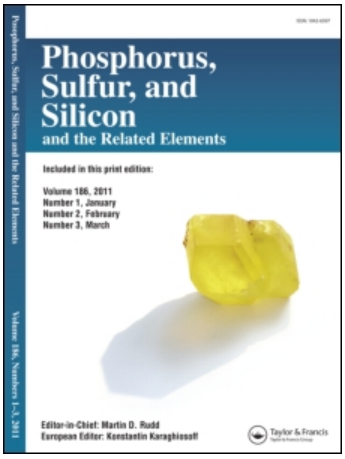


Phosphorus, Sulfur, and Silicon and the Related Elements

Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

Unexpected Reaction of Bis(Diethylamino)-Fluorophosphine with *N*-Benzimidazol-2-Yl-*N'*-Amidines

Noureddine Raouafi[a]; Khaled Boujlel[a]; Mohamed Lamine Benkhoud[a]
[a] Laboratoire de Chimie Analytique et Électrochimie, Department of Chemistry, Tunis El-Manar University, Campus Universitaire, Tunis El-Manar, Tunisia

To cite this Article Raouafi, Noureddine , Boujlel, Khaled and Benkhoud, Mohamed Lamine(2007) 'Unexpected Reaction of Bis(Diethylamino)-Fluorophosphine with *N*-Benzimidazol-2-Yl-*N'*-Amidines', Phosphorus, Sulfur, and Silicon and the Related Elements, 182: 4, 899 — 904
To link to this Article: DOI: 10.1080/10426500601088663
URL: http://dx.doi.org/10.1080/10426500601088663

Phosphorus, Sulfur, and Silicon, 182:899–904, 2007

ISSN: 1042-6507 print / 1563-5325 online
DOI: 10.1080/10426500601088663

Taylor & Francis
Taylor & Francis Group

Unexpected Reaction of Bis(Diethylamino)-Fluorophosphine with *N*-Benzimidazol-2-Yl-*N′*-Amidines

Noureddine Raouafi
Khaled Boujlel
Mohamed Lamine Benkhoud
Laboratoire de Chimie Analytique et Électrochimie, Department of Chemistry, Tunis El-Manar University, Campus Universitaire, Tunis El-Manar, Tunisia

Bis(diethylamino)fluorophosphine reacts with N-benzimidazol-2-yl-N′-amidines to undergo the elimination of HF and diethylamine leading to the corresponding 2-substituted benzimidazolo-1,3,5,2-λ³-triazaphosphorines.

Keywords Amidines; Bis(diethylamino)fluorophosphine; HF elimination; *N*-benzimidazol-2-yl-*N′*-amidines; triazaphosphorine

INTRODUCTION

Triazaphosphorine chemistry has been extensively studied by Kaukorat et al. and by Schmidpeter and Weingand, who developed many access routes to these substrates.[1–6] We are currently interested in developing new routes for the synthesis of new families of 2-substituted benzimidazolo-1,3,5,2-triazaphosphorines.[7,8] These substrates contain a triazaphosphorine ring fused with a benzimidazole moiety, which are both important pharmacophore groups.[9,10] We have been interested in the use of phosphines for accessing to triazaphosphorines. In this article, we report the unexpected condensation reaction of bis(diethylamino)fluorophosphine with amidines.

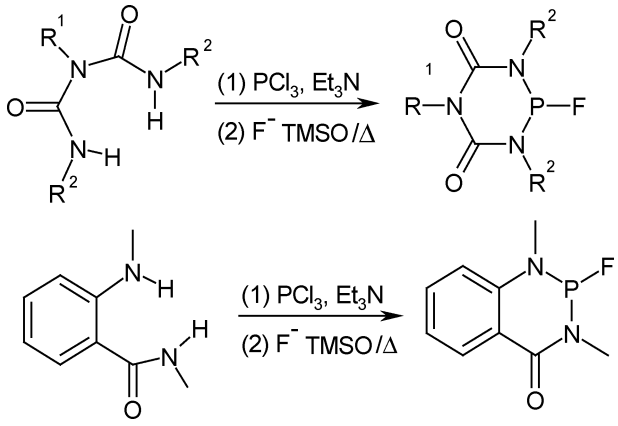
Received March 20, 2006; accepted September 11, 2006.

Authors thank Minstère de la Recherche Scientifique et Technique et Développement des Compétances for the financial support of this work code Lab CH-02. And Professor Jürgen Voss is deeply acknowledged for valuable comments during the preparation of the manuscript.

Address correspondence to Noureddine Raouafi, Laboratoire de Chimie Analytique et Électrochimie, Department of Chemistry, Faculty of Science of Tunis, Tunis El-Manar University, Campus Universitaire, Tunis El-Manar, 2092 Tunisia. E-mail: rdnnin@fst.rnu.tn

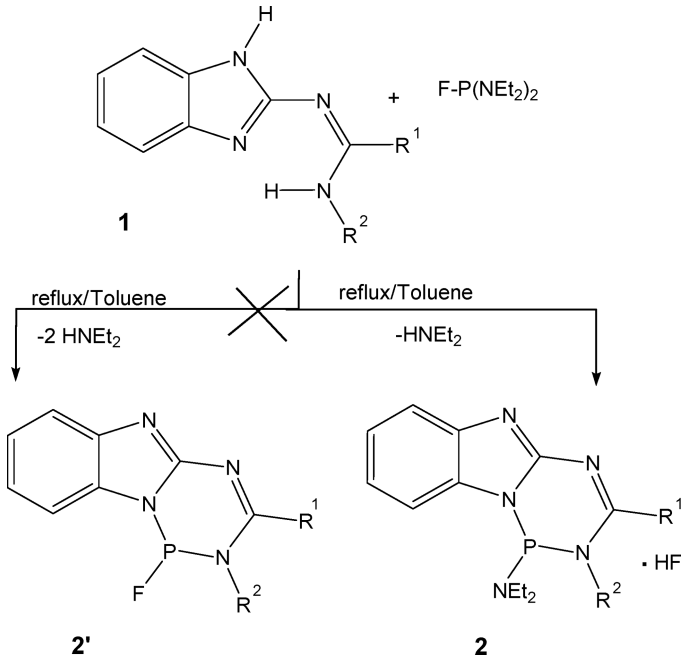
RESULTS AND DISCUSSION

Phosphines represent excellent starting compounds for the synthesis of triazaphosphorines when they are reacted with suitable reagents.[1–4,8] If phosphines bear a leaving group such as dialkylamino moiety or halogen atoms, they could yield cyclic compounds by condensation with binucleophilic substrates like disubstitued diurea or 2-acetamidoaniline.[1–4] Neda et al. prepared 2-fluoro-1,3,5,2-triazaphosphorine-4,6-dione in a two step reaction; the first step consists in the formation of the chlorinated compound, and the second step is a chlorine-fluorine exchange reaction (Scheme 1).[11,12]



SCHEME 1

Unlike bis(diethylamino)fluorophosphine, trifluorophosphine, mono-(alkyloxy)difluorophosphine and bis(alkyloxy)fluorophosphine, (RO_n PF_{3-n}, n = 0,1,2) did not release easily the fluorine atom or the alkoxy group. Instead, they acted as nucleophilic reagents by giving the corresponding addition products.[13–15] Bis(diethylamino)fluorophosphine carried two leaving groups and a fluorine atom and seemed to be an ideal starting product for the synthesis of 2-fluorinated benzimidazolo-1,3,5,2-λ^3-triazaphosphorines. In contrast the *N*-benzimidazol-2-yl-*N'*-amidines, the reaction did not yield the expected 2-fluorinated benzimidazolo-1,3,5,2-λ^3-triazaphosphorines, but gave a product bearing a diethylamino group at the phosphorus atom instead (Scheme 2). The formation of compounds **2** can be explained by the elimination of HF and $HNEt_2$. While the cleavage of the phosphorus-fluorine bond is more difficult than that of the phosphorus-nitrogen



SCHEME 2

bond, we find here the elimination of HF and $HNEt_2$ instead of two $HNEt_2$ molecules. The only one case of such a reaction was reported by Cavell, who showed that the substitution of a fluorine atom by NMe_2 is possible by reacting dimethylamine and PF_3under drastic conditions.[16]

The formation of compounds **2** was confirmed by proton decoupled ^{31}P NMR spectra in solution. The spectra showed the total absence of the doublet related to the P-F moiety ($\delta = 152$ ppm, $^1J_{PF} = 1022$ Hz) and the presence of a new signal at $\delta = 80$ ppm assigned to the P-NEt_2 phosphorus atom based on the results of our previous works.[7,8] Without proton decoupling, the ^{31}P NMR signal displayed a multiplet related to the P-NEt_2 group confirming the presence of the $^3J_{PH}$ coupling. The ^1H and ^{13}C NMR spectra, recorded for compound **2a**, confirmed the formation of product **2** and the total absence of compound **2′**.

In conclusion, in this article we report the unexpected reaction of bis(diethylamino)fluorophosphine with the *N*-benzimidazol-2-yl-*N*′-amidines, which leads to HF elimination, and which to our knowledge is observed here for the first time for this kind of compounds.

EXPERIMENTAL

General Procedure for the Synthesis of Triazaphosphosphorinse 2

To a solution of 2.0 mmol of amidine **1** in 10 mL of anhydrous toluene, 2.2 mmol of bis(diethylamino)fluorophosphine dissolved in 5 mL of toluene was added in dropwise. The mixture was refluxed for 3 to 6 h. The solution was allowed to reach r.t., the solvent was removed under vacuum, and the resulting yellowish solid was filtered off and washed twice with a mixture of diethyl ether/petroleum ether (1:1) to give the product **2** in a 90% yield.

NMR spectra were measured with a Bruker AC 200 spectrometer, and δ values are given in ppm using TMS as an internal standard for proton and ^{13}C as well as H_3PO_4 85% for ^{31}P as external standards. Melting points were recorded in an Electrothermal 9100 apparatus and are uncorrected. Elemental analysis were measured in a Perkin Elmer 2400 CHN elemental analyzer apparatus (Table I).

2a: m.p.: 139–141°C; yield: 93%; ^1H NMR ($CDCl_3$, 200.13 MHz): 0.80 (t, 6H, C<u>H</u>$_3$-CH$_2$); 2.20 (s, 3H, C<u>H</u>$_3$); 2.85 (t, 4H, CH$_3$-C<u>H</u>$_2$; $^3J_{P-H}$ = 9.0 Hz); 4.65 (m, 2H, Ph–C<u>H</u>$_2$); 6.95–8.90 (m, 9H, aromatics), 11.75 (br, 1H)-^{13}C NMR ($CDCl_3$, 50.32 MHz): 14.2; 14.2; 24.3; 40.4; 40.8; 52.9; 109.6–129.03; 133.3; 136.6; 143.9; 151.1; 160.56-^{31}P NMR ($CDCl_3$, 80.6 MHz): 80.0. Elemental analysis (calculated/found): C: 65.56/65.60; H: 6.88/6.89; N: 19.11/19.12.

2b: m.p.: 123–125°C; yield: 89%; ^1H NMR ($CDCl_3$, 200.13 MHz): 0.82 (t, 6H, C<u>H</u>$_3$-CH$_2$); 2.22 (s, 3H, C<u>H</u>$_3$); 2.85 (t, 4H, CH$_3$-C<u>H</u>$_2$; $^3J_{P-H}$ = 9.1 Hz); 4.55 (m, 2H, Py–C<u>H</u>$_2$); 6.90–8.95 (m, 9H, aromatics), 11.50 (br, 1H)-^{13}C NMR ($CDCl_3$, 50.32 MHz): 13.9; 14.2; 24.6; 40.1; 40.5; 52.5; 109.1–129.3; 133.5; 136.9; 144.4; 151.5; 160.9-^{31}P NMR ($CDCl_3$, 80.6 MHz): 79.8. Elemental analysis (calculated/found): C: 62.11/62.08; H: 6.58/6.55; N: 22.87/22.85.

TABLE I Synthesized Triazaphosphorines

Substrate	R^1	R^2	$\delta^{31}P$
2a	Me	Ph-CH$_2$	80.0
2b	Me	Py-CH$_2$	79.8
2c	Me	Ph-CH-CH$_3$	79.1
2d	Me	Ph	79.3
2e	Et	Fu-CH$_2$	79.5
2f	Et	Ph	80.9
2g	Et	*n*-Bu	79.1

2c: m.p.: 144–146°C; yield: 95%; ^{1}H NMR ($CDCl_3$, 200.13 MHz): 0.80 (t, 6H, $C\underline{H}_3$-CH_2); 1.38 (d, 3H, $C\underline{H}_3$,); 2.30 (s, 3H, $C\underline{H}_3$); 2.85 (t, 4H, CH_3—$C\underline{H}_2$; $^{3}J_{P-H} = 9.3$ Hz); 4.11 (q, H, CH_3—$C\underline{H}$); 7.00–7.95 (m, 9H, aromatics), 11.88 (br, 1H)-^{13}C NMR ($CDCl_3$, 50.32 MHz): 14.1; 14.2; 21.8; 39.4; 39.8; 42.9; 109.6–127.3; 137.3; 138.6; 141.9; 153.1; 162.1 - ^{31}P NMR ($CDCl_3$, 80.6 MHz): 79.1. Elemental analysis (calculated/found): C: 66.29/66.31; H: 7.17/7.15; N: 18.41/18.38.

2d: m.p.: 129–131°C; yield: 79%; NMR: ^{1}H: 0.79 (t, 6H, $C\underline{H}_3$-CH_2); 2.10 (s, 3H); 2.85 (t, 4H, CH_3-$C\underline{H}_2$; $^{3}J_{P-H} = 9.2$ Hz); 7.14–7.75 (m, 9H); 11.20 (br, 1H).^{13}C: 14.0; 14.2; 24.93; 39.2; 39.5; 109.5–129.2; 130.1; 133.3; 141.4; 143.6; 150.9; 159.3. ^{31}P: 79.3. Elemental analysis (calculated/found): C: 64.76/64.71; H: 6.58/6.50; N: 19.87/19.92.

2e: m.p.: 112–114°C; yield: 86%; NMR: ^{1}H: 0.84 (t, 6H, $C\underline{H}_3$-CH_2); 1.22 (t, $C\underline{H}_3$-CH_2); 2.30 (q, CH_3—$C\underline{H}_2$); 2.82 (d, 4H, $^{3}J_{P-H} = 9.0$ Hz); 3.82 (s, 2H); 6.37 (d, 1H); 7.24–7.72 (m, 6H); 11.80 (br, 1H). 13C: 10.9; 14.1; 14.2; 29.20; 38.3; 38.6; 40.7; 106.6–129.3; 140.3; 155.1; 164.0. ^{31}P: 79.5. Elemental analysis (calculated/found): C: 61.61/61.59; H: 6.80/6.74; N: 18.91/19.02; O: 4.32/4.35.

2f: m.p.: 151–153°C; yield: 97%; NMR: ^{1}H: 0.80 (t, 6H, $C\underline{H}_3$-CH_2); 1.21 (t, $C\underline{H}_3$-CH_2); 2.33 (q, CH_3-$C\underline{H}_2$); 2.80 (d, 4H, $^{3}J_{P-H} = 9.0$ Hz); 7.00–7.82 (m, 9H); 11.58 (br, 1H). ^{13}C: 11.2; 14.1; 14.2; 28.9; 38.3; 38.6; 107.1–124.3; 131.1; 140.9; 144.2; 146.7; 1490.8; 159.1. ^{31}P: 80.9. Elemental analysis (calculated/found): C: 65.59/65.56; H: 6.88/6.91; N: 19.11/19.09.

2g: m.p.: 118–120°C; yield: 91%; NMR: ^{1}H: 0.95 (t, 6H, $C\underline{H}_3$-CH_2); 1.06 (t, 3H, $C\underline{H}_3$-CH_2); 1.21 (t, $C\underline{H}_3$-CH_2); 1.33 (m, 2H, CH_3-$C\underline{H}_2$-CH_2); 1.55 (m, 2H, CH_2-$C\underline{H}_2$-CH_2); 2.33 (q, CH_3—$C\underline{H}_2$); 2.57 (m, 2H, $C\underline{H}_2$-N); 2.91 (d, 4H, $^{3}J_{P-H} = 9.0$ Hz); 7.24–7.52 (m, 4H); 11.28 (br, 1H). ^{13}C: 9.2; 13.7; 14.1; 14.2; 20.1; 25.3; 31.4; 38.2; 38.6; 39.7; 115.2–126.0; 137.9; 138.8; 143.5; 162.1. ^{31}P: 79.1. Elemental analysis (calculated/found): C: 62.59/62.41; H: 8.17/8.44; N: 20.27/20.22.

REFERENCES

[1] T. Kaukorat, I. Neda, A. Fischer, P. G. Jones, and R. Schmutzler, *Chem. Ber.*, **126,** 1265 (1993).

[2] R. Gast, T. Kaukorat, I. Neda, and R. Schmutzler, *Z. Naturforsch.*, **48B,** 867 (1993).

[3] I. Neda, M. Farkens, A. Fischer, P. G. Jones, and R. Schmutzler, *Z. Naturforsch.*, **48B,** 443 (1993).

[4] V. A. Pinchuk, I. Neda, C. Müller, H. Thönnessen, P. G. Jones, and R. Schmutzler, *Z. Naturforsch.*, **51B,** 1494 (1996).

[5] A. Schmidpeter and C. Weingand, *Angew. Chem. Int. Ed. Engl.,* **10,** 397 (1971).

[6] J. Ebeling, M. Avitabile Leva, H. Stary, and A. Schmidpeter, *Z. Naturforsch.*, **26B,** 650 (1971).

[7] R. Abderrahim, B. Baccar, and M. L. Benkhoud, *Phosphorus, Sulfur, and Silicon*, **177,** 1033 (2002).
[8] N. Raouafi, K. Boujlel, and M. L. Benkhoud, *Phosphorus, Sulfur, and Silicon*, **179,** 1387 (2004).
[9] L. A. Cates and V. S. Li, *J. Pharm. Sci.,* **71,** 308 (1982).
[10] L. Garuti, M. Roberti, D. Pizzirani, A. Pession, E. Leoncini, V. Cenci, et al., *Il Farmaco*, **59,** 663 (2004).
[11] M. Farkens, PhD Thesis, T. U. Braunschweig, Germany, 1994.
[12] I. Neda, A. Fischer, P. G. Jones, and R. Schmutzler, *Phosphorus, Sulfur, and Silicon*, **78,** 271 (1993).
[13] A. J. Kolka, *U.S. Patent n°* 2.866.809, (1958).
[14] K. A. Petrov, G. A. Sokolsky, and B. M. Polees, *Zh. Obshch. Khim.*, **26,** 3681 (1956).
[15] K. A. Petrov, A. A. Neimysheva, M. G. Fomenko, L. M. Chernushevich, and A. D. Knuntsevich, *Zh. Obshch. Khim.*, **31,** 516 (1961).
[16] R. G. Cavell, *J. Chem. Soc*., 1992, 1964.