A new and convenient method for the synthesis of strong non-ionic bases†

Marc Taillefer,* Nicolas Rahier, Aurélien Hameau and Jean-Noël Volle*

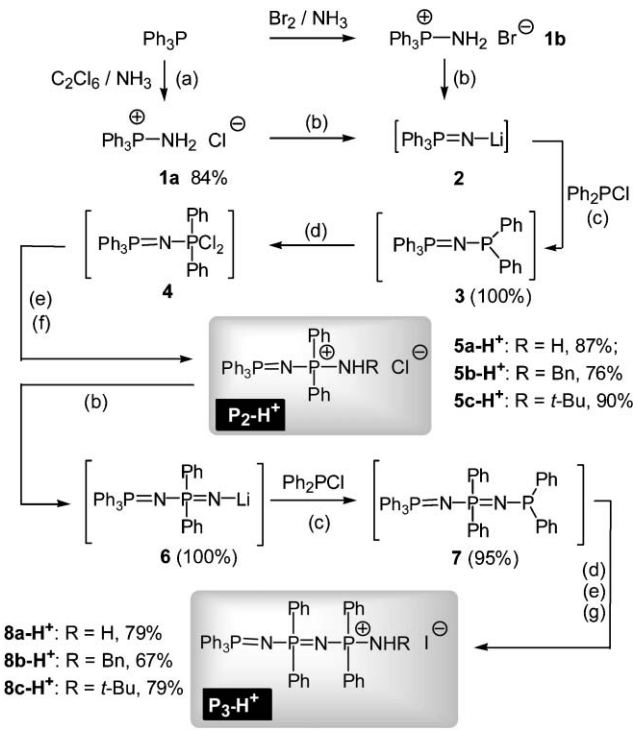
Received (in Cambridge, UK) 18th April 2006, Accepted 12th June 2006
First published as an Advance Article on the web 28th June 2006
DOI: 10.1039/b603677e

Various strong non-ionic phosphazene bases were obtained by a new, efficient and very simple method involving the lithium phosphonium azayldiide Ph_3P=NLi (2) as a precursor.

Commercial nitrogenous non-ionic organic bases such as, for example, triethylamine (TEA), or 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) have often been used as catalysts or deprotonating reagents. However, because their application fields have been limited by their relatively weak basicity, many investigations have been led during the last two decades in order to obtain non-ionic and very strong bases. This research has resulted in the disclosure of nitrogenous and phosphorus non-ionic bases called phosphazenes (Schwesinger's bases[1]) and proazaphosphatranes (Verkade's base[2]). These structures revealed high basicities[1d–2d] and have become a credible alternative to strong ionic bases as *t*-BuOK, NaH, LDA, LTMP, NaHMDS or BuLi.[2c,d,3]

As part of our studies on metallated diylides[4] and diazaylides[5] exhibiting a high nucleophilicity, we recently became interested in the reactivity of the lithium azayldiide Ph_3P=NLi (**2**)[6] (isoelectronic with the methylide Ph_3P=CHLi)[7] towards various and commercially available phosphorus electrophiles. Related to that subject, we report herein a new method for the preparation of various non-ionic and very strong phosphazene type bases ($P_{2\text{–}3\text{–}4}$, Scheme 3) and of their corresponding acids ($P_{2\text{–}3\text{–}4}$–H^+, Scheme 1,2). Our protocol displays several important features such as the use of a unique starting reagent (the phosphonium salt **1**) and the implementation of a simple and convenient procedure for the synthesis of these compounds.

We were first interested in the acquisition of the protonated phosphazene bases P_2–H^+ and linear P_3–H^+ (Scheme 1). As a preliminary we perfected a new and useful method for the synthesis of the phosphonium salt **1**, precursor of Ph_3P=NLi and starting reagent for all the syntheses described herein. In the past, we showed that Ph_3P=NLi could be prepared by double deprotonation of aminotriphenylphosphonium bromide salt **1b** but the synthesis of the latter, however, required the use of harmful and unpractical bromine (Scheme 1). In order to minimize these drawbacks, we have here tested hexachloroethane because of its easier handling. We could thus obtain from triphenylphosphine and C_2Cl_6 the formation of a dichlorophosphorane species, which was trapped with gaseous ammonia to give the expected aminotriphenylphosphonium chloride **1a** (Scheme 1, isolated yield: 84%).

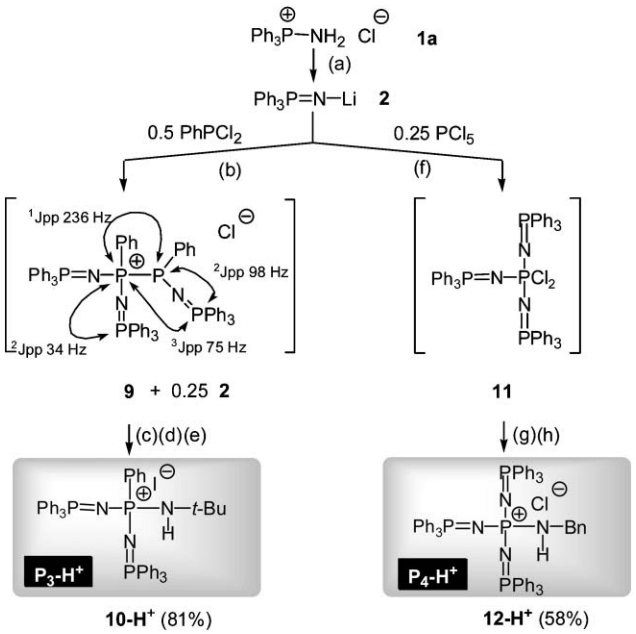


Scheme 1 Reagents and conditions for synthesis of $P_{2/3}$–H^+: (a) (1) 1.1 C_2Cl_6, THF, 25 °C, 2 h; (2) NH_3, −25 °C to RT; (b) 2 *n*-BuLi, THF, −20 °C, 30 min; (c) 1.1 Ph_2PCl, −20 °C to RT; (d) 1.1 C_2Cl_6, 25 °C, 2 h; (e) 4 RNH_2, reflux, 2 h (R = H, 25 °C); (f) NaCl (10%), H_2O; (g) NaI (5%), H_2O.

Ph_3P=NLi was then generated by double deprotonation of **1a**, and revealed a strong reactivity towards chlorodiphenylphosphine. Indeed, after few minutes at −20 °C, it gave quantitatively the *N*-diphenylphosphino-*P*,*P*,*P*-triphenylphosphinimide **3**,[8] identified by ^{31}P NMR {THF: δ (ppm) 40.43 (d, J = 103 Hz, *P*–Ph), 16.81 (d, J = 103 Hz, *P*=N)} (Scheme 1(c)). The latter was treated *in situ* with hexachloroethane (Scheme 1(d)), and subsequently with an alkylamine or gaseous ammonia (Scheme 1(e)). This one-pot strategy gave the structures P_2–H^+ (**5a–c–H$^+$**), precursors of the corresponding P_2 bases, with a yield of 76–90%. According to a similar method, we showed that it was possible to gain a direct access to linear P_3–H^+. Indeed, the phosphonium species P_2–H^+ could also be quantitatively deprotonated in presence of *n*-butyllithium to give the corresponding lithiophosphinimide intermediate **6** {^{31}P NMR, THF: δ (ppm) −5.28 (d, J = 6.0 Hz,

Architectures Moléculaires et Matériaux Nanostructurés, UMR CNRS 5076, Ecole Nationale Supérieure de Chimie de Montpellier, F-34296, Montpellier, France. E-mail: marc.taillefer@enscm.fr; Fax: +33 (0)4 67 14 43 19; Tel: +33 (0)4 67 14 43 52

† Electronic supplementary information (ESI) available: Experimental procedures and physical data for each new compound. See DOI: 10.1039/b603677e



Scheme 2 (a) 2 *n*-BuLi, THF, −20 °C, 30 min; (b) 0.5 $PhPCl_2$, THF, −20 °C to RT; (c) 1.1 C_2Cl_6, RT, 2 h; (d) 4 *t*-$BuNH_2$, reflux, 2 h; (e) NaI (5%), H_2O; (f) 0.25 PCl_5, −65 °C, 1 h and 25 °C, 12 h; (g) $BnNH_2$, 100 °C, 4 h; (h) NaCl (10%), H_2O.

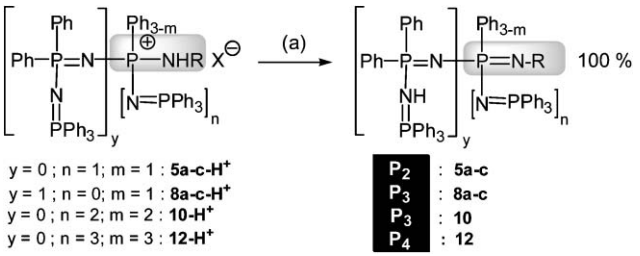
1P), −14.88 (s br, 1P)}. This was then trapped with a slight excess of chlorodiphenylphosphine to generate almost quantitatively after few minutes, the linear P_3 phosphazene **7** {^{31}P NMR, THF: three peaks (relative area 1 : 1 : 1): δ (ppm) 37.84 (d, $^2J_{pp}$ = 114.4 Hz), 11.91 (d, $^2J_{pp}$ = 1.6 Hz), 10.89 (dd, $^2J_{pp}$ = 114.4 Hz, $^2J_{pp}$ = 1.6 Hz, N–*P*=N)}. Finally, after a treatment with C_2Cl_6, followed by an amine, the desired P_3–H^+ salts (**8a–c–H$^+$**), precursors of the expected linear P_3 bases, were isolated in 67–79% yields.

We were also interested in the synthesis of branched bases P_3 (iso structure of **8**) and P_4, potentially more basic than the linear P_2 and P_3 phosphazenes.[1d] In order to obtain the corresponding protonated bases, the quenching of Ph_3P=NLi with half an equivalent of dichlorophenylphosphine was first performed. Following the procedure used for P_2 and linear P_3 structures we could thus synthesise without any difficulty the expected precursor P_3–H^+ salt (**10–H$^+$**, yield 81%) (Scheme 2).[9]

Following another method, we also observed that Ph_3P=NLi could substitute three chlorine atoms from PCl_5 (0.25 equiv.) to form the branched P_4–H^+ salt **12–H$^+$** (Scheme 2). The addition of electrophile was performed at very low temperature (−65 °C) in order to minimize the formation of by-products, the precipitate **11** being recovered by filtration {^{31}P, DMSO-d_6: δ (ppm) 12.71 (s, 3P), −3.28 (s, 1P)} and subsequently treated without any other purification with benzylamine to give **12–H$^+$** (isolated yield 58%).

Finally, the corresponding bases were prepared *in situ* in dimethyl sulfoxide (or DMSO-d_6) by deprotonation of the corresponding salts with sodium hydride for the P_2 and P_3 series and sodium amide for the P_4 structure (Scheme 3). All the bases were quantitatively obtained and analyzed by ^{1}H, ^{13}C and ^{31}P NMR.

In other respects, determination in DMSO of the acid–base equilibria was performed with couples **5c/5c–H$^+$**, **8c/8c–H$^+$** and **10/10–H$^+$**, on the basis of an overlapping indicator method.[10] The



Scheme 3 (a) *n* = 0, 1 and 2; 1 NaH, DMSO, vacuum (30 Torr), 25 °C, 1 h; (b) *n* = 3, 1.5 $NaNH_2$, DMSO, 25 °C, 1 h.

first equilibrium acidity corresponds to a $^{DMSO}pK_a$ of 18.0 ± 0.5 (**5c–H$^+$**), the second to a $^{DMSO}pK_a$ of 19.8 ± 0.5 (**8c–H$^+$**), and the last to a $^{DMSO}pK_a$ of 23.6 ± 0.5 (**10–H$^+$**). It is worthy of note that these high pK_a values are slightly weaker than those reported by Schwesinger for the corresponding bases, probably owing to the different nature of the phosphorus substituents.

In conclusion, with these preliminary, results we have developed from Ph_3P=NLi[6] a new, efficient and simple method for the synthesis of various strong non-ionic bases. Work is now in progress to extend this new method to the synthesis of still stronger bases with the use of other azayldiides and phosphorus halides, R_3P=NLi and R'_xPCl_y (R, R′ = NMe_2 or *tert*-butyl), respectively.

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9 **9** is proposed as an intermediate; ^{31}P NMR {THF–DMSO-d_6: δ 51.49 (dd, $^1J_{P=P}$ = 236, 98 Hz, 1P); 21.67 (dd, *J* = 98.1, 75.2 Hz, 1P); 17.56 (ddt, $^1J_{P-P^+}$ = 236.5, 75.2, 34.3 Hz, 1P); 11.16 (d, *J* = 34.3 Hz, 1P); 10.85 (d, *J* = 34.8 Hz, 1P). For such a $^1J_{P=P}$ value see: R. W. Alder, D. D. Ellis, R. Gleiter, C. J. Harris, H. Lange, A. G. Orpen, D. Read and P. N. Taylor, *J. Chem. Soc., Perkin Trans. 1*, 1998, 1657. Another indication of the existence of **9** is the presence in the mixture of the expected corresponding unreacted 0.25 equivalent of Ph_3P=NLi.
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