4.08 (2qt, 4H, J = 7.0) $2CH_2O$; 7.90, 8.09 (2d, 1H, J = 24.0, 21.6) CH═N	11.3 (100)
d	3240, 3062, 1638, 1617, 1220, 1050, 990, 965	1.31, 1.32 (2t, 6H, J = 7.2) $2CH_3$; 1.10–2.22 (m, 10H)$(CH_2)_5$; 2.80–3.35 (m, 1H) CHN; 4.04, 4.10 (2qt, 4H, J = 7.2) $2CH_2O$; 7.87 (bd, 1H, J = 22.5) CH═N	12.0, 10 (62:38
e	3290, 3220, 3150, 3000, 1650, 1610, 1226, 1064, 990, 830, 770	1.31, 1.32 (2t, 6H, J = 7.2) $2CH_3$; 4.10 (qt, 4H, J = 7.2) $2CH_2O$; 6.92–7.83 (m, 5H) C_6H_5; 8.54, 8.62 (2d, 1H, J = 23.8, 24.3) CH═N	11.3, 10.3, 2 (12:50:13
f	3260, 3140, 1670, 1575, 1200, 1047, 975, 802, 750	1.26, 1.27 (2t, 6H, J = 7.1) $2CH_3$; 3.98, 4.01 (2qt, 4H, J = 7.1) $2CH_2O$; 4.36–4.66 (m, 2H) CH_2Ph; 7.29 (s, 5H) C_6H_5; 8.07 (d, J = 25.0), 8.17 (bd, 1H, J = 21.6) CH═N	11.6, 10 (69:31
g	3000, 2945, 1644, 1630, 1205, 1065, 980	1.32, 1.33 (2t, 6H, J = 7.2) $2CH_3$; 3.00, 3.07 (2s, 6H) $2CH_3N$; 4.06, 4.09 (2qt, 4H, J = 7.2) $2CH_2O$; 8.02 (d, 1H, J = 20.7) CH═N	13.9, 13 (19:81
h	3000, 2950, 1640, 1630, 1245, 1050, 980	1.15 (t, 6H, J = 7.2) $2CH_3$; 1.31, 1.32 (2t, 6H, J = 7.1) $2CH_3$; 3.40, 3.48 (2q, 4H, J = 7.2) $2CH_2N$; 4.06 (qt, 4H, J = 7.1) $2CH_2O$; 8.03 (d, 1H, J = 21.2) CH═N	11.8, 10 (25:75
i	2990, 2956, 1640, 1620, 1250, 1075, 1050, 970	0.90 (t, 6H, J = 7.2) $2CH_3$; 1.31, 1.32 (2t, 6H, J = 7.2) $2CH_3$; 1.60 (sx, 4H, J = 7.2) $2CH_2$; 3.22, 3.38 (2t, 4H, J = 7.2) $2CH_2N$; 4.05 (qt, 4H, J = 7.2) $2CH_2O$; 8.05 (d, 1H, J = 21.2) CH═N	11.7, 10 (21:79
j	2980, 2940, 1622, 1604, 1222, 1048, 1030, 980	1.22, 1.30 (2d, 12H, J = 6.9) $4CH_3$; 1.31, 1.32 (2t, 6H, J = 7.1) $2CH_3$; 3.64, 4.64 (2sp, 2H, J = 6.9) 2CH; 4.05, 4.10 (2qt, 4H, J = 7.1) $2CH_2O$; 8.13 (d, 1H, J = 21.9) CH═N	11.5, 10 (34:66

TABLE II (*continued*)

pound lo	IR(film)[a] $\nu(cm^{-1})$	^1H NMR ($CDCl_3$/TMS)[b] δ (ppm)J(Hz)	^{31}P NM δ(ppm)(H
k	2970, 2900, 1665, 1620, 1600, 1220, 1060, 1036, 974, 880	1.31, 1.32 (2t, 6H, $J = 7.2$) $2CH_3$; 1.83–2.15 (m, 4H) CH_2CH_2; 3.31 3.70 (m, 4H) $2CH_2N$; 4.06, 4.09 (2qt, 4H, $J = 7.2$) $2CH_2O$; 8.22 (d, 1H, $J = 21.3$) CH=N	11.8, 1 (24:6
l	3015, 2960, 1650, 1630, 1250, 1080, 1050, 970, 840, 768	1.33, 1.36 (2t, 6H, $J = 7.1$) $2CH_3$; 4.09, 4.18 (2qt, 4H, $J = 7.1$) $2CH_2O$; 6.90–7.60 (m, 3H) CH=NCH=CH); 8.23 (bd, 1H, $J =$ 15.0) CH=N	8.5, 8 (53:4

corded on a Specord M80 Spectrometer.
asured at 80 MHz with a TESLA BS 587A spectrometer. Abbrevations used: s-singlet, d-dublet, t-triplet, q-quartet, qt-quintet, tet, m-multiplet, b-broad.
asured at 24.3 MHz with a Jeol INM-FX60 spectrometer.
tio of geometrical isomers is given in brackets.

mine, the appropriate formamidine **3g** was obtained by treatment of **1** with an excess of dimethylamine in benzene at room temperature for 4 days.

As proven by ^{1}H and ^{31}P NMR spectroscopy, crude formamidines **3** are practically pure and sufficiently stable to be distilled in vacuo. Some of them, (i.e. **3e**), however, decompose partially during distillation and cannot be obtained in analytically pure state. Distilled samples are colorless or pale-yellow oils of an amine odour. Yields and physical constants of *N*-diethoxyphosphorylformamidines **3** are compiled in Table I. Their spectroscopic data (Table II) are consistent with the anticipated structures. All specimens of **3** are mixtures of both geometrical isomers and exhibit two independent signals in their ^{31}P NMR spectra. Owing to accessibility of various *N*-phosphorylated imidates,[18] the reported approach offers a general, operationally simple method for preparing a wide spectrum of *N*-phosphorylated amidines.

EXPERIMENTAL

Ethyl [*N*-(diethoxyphosphoryl)]formimidate **1** was prepared, according to the previously described procedure,[16] from diethyl phosphoramidate and a slight excess of ethyl orthoformate.

N-Diethoxyphosphorylformamidines **3a–f**; *Method B.* To a solution of ethyl[*N*-diethoxyphosphoryl)]-formimidate (**1**; 4.2 g, 0.02 mol) in benzene (20 ml) is added dropwise a solution of corresponding amine (**2a–f**; 0.02 mol) in 8 ml of benzene. The mixture is refluxed for 4–8 h, (Table I) and then evaporated under reduced pressure. The oily residue is distilled in vacuo. Yields and physical data are given in Table I.

Method A: A mixture of ethyl[*N*(diethoxyphosphoryl)]formimidate (**1**; 4.2 g, 0.02 mol) and the appropriate amine (**2h–l**; 0.08 mol) in 30 ml of benzene is refluxed for 4 h. The excess of amine and the solvent are then evaporated under reduced pressure. The oily residue is distilled in vacuo. Physical data are given in Table I.

ACKNOWLEDGEMENT

This work was supported by the Polish Academy of Sciences, grant CPBP-01.13.3.3.

REFERENCES

1. H. E. Windberg, U.S. Pat. 3121084 (1964); *C.A.*, **60,** 13197d (1964).
2. K. D. Berlin and L. A. Wilson, *Chem. and Ind.*, **1965,** 1522.
3. K. Sasse, in: Houben-Weyl XII/2, 490 (1963).
4. F. Cramer and A. Vollmar, *Chem. Ber.*, **91,** 704, 911, 918 (1958).
5. V. I. Shevchenko, V. I. Kalchenko and A. D. Sinitsa, *Zh. Obshch. Khim.*, **47,** 2157 (1977).
6. A. V. Kirsanov and G. I. Derkach, *Zh. Obshch. Khim.*, **32,** 2254 (1962).
7. A. V. Kirsanov and V. A. Shokol, *Zh. Obshch. Khim.*, **31,** 582 (1961).
8. G. I. Derkach, M. A. Lepesa and A. V. Kirsanov, *Zh. Obshch. Khim.*, **31,** 3424 (1961).
9. G. I. Derkach and A. V. Kirsanov, *Zh. Obshch. Khim.*, **29,** 3424 (1959).
10. A. A. Kropacheva, G. I. Derkach and A. V. Kirsanov, *Zh. Obshch. Khim.*, **31,** 1601 (1961).
11. G. I. Derkach, E. S. Gubnitzkaja and A. V. Kirsanov, *Zh. Obshch. Khim.*, **31,** 3746 (1961).
12. T. Shioiri, N. Kawai and M. Ban, *Jpn. Kokai* 7959238 (1979); *C.A.*, **91,** 156827q (1979).
13. M. A. R. Khayat and F. S. Al-Isa, *J. Prakt. Chem.*, **331,** 149 (1989).
14. F. L. Scott, R. Riorden and P. D. Martin, *J. Org. Chem.*, **27,** 4255 (1962).
15. K. D. Berlin and M. A. R. Khayat, *Tetrahedron* **22,** 975 (1966).
16. S. Zawadzki, *Phosphorus and Sulfur* **40,** 263 (1988).
17. D. M. Vyas, Y. Chiang, D. Benigni and T. W. Doyle, *J. Org. Chem.*, **52,** 5601 (1987).
18. V. V. Moskva, A. I. Maikova and A. I. Razumov, *Zh. Obshch. Khim.*, **38,** 2586 (1968).