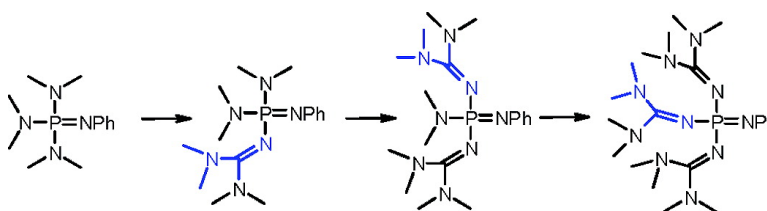


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Guanidinophosphazenes: Design, Synthesis, and Basicity in THF and in the Gas Phase

Alexander A. Kolomeitsev,^{*,†} Ilmar A. Koppel,^{*,‡} Toomas Rodima,[‡] Jan Barten,[§] Enno Lork,[†] Gerd-Volker Röschenhaler,[†] Ivari Kaljurand,[‡] Agnes Kütt,[‡] Ivar Koppel,[‡] Vahur Mäemets,[‡] and Ivo Leito^{*,‡}

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Abstract: A principle for creating a new generation of nonionic superbases is presented. It is based on attachment of tetraalkylguanidino, 1,3-dimethylimidazolidine-2-imino, or bis(tetraalkylguanidino)carbimino groups to the phosphorus atom of the iminophosphorane group using tetramethylguanidine or easily available 1,3-dimethylimidazolidine-2-imine. Seven new nonionic superbasic phosphazene bases, tetramethylguanidino-substituted at the P atom, have been synthesized. Their base strengths are established in tetrahydrofuran (THF) solution by means of spectrophotometric titration and compared with those of eight reference superbases designed specially for this study, P₂- and P₄-iminophosphoranes. The gas-phase basicities of several guanidino- and N,N,N',N'-tetramethylguanidino (tmg)-substituted phosphazenes and their cyclic analogues are calculated, and the crystal structures of (tmg)₃P=N-t-Bu and (tmg)₃P=N-t-Bu·HBF₄ are determined. The enormous basicity-increasing effect of this principle is experimentally verified for the tetramethylguanidino groups in the THF medium: the basicity increase when moving from (dma)₃P=N-t-Bu (pK_a = 18.9) to (tmg)₃P=N-t-Bu (pK_a = 29.1) is 10 orders of magnitude. A significantly larger basicity increase (up to 20 powers of 10) is expected (based on the high-level density functional theory calculations) to accompany the similar gas-phase transfer between the (dma)₃P=NH and (tmg)₃P=NH bases. Far stronger basicities still are expected when, in the latter two compounds, all three dimethylamino (or tetramethylguanidino) fragments are replaced by methylated triguanide fragments, (tmg)₂C=N-. The gas-phase basicity (around 300–310 kcal/mol) of the resulting base, [(tmg)₂C=N-]₃P=NH, having only one phosphorus atom, is predicted to exceed the basicity of (dma)₃P=NH by more than 40 powers of 10 and to surpass also the basicity of the widely used commercial [(dma)₃P=N]₃P=N-t-Bu (t-BuP₄) superbase.

Introduction

Organic chemists routinely face the crucial problem of selecting the appropriate base for the reaction to be performed. Although uncharged organic bases are usually weaker than their inorganic counterparts, i.e., alkali-metal hydroxides, oxides, and alkoxides, they have become widely used standard reagents in organic synthesis. They offer several advantages over the ionic bases, such as milder reaction conditions, better solubility, and absence of a coordinating metal ion.¹ In the past decade, particular attention has been focused on the computational design and preparation of neutral organic superbases and proton sponges.^{2–4} The cation-free strong neutral bases are strong

nonionic systems, allowing the deprotonation of a wide range of weak acids, to give highly reactive weakly coordinated “naked” anions.

In this respect, the strong and hindered bases of the families of cyclic amidines,⁵ phosphatranes,⁶ and phosphazenes are of special interest for general and synthetic organic chemistry.⁷

The first representative of a phosphazene base was prepared by Issleib in the 1970s.^{8a} Subsequently, a simple, molar-scale

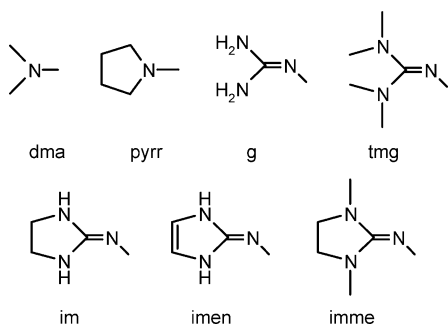
[†] University of Bremen.

[‡] University of Tartu.

[§] Hansa Fine Chemicals GmbH.

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Scheme 1. Designations of the Substituents^a

^a IUPAC names of the substituents: dma, dimethylamino; pyr, tetramethyleneamino; g, (diaminomethylene)amino; tmg, [bis(dimethylamino)methylene]amino; im, imidazolidin-2-ylideneamino; imen, 1,3-dihydro-2H-imidazol-2-ylideneamino; imme, (1,3-dimethylimidazolidin-2-ylidene)amino.

synthesis of tris(dialkylamino)iminophosphoranes and tris(dialkylamino)-*N*-alkyliminophosphoranes (the P₁ phosphazene bases (dma)₃P=N-R, see Scheme 1 for substituent designations) was developed by Marchenko et al.^{8,9} Furthermore, the homologization principle — the use of a (dma)₃P=N— ligand on phosphorus for synthesizing highly nucleophilic tris[tris(dimethylamino)phosphinimino]phosphine and -phosphine oxide — was introduced⁹ and later used⁷ for construction of a big family of extremely strong noncharged organic bases: P₁–P₅ phosphazene bases or iminophosphoranes, which are stronger bases than the well-known diazabicycloundecene (DBU) or triaza-bicyclodecene (TBD) bases.^{7,10,11}

These hydrolytically stable phosphazophosphazene bases, especially [(dma)₃P=N]₃P=N-*t*-Bu (*t*-BuP₄), immediately became rather useful organic reagents. Besides the enhanced basicity, they combine (i) high solubility in apolar to moderately polar organic solvents, (ii) easy handling and easier workup through cleaner reactions, (iii) low sensitivity to moisture and oxygen, and (iv) the possibility to operate at lower temperature and higher selectivity. There are many examples demonstrating the superiority of the polyaminophosphazenes¹ and polymer-supported polyaminophosphazene reagents^{1,12} over common inorganic and organic nitrogen bases in laboratory and industrial organic syntheses.

A relative self-consistent basicity scale in tetrahydrofuran (THF) medium has been created, now spanning 24 orders of magnitude.^{11,13} On going from phosphazenes with alkyl substituents, e.g., Me₃P=N-R, to amino-substituted phosphazenes, e.g., (dma)₃P=N-R, and especially to the phosphazo-substituted phosphazenes, e.g., [(dma)₃P=N]₃P=N-R, a significant enhancement in the gas-phase basicity has been predicted² and observed.¹¹

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However, the high cost and possible toxicity of the tris-(dimethylamino)iminophosphorane bases derived from the cytotoxic hexamethylphosphoramide (HMPTA) restrict the broad application of polyphosphazene bases. Also, as shown by Schwesinger,⁷ the progressive increase of the basicity of phosphazene bases with increasing number of phosphorus atoms levels out at $n \geq 5$.

In this paper we report a novel family of phosphazene bases — guanidinophosphazenes — designed by introduction of guanidino or substituted guanidino (cyclic or acyclic) fragments into the phosphazene structure (vide infra for detailed presentation of this approach). The structures of the studied guanidinophosphazenes are presented in Scheme 2 (see Scheme 3 for related bases and Scheme 1 for designations of substituents).

The tetramethylguanidino-substituted phosphine oxides, including the [(dma)₂C=N]₃P=O, which was prepared from POCl₃ and tetramethylguanidine (TMG), were synthesized by Terry and Borkovec.¹⁴ In contrast to HMPTA, the tmg-substituted phosphine oxides showed no insect chemosterilizing power. This led us to expect also the lower cytotoxicity for the tetraalkylguanidinophosphazenes, especially for imme derivatives.

Altogether 15 new superbasic phosphazene compounds (8 of them with tetraalkylguanidino substituents) and their HBF₄ or HBPh₄ salts were synthesized. Their basic strength in THF (and the basicity of the (tmg)₂(Et₂N)P=N-Ph in MeCN) was measured. The basicity of some related compounds in THF was also measured. The gas-phase basicities of several “classical” P₁–P₄ aminophosphazenes, open-chain acyclic guanidino- or tetramethylguanidino-substituted P₁ and P₂ phosphazenes, and their cyclic counterparts, substituted by the im, imen, and imme groups (see Scheme 1), were predicted computationally using the density functional theory (DFT) B3LYP approach with the 6-311+G** basis set. We also report the crystal structure data for the **8c** free base and **8c**·HBF₄.

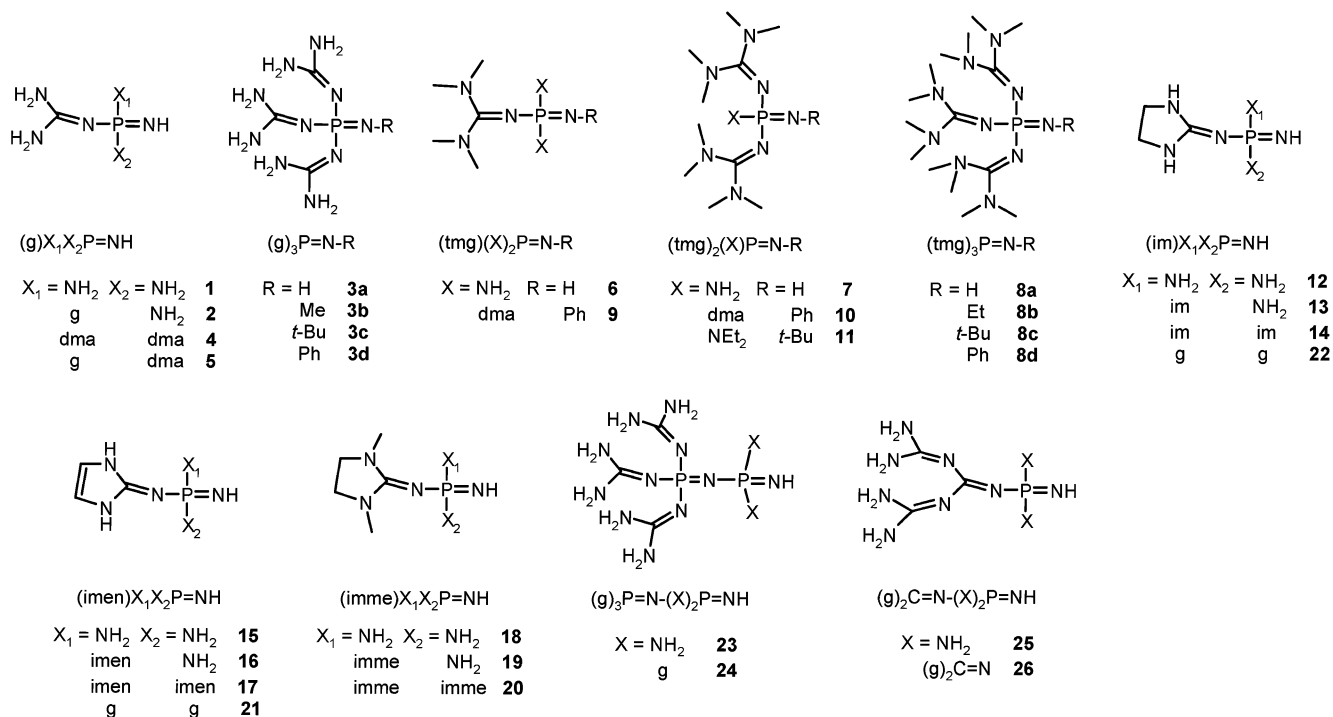
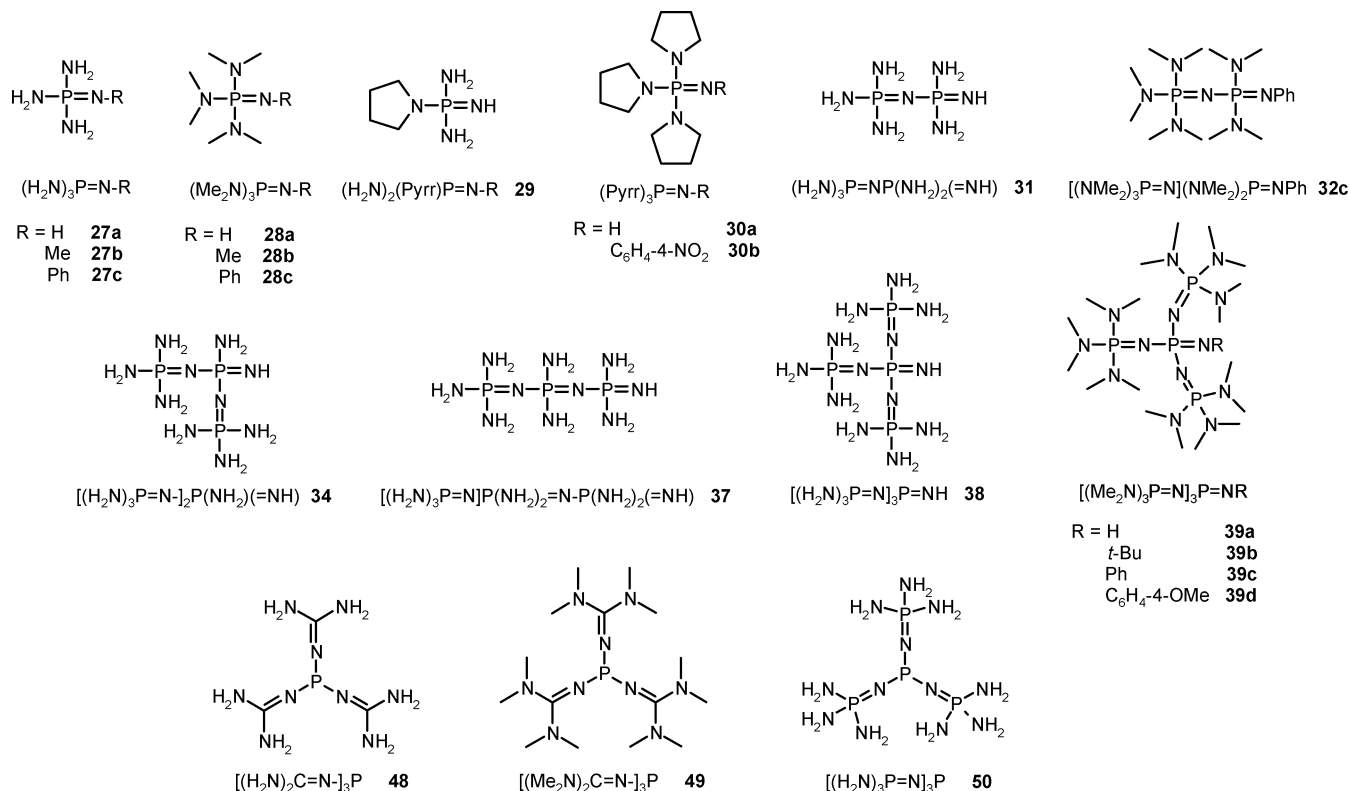
The Principle of Design of the New Family of Superbases

The main idea for construction of the new family of superstrong uncharged bases of the guanidinophosphazene type (Scheme 2) is to apply, instead of the cytotoxic dialkylamine and tris(dimethylamino)phosphazene, the strongly electron-donating and presumably less toxic¹⁵ tetramethylguanidino⁴ (tmg) and (1,3-dimethylimidazolidin-2-ylidene)amino (imme) fragments (see Scheme 1) as the building units and furthermore to synthesize acyclic and cyclic bis(tetraalkylguanidino)carbamines (triguanides) [(Alk₂N)₂C=N]₂C=NH for use as ligands on phosphorus.

TMG combines strong basic ($pK_{ip}(\text{THF}) = 17.0$, $pK_a(\text{THF}) = 15.5$)¹¹ and nucleophilic properties. Therefore, it is advantageous to apply this compound and its easily available cyclic analogue, 1,3-dimethylimidazolidine-2-imine (derived from nontoxic 1,3-dimethyl-2-imidazolidone), as building blocks for designing new cheap organic superbases for common use in organic synthesis.

To be synthetically useful, the organic superbase (along with having high intrinsic basicity) has to be a hydrolytically stable

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Scheme 2. Representative Structures of the Novel Guanidinophosphazenes**Scheme 3.** Structures of Some Related Bases

compound. This requirement also applies to its protonated form — the respective salt with a highly reactive “naked” anion (counterion). We assume that significant delocalization of the positive charge over the tmg groups due to the conjugation of guanidino moieties with either a phosphorus atom of guanidinophosphazene or a phosphonium center will reduce the electrophilic character of phosphorus, providing the respective bases and phosphonium salts with high hydrolytic stability. This

assumption is supported by our previous results on the use of TMG for synthesizing a new generation of robust phase-transfer (PT) catalysts with delocalized lipophilic cations (DLCs).¹⁶ The introduction of one electron-donating tmg group into carbonium

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or phosphonium centers and three tmg substituents to a sulfonium center provided cations with enhanced stability under extreme conditions (e.g., high temperature, strongly basic media, powerful nucleophiles).^{17,18} This led us to expect similar hydrolytic stability also for the tmg-substituted carbimines and phosphazenes.

Incorporation of amino groups into rings (e.g., pyrrolidinyl) has been demonstrated to enhance the basicity of phosphazene bases.^{7b} Thus, the guanidinophosphazenes derived from imidazolidine-2-imine (e.g., **12**, **13**, **14**, and **22**; see Scheme 2) or 1,3-dimethylimidazolidine-2-imine (e.g., **18–20**) could be even more potent (bases) compared to acyclic guanidinophosphazenes. The second reason for introduction of these subunits into the phosphazene structure is the low toxicity of 1,3-dimethylimidazolidinone, which is a potential final product of hydrolysis of 1,3-dimethylimidazolidine-2-imine or may be derived from guanidinophosphazenes.

Experimental Section

Synthesis. The Kirsanov and Staudinger reaction schemes were used for the synthesis of the guanidinophosphazene bases. A representative synthesis procedure is presented for (tmg)₃P=NH (**8a**). The syntheses of the rest of the new compounds are described in the Supporting Information.

(tmg)₃P=NH (8a). In a 1-L three-neck flask, equipped with a mechanical stirrer, a dropping funnel with a N₂ outlet, and a thermometer, were placed 40.1 g (192.8 mmol) of phosphorus pentachloride and 400 mL of dried chlorobenzene. The mixture was cooled to –30 °C and vigorously stirred. Then 135.0 g (1173.9 mmol) of tetramethylguanidine was added dropwise during 0.5 h at such a rate as to prevent the temperature from rising above –10 °C. The resulting slurry was kept at –30 °C for 1 h, allowed to warm to ambient temperature during 1 h, and then stirred for an additional 1 h at this temperature. The dropping funnel was replaced with a gas inlet, the mixture was cooled to –30 °C again, and an excess of NH₃ (10 g, 588.2 mmol) was added into the mixture with vigorous stirring at a rate that kept the temperature of the solution at –20 to –10 °C. The mixture was kept at this temperature for an additional 4 h. The solid (tetramethylguanidine hydrochloride and ammonium chloride) was filtered off and washed two times with chlorobenzene (2 × 50 mL), and the solvent was evaporated at reduced pressure (10^{–2} Torr) to dryness to leave a light yellow solid (imino-tris(tetramethylguanidino)phosphonium chloride). This solid was dissolved in water (200 mL), and a solution of 23.0 g (209.1 mmol) of NaBF₄ was added in one portion. The resulting (tmg)₃P=NH·HBF₄ (**8a**·HBF₄) was extracted with methylene chloride (3 × 100 mL). The solvent was removed in vacuo to give 90.1 g (98.2%) of colorless solid, mp 114–115 °C (from acetone/water).

¹H NMR (200.13 MHz, CDCl₃): δ 2.88 (s, 36H), 3.0 (s, 36H), 4.18 (s, 2H). ³¹P NMR (81.00 MHz, CDCl₃): δ –8.7 (s). ¹³C NMR (50.32 MHz, THF-*d*₆): δ 40.5, 160.5. ¹⁹F NMR (188.31 MHz, CDCl₃): δ –151.1. HRMS (FAB+): calcd for C₁₅H₃₈N₁₀P, 389.30185; found, 389.30028.

Anal. Calcd for C₁₅H₃₈N₁₀P: C, 37.83; H, 8.04; N, 29.41. Found: C, 37.38; H, 7.93; N, 28.62.

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The free base was prepared according to the general procedure described below. To 15.9 g (33.4 mmol) of **8a**·HBF₄ was added 33.4 mL of a 1 M solution of *t*-BuOK. The raw product — a yellow oil — was recrystallized from hexane at –30 °C to give 11.3 g (87%) of colorless crystals, mp 101–102 °C (in a sealed capillary).

³¹P NMR (81.00 MHz, C₆D₆): δ 7.4. ¹H NMR (200.13 MHz, C₆D₆): δ 2.74 (s, 36H), 1.42 (1H). ¹³C NMR (50.32 MHz, C₆D₆): δ 40.2, 157.7. HRMS (ED): calcd for C₁₅H₃₇N₁₀P, 388.29404; found, 388.29273.

General Procedure for the Liberation of Phosphazene Bases from Their HBF₄ or HBPh₄ Salts. The corresponding salts of **8d**, **9**, **10**, and **31–33** bases were dissolved in as small an amount as possible of dry MeOH (or in a mixture of MeOH with MeCN or THF), and the calculated amount of 30% MeOK in MeOH was added. In the cases of **8a**, **8b**, **8c**, and **11**, the corresponding salts were dissolved in dimethoxyethane (DME) or suspended in THF and the calculated amount of *t*-BuOK in DME was added at reduced temperature. The mixture was stirred, and the temperature was allowed to rise to room temperature. The solid (KBF₄ or KBPh₄, respectively) was filtered off in a glovebox or by use of a Schlenk-type filter. The volatile components were removed under reduced pressure, and the residue was extracted with dry hexane. The extract was filtered, hexane was removed in vacuo, and the residue was dried under high vacuum.

Spectra. The NMR spectra were recorded on a Bruker AC-200 NMR spectrometer. Standard 5-mm NMR tubes were used for the measurements, except for those of the samples of the free phosphazene bases, which were prepared in the glovebox under an Ar atmosphere in special NMR tubes with screwable stoppers. TMS was added as the internal standard.

The mass spectra were recorded on an Agilent 1100 Series LC-MSD Trap-XCT instrument.

X-ray Crystallography. X-ray-quality crystals of **8c** and **8c**·HBF₄ were grown from hexane at –30 °C and from water, respectively. They were mounted on a glass fiber with KEL-F oil, and data were collected on a Siemens P4 diffractometer at a temperature of 173 K. Structures were determined using direct methods with the SHELX program package. The full crystallographic tables are included in the Supporting Information. The most important pieces of evidence for the increasing extent of delocalization of tmg groups with phosphorus atom on going from **8c** to **8c**·HBF₄ are given below.

(tmg)₃P=N-*t*-Bu (8c). All three guanidine centers, C(1), C(6), and C(11), are almost trigonal planar (Σ ≤ 360°). The average P–N–C–N torsion angle (30.2°) for the evaluation of planarity at the C–N double bond indicates a deviation of the C–N double bond from the expected planar geometry. In agreement with this trend are the angles P1–N1–C1, 134.5°, P1–N7–C11, 127.8°, and P1–N10–C16, 129.13° (average P–N–C angle of 130.5°), which are greater than the angle expected for sp²-hybridized nitrogen. Meanwhile, there is still a distinct difference in bond lengths between guanidine C–N double bonds on one hand and the distances from carbon atoms of the guanidine imino group, C(1), C(6), and C(11), to the nitrogen atoms on the periphery, N(2), N(3), N(5), N(6), N(8), and N(9) (average 138.3 pm), on the other hand. An ORTEP diagram of the molecular structure of **8c** is shown in Figure 1.

(tmg)₃P=N-*t*-Bu·HBF₄ (8c·HBF₄). The position of the proton was taken from the difference Fourier map and refined isotropically. Its location on the former phosphoimino nitrogen is in accordance with the observation of the ²J_{PH} constant in the ¹H and ³¹P NMR spectra. For the protonated **8c**, only a slight deviation from tetrahedral arrangement of the phosphorus atom was revealed. On protonation of the free base **8c**, the bonds between C1, C6, C11 and N1, N4, N7, respectively, of the imino groups became elongated. In contrast to the neutral form, the average C–N guanidine double bond lengths (131.2 pm) in the protonated form became more similar to the average bond length (136.5 pm) between the C1, C6, and C11 carbons and the nitrogens of the NMe₂ groups. These observations imply significant

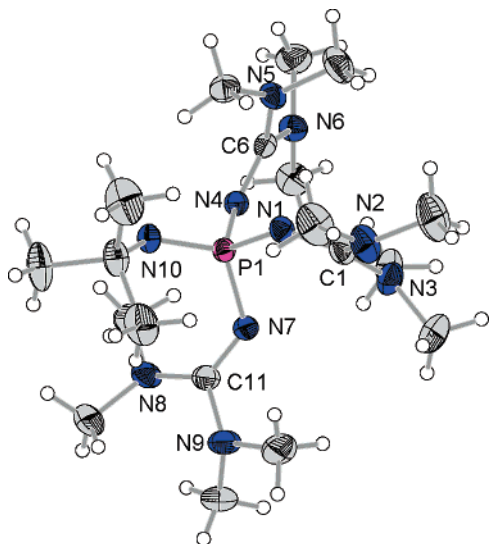


Figure 1. Molecular structure of $[(\text{dma})_2\text{C}=\text{N}]_3\text{P}=\text{N}-\text{Bu}-t$ (**8c**) with 50% thermal ellipsoids.

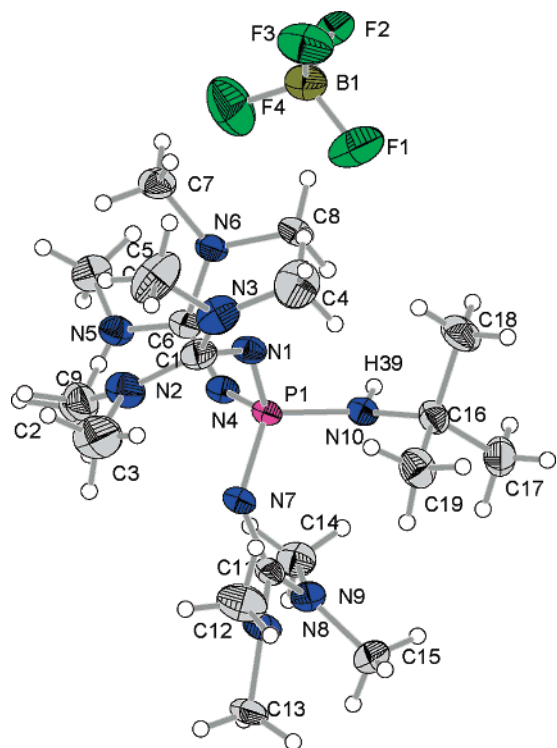
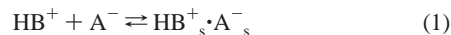


Figure 2. Molecular structure of $[(\text{dma})_2\text{C}=\text{N}]_3\text{P}^+-\text{N}(\text{H})\text{Bu}-t \text{ BF}_4^-$ (**8c**· HBF_4) with 50% thermal ellipsoids.

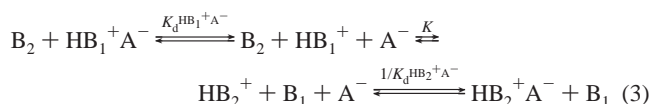
delocalization of positive charge in the protonated **8c** over the three tmg groups due to conjugation of guanidino moieties with the phosphonium center. Therefore, the P–N bonds to guanidino groups [P1–N1 163.3(2), P1–N4 162.0(2), P1–N7 161.9(2) pm, average 162.4 pm] reveal partial double bond character. An ORTEP diagram of the molecular structure of **8c**· HBF_4 is shown in Figure 2.

pK_{ip} Measurements. The spectrophotometric titration method and calculation methods used in this work are the same as those described earlier,¹³ i.e., the simultaneous titration of two free bases of comparable basicity in THF solution and mathematical treatment of the spectral data. The measurements are relative, i.e., the basicity difference (expressed either as ΔpK_{ip} or ΔpK_{α}) between the two bases is obtained. In THF – a moderately polar solvent ($D = 7.47$) – the ions are not

fully dissociated even at very low concentrations, and both solvent-separated (eq 1) and contact (eq 2) ion pairs are formed:



In the framework of our method, the following equilibrium between two bases B_1 and B_2 is studied:



The K_d 's are the dissociation constants of the respective ion pairs. The directly measured quantity is the relative ion-pair basicity – ΔpK_{ip} – of bases B_1 and B_2 . It is expressed as follows:

$$\begin{aligned} \Delta pK_{\text{ip}} &= pK_{\text{ip}}(\text{HB}_2^+ \text{A}^-) - pK_{\text{ip}}(\text{HB}_1^+ \text{A}^-) \\ &= \log \frac{K K_d^{\text{HB}_1^+ \text{A}^-}}{K_d^{\text{HB}_2^+ \text{A}^-}} = \log \frac{a(\text{HB}_2^+ \text{A}^-) a(B_1)}{a(\text{HB}_1^+ \text{A}^-) a(B_2)} \quad (4) \end{aligned}$$

The K_d values were estimated using the Fuoss equation as described in refs 13 and 19. Ionic radii are given in Table S1 in the Supporting Information.

Using the K_d values, the pK_{α} (an estimate of the pK_a) can be found as follows:

$$\Delta pK_{\alpha} = pK_{\alpha}(\text{HB}_2^+) - pK_{\alpha}(\text{HB}_1^+) = \Delta pK_{\text{ip}} - \log \frac{K_d^{\text{HB}_1^+ \text{A}^-}}{K_d^{\text{HB}_2^+ \text{A}^-}} \quad (5)$$

The preparation of solutions and measurements were carried out in a professional glovebox under an argon atmosphere, where the contents of O_2 and H_2O were less than 1 ppm. Individual concentrations of bases in the mixtures were $(1.7\text{--}4.9) \times 10^{-5}$ M, and the overall concentration of bases never exceeded 8.5×10^{-5} M.

Solutions of methanesulfonic acid and $[(\text{dma})_3\text{P}=\text{N}](\text{dma})_2\text{P}=\text{N}-\text{Et}$ or $[(\text{dma})_3\text{P}=\text{N}]_3\text{P}=\text{N}-t\text{-Bu}$ were used as acidic and basic titrants, respectively. The measurements were carried out in an external cell compartment, situated in the glovebox. The cell compartment was connected to the UV–vis spectrophotometer by means of two quartz fiber-optic cables. Further details of the measurement method can be found in the Supporting Information.

NMR pK_{ip} Determination. The standard 1D ^1H and proton-decoupled ^{13}C NMR spectra were recorded on a Bruker AC-200 NMR spectrometer at 200.13 and 50.34 MHz, respectively. Solutions (~ 0.1 M) were prepared and sealed in 5-mm NMR tubes. Chemical shifts were determined relative to TMS as an internal standard. The NMR spectra of phosphazenes and the method used for determination of their ΔpK_{ip} in THF were analogous to the corresponding NMR spectra and ΔpK_a calculations applied for phosphazenes in acetonitrile.²⁰ The ΔpK_{ip} values of phosphazenes were determined using an approximately equimolar mixture of phosphazene and indicator in THF. There is a fast (on the NMR time scale) exchange between phosphazene and the indicator base and their acid forms, leading to the coalescence of NMR lines in the ^{13}C and ^1H NMR spectra. Correspondingly, the chemical shifts of these forms were determined separately from the single-component THF solutions of these species. The ΔpK_{ip} values were calculated as was done previously with ΔpK_a values.²⁰

(19) Abdur-Rashid, K.; Fong, T. P.; Greaves, B.; Gusev, D. G.; Hinman, J. G.; Landau, S. E.; Lough, A. J.; Morris, R. H. *J. Am. Chem. Soc.* **2000**, *122*, 9155–9171.

(20) Rodima, T.; Mäemets, V.; Koppel, I. *J. Chem. Soc., Perkin Trans. 1* **2000**, 2637–2644.

The indicator ratios were calculated (eqs 6 and 7) from chemical shifts of the individual species (both neutral and protonated forms of the bases) and their averaged values in the mixtures containing both forms:

$$\frac{a(\text{HB}_2^+\text{A}^-)}{a(\text{B}_2)} = \frac{\delta_{\text{B}_2} - \delta}{\delta - \delta_{\text{HB}_2^+\text{A}^-}}$$

$$\frac{a(\text{B}_1)}{a(\text{HB}_1^+\text{A}^-)} = \frac{\delta - \delta_{\text{B}_1}}{\delta_{\text{HB}_1^+\text{A}^-} - \delta} \quad (7)$$

In the case of alkylphosphazenes, the differences in the ^{13}C chemical shifts for the alkyl substituents between the free phosphazene base and the protonated form were markedly lower than the corresponding differences for the aryl carbons of arylphosphazenes²⁰ and were in the range of 3–6 ppm for the ones measured. In the case of arylphosphazenes, this difference was up to 14.5 ppm for the C1 carbon of the substituent.

Computations. The quantum-chemical computations reported in this work were carried out using the Gaussian 03 series of programs.²¹ DFT calculations were performed using the B3LYP hybrid functional. Full geometry optimizations and vibrational analyses were performed using the 6-311+G** basis set. This approach has been demonstrated by some of us to describe, with reasonable accuracy, the gas-phase basicities^{2,22} and acidities²² of a wide variety of relatively simple molecules. All stationary points were found to be true minima ($N_{\text{imag}} = 0$). Unscaled B3LYP 6-311+G** frequencies were used to calculate the gas-phase basicities and proton affinities of the neutral bases, taking into account the zero-point frequencies, the finite temperature 0–298 K correction, the pressure–volume work term, and the entropy term as appropriate. The terms gas-phase basicity (GB) and proton affinity (PA) refer to the following equilibrium:



GB and PA are defined as follows:

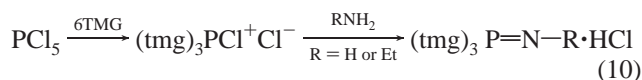
$$\text{GB} = -\Delta G_b \quad \text{PA} = -\Delta H_b \quad (9)$$

Results and Discussion

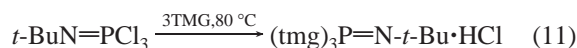
Synthesis. The interaction of primary and secondary amines with phosphorus pentachloride is a well-studied process.^{7b} Depending on the ratio of the reactants and the steric hindrance of the amine, either tris(alkylamino)chlorophosphonium chloride or tetrakis(alkylamino)phosphonium chloride was synthesized. It has been shown that the reaction of PCl_5 with tetramethyl-*N*-trimethylsilylguanidine afforded bis(tetramethylguanido)-dichlorophosphonium chloride.²³ In a more recent publication, a possibility to generate tris(guanidino)chlorophosphonium chloride in 60% yield from $\text{Me}_3\text{Si-TMG}$ was mentioned, but no characterization data for the compound were given.²⁴

We have found that PCl_5 reacts exothermically with an excess of TMG in methylene chloride, toluene, or chlorobenzene at -30°C to give $(\text{tmg})_3\text{PCl}^+\text{Cl}^-$ (see also ref 23b) as the only phosphorus-containing product (^{31}P NMR: -17.1 ppm). This

salt is a key precursor for preparation of the HCl or HBF_4 salts of $(\text{tmg})_3\text{P}=\text{NH}$ and $(\text{tmg})_3\text{P}=\text{N-Et}$, which were synthesized by passing ammonia through or adding ethylamine/triethylamine (1:1 mixture) to the chlorobenzene (methylene chloride) solution of $(\text{tmg})_3\text{PCl}^+\text{Cl}^-$, respectively (monitored by means of ^{31}P NMR, eq 10):



The *tert*-butylimino-tris(tetramethylguanidino)phosphazene·HCl salt, a precursor to *tert*-butylimino-tris(tetramethylguanidino)-phosphazene, was synthesized by the Kirsanov method²⁵ (eq 11):



The following inorganic bases were tried for the liberation of the free organic bases $(\text{tmg})_3\text{P}=\text{N-R}$ ($\text{R} = \text{H}, t\text{-Bu}$) from their HBF_4 salts: (a) pregenerated NaNH_2 in liquid NH_3 ; (b) pregenerated NaNH_2 in liquid NH_3/THF ; (c) $\text{NaH}/\text{NH}_3/\text{THF}$ and $\text{KH}/\text{NH}_3/\text{THF}$; (d) KOMe in MeOH; (e) $\text{KOBu-}t$ in $\text{HOBu-}t$; and (f) $\text{KOBu-}t$ in THF or monoglyme. The inorganic base of choice for liberation of the guanidinophosphazenes proved to be potassium *tert*-butylate/monoglyme.

The simplest purification method, also useful for obtaining single crystals of guanidinophosphazenes, was low-temperature recrystallization from petroleum ether.

The possibility of one-pot synthesis, cheap and available starting compounds, good solubility in organic solvents, and, as it will be shown below, especially the strong basicity of the *N*-alkyl(tetramethylguanidino)phosphazenes should make these compounds useful tools in organic synthesis.

The Staudinger reaction between phenyl azide and suitable substituted chlorophosphines (followed by replacement of the chlorine atoms with tmg groups) was used to synthesize tmg-substituted phenyliminophosphoranes **8d**, **9**, and **10**.

Solution Basicity Measurements. The results of the basicity measurements in THF medium made using the UV–vis spectrophotometric method^{11,13} and the ^{13}C NMR method¹³ are presented in Table 1.

In the papers of Raab et al.,⁴ it was found that in acetonitrile solution the basicity of Alder's "proton sponge" increased by ca. 6.9 $\text{p}K_a$ units when the 1,8-bis(dimethylamino) substituents in the naphthalene ring were replaced with 1,8-bis(tetramethylguanidino) groups. As evidenced in this work, in THF solution a similar change of the substituents in the naphthalene ring results in a somewhat more modest (by 5.8 $\text{p}K_a$ units) increase in the basicity of the "proton sponge". In THF, changing all three dimethylamino groups in $(\text{dma})_3\text{P}=\text{N-}t\text{-Bu}$, $(\text{dma})_3\text{P}=\text{N-Ph}$, and $(\text{dma})_3\text{P}=\text{NH}$ phosphazenes (see refs 11 and 13 for the $\text{p}K_a$ values in THF) to tetramethylguanidino groups increases the basicity enormously: by 10.2, 9.0, and 8.9 powers of 10, respectively. The basicity increase in the pyrrolidinyll phosphazenes — $(\text{pyrr})_3\text{P}=\text{N-}t\text{-Bu}$, $(\text{pyrr})_3\text{P}=\text{N-Ph}$, and $(\text{pyrr})_3\text{P}=\text{NH}$ — initially somewhat stronger, is 8.9, 8.3, and 7.8 $\text{p}K_a$ units, respectively.

(21) Frisch, M. J.; et al. *Gaussian 03*, Revision C.02; Gaussian, Inc.: Wallingford, CT, 2004.

(22) (a) Burk, P.; Koppel, I. A.; Koppel, I.; Leito, I. Travnikova, O. *Chem. Phys. Lett.* **2000**, *323*, 482–489. (b) Koppel, I. A.; Burk, P.; Koppel, I.; Leito, I.; Sonoda, T.; Mishima, M. *J. Am. Chem. Soc.* **2000**, *122*, 5114–5124.

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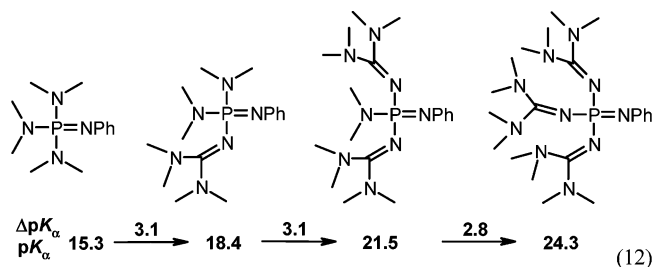
Table 1. Results of Basicity Measurements of Guanidinophosphazenes and Related Compounds in THF

No	Compound	Measurement Results ^a	$pK_{ip}(\text{THF})^b$	$pK_a(\text{THF})^b$
8b	(tmg) ₃ P=N-Et		29.0 ^{c,d}	29.7 ^{c,d}
8c	(tmg) ₃ P=N- <i>t</i> -Bu	0.6	28.4 ^c	29.1 ^c
8a	(tmg) ₃ P=N-H		27.9	28.6
40b	[(pyrr) ₃ P=N-] ₃ P=N-C ₆ H ₄ -4-OMe	0.07, 0.85	27.8	28.9
40a	[(pyrr) ₃ P=N-] ₃ P=N-Ph	0.75	27.1	28.1
39d	[(dma) ₃ P=N-] ₃ P=N-C ₆ H ₄ -4-OMe	0.08, 0.70, 1.50	27.0	27.7
11	(tmg) ₂ (NEt ₂)P=N- <i>t</i> -Bu		26.3	26.8
39c	[(dma) ₃ P=N-] ₃ P=N-Ph	1.17, 0.02, 0.67	26.3	27.0
33a	(pyrr) ₃ P=N-(pyrr) ₂ P=N-Et	0.77, 0.35	25.9	26.6
40c	[(pyrr) ₃ P=N-] ₃ P=N-C ₆ H ₄ -4-Br		25.8	26.9
	[(pyrr) ₃ P=N-] ₃ P=N-C ₆ H ₄ -2-Cl	0.27, 1.05, 0.97	25.6 ^e	26.6 ^e
36b	[(pyrr) ₃ P=N-] ₂ (pyrr)P=N-C ₆ H ₄ -4-OMe		24.8 ^e	25.7 ^e
36a	[(pyrr) ₃ P=N-] ₂ (pyrr)P=N-Ph		24.2 ^e	25.0 ^e
8d	(tmg) ₃ P=N-Ph	0.52	23.7	24.3
35b	[(dma) ₃ P=N-] ₂ (dma)P=N-C ₆ H ₄ -4-OMe	0.70, 0.11	23.6 ^e	24.0 ^e
35a	[(dma) ₃ P=N-] ₂ (dma)P=N-Ph		23.0 ^e	23.5 ^e
	[(pyrr) ₃ P=N-] ₂ (pyrr)P=N-C ₆ H ₄ -4-CF ₃		22.3 ^e	23.2 ^e
	[(dma) ₃ P=N-] ₂ (dma)P=N-C ₆ H ₄ -4-CF ₃	-1.20, 0.10	21.2 ^e	21.7 ^e
10	(tmg) ₂ (dma)P=N-Ph ^f	0.23	21.1	21.5
	(pyrr) ₃ P=N-(pyrr) ₂ P=N-C ₆ H ₄ -4-OMe		20.9 ^e	21.5 ^e
	(dma) ₃ P=N-(dma) ₂ P=N-Ph		19.4 ^e	19.9 ^e
	[(pyrr) ₃ P=N-] ₂ (NEt ₂)P=N-C ₆ H ₃ -2,5-Cl ₂	0.13	19.3 ^e	20.2 ^e
33b	(pyrr) ₃ P=N-(pyrr) ₂ P=N-C ₆ H ₄ -4-Br		19.3	20.0
	MTBD ^g	1.08, 1.25, 0.58	18.7 ^e	18.0 ^e
	DBU ^g		18.1 ^e	16.9 ^e
9	(tmg)(dma) ₂ P=N-Ph	1.44, 0.10	18.1	18.4
	(pyrr) ₃ P=N-C ₆ H ₄ -4-OMe		16.8 ^e	16.8 ^e
	TMGN ^g	0.98, 0.27, 0.36	16.5	16.8
	(pyrr) ₃ P=N-Ph		16.0 ^e	16.0 ^e
32d	(dma) ₃ P=N-(dma) ₂ P=N-C ₆ H ₄ -2-Cl	0.66	15.8	16.3
	(Me)(dma) ₂ P=N-Ph	0.51	15.4 ^e	15.4 ^e
30b	(pyrr) ₃ P=N-C ₆ H ₄ -4-NO ₂		13.2	13.3
	(pyrr) ₃ P=N-C ₆ H ₄ -2-Cl	0.80, 0.01	13.2 ^e	13.2 ^e
	(dma) ₃ P=N-C ₆ H ₄ -2-Cl		12.5 ^e	12.5 ^e

^a The numbers on the arrows are the direct experimental ΔpK_{ip} values, obtained from UV-vis spectrophotometric titration of neutral bases with methanesulfonic acid unless indicated otherwise. The part of the scale starting from the compound **40c** is an extension to the previously published basicity scale.¹¹ Below **40c**, only new measurements are shown. The results of the earlier measurements making up the continuous scale can be found in ref 11.

^b Absolute $pK_{ip}(\text{THF})$ and $pK_a(\text{THF})$ values estimated for conjugate acids of the respective bases; see Experimental Section. ^c Approximate values. ^d NMR data; BF_4^- was used as the counterion; measurements performed as in ref 13. ^e Values from ref 11; some are slightly corrected. ^f The pK_a in CH_3CN is determined to be 29.08 using the method from ref 10. ^g Abbreviations: MTBD, 7-methyl-1,5,7-triazabicyclo[4.4.0]dec-5-ene; DBU, 1,8-diazabicyclo[5.4.0]undec-7-ene; TMGN, N''',N'''' -naphthalene-1,8-diylylbis(N,N,N',N' -tetramethylguanidine).

The following pattern of basicity change is observed in the THF solution:



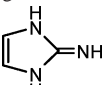
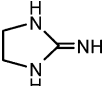
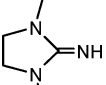
The basicity increase is nearly additive: the consecutive replacements of dma groups by tmg fragments contribute 34.4, 34.4, and 31.2%, respectively, to the total basicity increase of 9 pK_a units. This is in contrast to the findings in the gas phase, where the consecutive introduction of guanidino and tetramethylguanidino fragments seems to be nonadditive (vide infra).

The comparison of differences (ca. 2.3 pK_a units) in pK_a values between two pairs of compounds with sterically more demanding *t*-Bu groups on the imino nitrogen, **8c** and **11** on one hand and **8d** and **10** on the other hand, indicates that the introduction of the first two tmg groups accounts for ca. 70–80% of the overall basicity increase when going from the $(\text{dma})_3\text{P=N-}t\text{-Bu}$ and $(\text{dma})_3\text{P=N-Ph}$ to their double tmg-substituted analogues.

Gas-Phase Basicity Calculations. The results of calculation of the basicities of the model compounds of phosphazene superbases described in this work are summarized in Table 2. Detailed results of the calculations and the Cartesian coordinates of the calculated species are available in the Supporting Information.

Ab initio and DFT methods have been used previously for quantum-chemical studies of gas-phase basicities of some phosphazene bases.^{2,3c} In particular, it could be demonstrated that the calculated DFT B3LYP/6-311+G** gas-phase basicities

Table 2. Results of Basicity Calculations of Guanidinophosphazenes and Related Bases at the DFT B3LYP 6-311+G** Level^a

no.	base	GB	PA
Guanidinophosphazenes			
1	(H ₂ N) ₂ [(H ₂ N) ₂ C=N]P=NH ^b	253.1	259.1
2	H ₂ N[(H ₂ N) ₂ C=N] ₂ P=NH	261.7	267.7
3a	[(H ₂ N) ₂ C=N] ₃ P=NH ^b	266.5	272.6
3b	[(H ₂ N) ₂ C=N] ₃ P=N-Me	271.7	278.0
3c	[(H ₂ N) ₂ C=N] ₃ P=N- <i>t</i> -Bu	273.0	278.6
3d	[(H ₂ N) ₂ C=N] ₃ P=N-Ph	264.3	269.6
4	(dma) ₂ [(H ₂ N) ₂ C=N]P=NH	260.1	264.8
5	(dma)[(H ₂ N) ₂ C=N] ₂ P=NH	265.0	270.4
6	[(dma) ₂ C=N](H ₂ N) ₂ P=NH	258.4	266.1
7	[(dma) ₂ C=N] ₂ (H ₂ N)P=NH	269.7	278.1
8a	[(dma) ₂ C=N] ₃ P=NH	276.1	283.9
12	[im](H ₂ N) ₂ P=NH	254.3	261.4
13	[im] ₂ (H ₂ N)P=NH	261.5	267.9
14	[im] ₃ P=NH	270.5	277.6
15	(H ₂ N) ₂ (imen)P=NH	253.8	261.4
16	(H ₂ N)(imen) ₂ P=NH	260.2	267.5
17	(imen) ₃ P=NH	271.5	279.2
18	(H ₂ N) ₂ [imme]P=NH	257.9	265.7
19	(imme) ₂ (H ₂ N)P=NH	267.9	275.0
20	(imme) ₃ P=NH	280.8	287.0
21	(imen)[(H ₂ N) ₂ C=N] ₂ P=NH	266.8	273.1
22	(im)[(H ₂ N) ₂ C=N] ₂ P=NH	267.7	273.6
23	[(H ₂ N) ₂ C=N] ₃ P=N[(H ₂ N) ₂ C=N]P=NH	276.2	281.9
24	[(H ₂ N) ₂ C=N] ₃ P=N-P[(H ₂ N) ₂ C=N] ₂ =NH	290.8	296.7
25	(H ₂ N) ₂ [(H ₂ N) ₂ C=N] ₂ C=N]P=NH	272.6	278.3
26	[(H ₂ N) ₂ C=N] ₂ C=N] ₃ P=NH	296.2	302.3
Other Bases Phosphazenes			
27a	(H ₂ N) ₃ P=NH	241.7	249.7
27b	(H ₂ N) ₃ P=N-Me ^c	245.6	253.8
27c	(H ₂ N) ₃ P=N-Ph	238.9	246.9
28a	(dma) ₃ P=NH ^c	249.6	256.3
28b	(dma) ₃ P=N-Me ^c	252.3	260.3
28c	(dma) ₃ P=N-Ph	245.3	252.7
29	(H ₂ N) ₂ (pyrr)P=NH	246.8	254.9
30a	(pyrr) ₃ P=NH	255.0	262.8
31	(H ₂ N) ₃ P=NP(NH ₂) ₂ (=NH)	257.0	262.9
32c	[(dma) ₃ P=N](dma) ₂ P=N-Ph	259.2	266.9
34	[(H ₂ N) ₃ P=N-] ₂ P(NH ₂) ₂ (=NH)	269.3	276.2
37	[(H ₂ N) ₃ P=N]P(NH ₂) ₂ =N-P(NH ₂) ₂ (=NH)	264.8	271.9
38	[(H ₂ N) ₃ P=N] ₃ P=NH	273.2	279.1
39a	[(dma) ₃ P=N] ₃ P=NH	~290	
Guanidines			
41	guanidine ^c	230.6	237.5
42		234.3	241.2
43		235.5	242.4
44		239.6	246.2
45	tetramethylguanidine ^c	240.7	248.2
46	[(H ₂ N) ₂ C=N] ₂ C=NH	248.4	255.1
47	[(dma) ₂ C=N] ₂ C=NH	268.4	276.2
Phosphines			
48	[(H ₂ N) ₂ C=N-] ₃ P ^b	258.9	263.7
49	[(dma) ₂ C=N-] ₃ P ^b	267.1	276.7
50	[(H ₂ N) ₃ P=N-] ₃ P	275.0	283.3

^a Data are given in kcal/mol. Basicity data are from this work, unless indicated otherwise. All calculations were run using the DFT B3LYP 6-311+G** method. ^b The preferential protonation site is indicated in bold. Protonation on the C=N nitrogen will lead to the following GB and PA values, respectively: **1**, 227.4, 234.5; **3a**, 251.4, 257.3; **48**, 250.9, 256.9; **49**, GB ca. 269. ^c Data from ref 2.

for (dma)₃P=NH,² (dma)₃P=N-Me,² and (pyrr)₃P=NH (this work) match the experimentally measured intrinsic basicities²⁶ of these bases within ±1 kcal/mol. In the following, the calculations at the same level of theory are used for studying the major trends in structure–basicity relationships of the guanidinophosphazenes and related bases.

Effects of Substitution in Simple Model Amino-Substituted Phosphazene Bases, e.g., (H₂N)₃P=NH, (dma)₃P=NH, etc. Inspection of the data from Table 2 shows evidence that the replacement of an amino group in (H₂N)₃P=NH by a guanidino group, (H₂N)₂C=N–, increases the GB of this relatively strong base (GB = 241.7 kcal/mol) by 11.4 kcal/mol, whereas the analogous introduction of the second and third guanidino groups is predicted to result in further significant increases of the GB by 8.6 and 4.8 kcal/mol, respectively. This leads to a total basicity increase of 24.8 kcal/mol on going from (H₂N)₃P=NH to **3a**. The GB of **3a** is predicted to be 266.5 kcal/mol,⁴ which is ca. 11 kcal/mol higher than the GB directly experimentally measured¹⁵ for phosphazene superbase (pyrr)₃P=N-C₆H₄-4-OMe (GB = 255.2 kcal/mol).⁴ Here the calculations predict that the imino group at the phosphorus atom is clearly the preferable protonation site (by ca. 15 kcal/mol) compared to the imino nitrogen atom in the guanidino group attached to the P atom (amino groups of the guanidino group are much weaker basicity centers as compared with the =NH group of guanidine¹⁵). Similar protonation of the **8a** molecule shows that, in this case, the protonation at the =NH group is more favorable by 20.5 kcal/mol than protonation on the imino nitrogen of the tmg group.

The preferred protonation on the imino group is indirectly supported by the geometry calculations, which show that, upon protonation, the P–NH bond length increases from ca. 1.55 to 1.6–1.7 Å and approaches the length of the P–N bonds between P and amino groups. Similar conclusions follow from the X-ray data for **8c** and its BF₄[–] salt.

The effects of consecutive replacement of the amino groups by guanidino groups in (H₂N)₃P=NH are nonadditive, and the individual contributions of introduction of the guanidino substituents are 46.0, 34.7, and 19.4%, respectively, of the total basicity increase of 34.8 kcal/mol.

In a similar way, the consecutive replacement of the three dimethylamino groups in (dma)₃P=NH by guanidino fragments is predicted to be nonadditive, where the contributions of the first, second, and third guanidino substituents to the total basicity increase of 16.9 kcal/mol are ca. 54, 37, and 9%, respectively.

Similar to the two previous cases of consecutive introduction of guanidino fragments into (H₂N)₃P=NH and (dma)₃P=NH, the stepwise replacement of three amino groups in (H₂N)₃P=NH by tetramethylguanidino groups leads to the enormous (34.4 kcal/mol) nonadditive basicity increase, where the shares of the first, second, and third tmg substituents are 48.5, 32.8, and 18.7%, respectively.

At the same time, and in contrast to the gas-phase data, additivity is observed in THF solution for the **28c** → **8d** triple-replacement transformation (see above).

Effect of Introduction of the Cyclic Guanidino Fragment. The replacement of one amino fragment in (H₂N)₃P=NH with the cyclic 1,3-dihydro-2*H*-imidazol-2-ylideneamino fragment

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(imen, see Scheme 1), yielding **15**, is expected to increase its basicity by ca. 12.1 kcal/mol, practically the same amount as the similar introduction of one guanidino fragment (11.4 kcal/mol).

Replacement in the same base of one amino group by the imidazolidin-2-ylideneamino group (im, see Scheme 1), yielding **12**, is calculated to increase the basicity of the same model compound only slightly more — by 12.6 kcal/mol. The CNNN fragment is predicted to be planar in both neutral and protonated forms, whereas the pyramidalization of the ring NH groups decreases significantly on protonation, as evidenced by changes in the respective average sums of angles at the $-\text{NH}-$ fragments from 349° in the neutral form to 356.8° in the protonated base. The analogous replacement of a single amino group in $(\text{H}_2\text{N})_3\text{P}=\text{NH}$ by the (1,3-dimethylimidazolidin-2-ylidene)amino substituent (imme, Scheme 1), yielding **18**, is predicted to have a somewhat stronger basicity-increasing effect (16.2 kcal/mol); i.e., the effect of the two *N*-methyl groups in the imidazolidine ring is ca. 3.6 kcal/mol.

The replacement of a single amino group in $(\text{H}_2\text{N})_3\text{P}=\text{NH}$ phosphazene by a tmg group is calculated to lead to only a slightly larger basicity increase than the similar exchange of one amino group in $(\text{H}_2\text{N})_3\text{P}=\text{NH}$ for the cyclic imme fragment and to a ca. 4 kcal/mol larger basicity increase than in the cases of similar replacements by the smaller and less polarizable guanidino, imen, and im fragments.

Similar to the consecutive replacement of amino groups in $(\text{H}_2\text{N})_3\text{P}=\text{NH}$ and $(\text{dma})_3\text{P}=\text{NH}$ by guanidino or tetramethylguanidino groups (vide supra), the analogous introduction of first imen, im, imme, and tmg groups accounts for 40.6, 44.0, and 41.0%, respectively, of the total effect of replacement of all three amino groups in the reference base. The effect of introduction of the second substituent accounts for 21.4, 23.6, and 25.0%, respectively, and the replacement of the last amino group is responsible for 37.9, 32.6, and 33.0%, respectively, of the total calculated effects of the basicity increase.

In the case of the open-chain guanidino and tetramethylguanidino derivatives, the calculated basicity is rather similar and telescopically decreases upon addition of an increasing number of substituents. Quite unexpectedly, in the case of three considered cyclic guanidino derivatives, including imen, im, and imme substituents, the effect of the introduction of the third substituent is somewhat more pronounced than the effect of the introduction of the second substituent.

From the practical viewpoint, it is important to notice that all these trisubstituted cyclic or open-chain guanidino phosphazenes are expected to be extremely strong superbases whose gas-phase basicity exceeds those of such widely used organic superbases as DBU, MTBD, BEMP, $(\text{dma})_3\text{P}=\text{N}-t\text{-Bu}$, $(\text{dma})_3\text{P}=\text{N}-\text{Et}$, the phosphatrane superbase of Verkade, etc.²⁷ At the same time, $(\text{imme})_3\text{P}=\text{NH}$, which is predicted to be by 39.1 kcal/mol or 28.8 powers of 10 a stronger base than the simple reference superbase $(\text{H}_2\text{N})_3\text{P}=\text{NH}$, is expected to surpass by its basicity (ca. 280 kcal/mol) even **8**.

Replacement of the imino hydrogen atom in $(\text{H}_2\text{N})_3\text{P}=\text{NH}$ with a phenyl group is expected to reduce its gas-phase basicity slightly (compare with ref 3c) by 2.8 kcal/mol, to 238.9 kcal/mol. However, analogous to the situation in the case of

$(\text{H}_2\text{N})_3\text{P}=\text{NH}$, the introduction of three guanidino-groups into $(\text{NH}_2)_3\text{P}=\text{N}-\text{Ph}$ is expected to increase the basicity of the latter by around the same magnitude (24.8 kcal/mol) as in the case of $(\text{H}_2\text{N})_3\text{P}=\text{NH}$.

Effect of Replacement of the Guanidino Fragment with an *N,N,N',N''*-Tetramethylguanidino Substituent (tmg). The primary cause of the relatively high basicity of guanidine (GB = 224.2 kcal/mol)²⁸ is believed to be the strong resonance, often termed as “Y-aromaticity” (see refs 2, 3, and 6 and references therein), and the polarizability stabilization of the guanidinium cation.

Naturally, the introduction of alkyl groups into the guanidine moiety also significantly increases the basicity of the resulting molecules (TMG, etc.) due to the polarizability increase and the change in charge delocalization effects, etc.^{2,6} In the specific case of comparison of the experimental gas-phase basicities of guanidine and TMG, the basicity increase is 7.9 kcal/mol. Table 2 shows that similar basicity-increasing alkylation effects are also present in the cases of transfer from $(\text{H}_2\text{N})_3\text{P}=\text{NH}$ to $(\text{dma})_3\text{P}=\text{NH}$ (7.9 kcal/mol) and from $(\text{H}_2\text{N})_3\text{P}=\text{N}-\text{Ph}$ to $(\text{dma})_3\text{P}=\text{N}-\text{Ph}$ (6.4 kcal/mol). As it was mentioned before (vide supra), alkylation of the nitrogen sp^3 atoms of the imidazolidin-2-ylideneamino substituent increases somewhat the basicity of the derivatives of the latter by ca. 3.6 kcal/mol.

Similar rather significant (9.6 kcal/mol) basicity-increasing alkylation effects (transfer from guanidino to tetramethylguanidino fragments) are expected to accompany the transfer from the tris-guanidino base **3a** to the respective tris-tmg derivative **8a**.

The imino *N*-alkylation effect on the basicity of the novel guanidino- and tmg-substituted phosphazenes is expected to be not significantly different from the known cases of $(\text{dma})_3\text{P}=\text{NH}$ and $(\text{dma})_3\text{P}=\text{N}-\text{Me}$ (calculated, 2.7 kcal/mol; experimental, 2.2 kcal/mol¹¹): for the transfer from **3a** to its imino-methylated (**3b**) and *t*-Bu-substituted (**3c**) derivatives, the basicity increase is predicted to be 5.2 and 6.5 kcal/mol, respectively. Similar increments have been found¹⁵ from gas-phase experiments for the transfer from TMG to *N*-methyl-TMG (4.3 kcal/mol) and *N-t*-Bu-TMG (7.8 kcal/mol).

Taking into account the probable basicity increase due to *N*-alkylation as 5–8 kcal/mol, one can expect that the predicted basicity change for the transfer from **8a** to **8b**, **8c**, or its cyclic analogues $(\text{imme})_3\text{P}=\text{N}-\text{Alk}$ would result in phosphazene superbases with only one phosphorus atom, having a GB value around 280 kcal/mol (see also refs 2 and 3b).

Even more so, our calculations indicate that the use of bis-guanidinocarbimines **46** (GB = 248.4 kcal/mol) and **47** (GB = 268.4 kcal/mol) as building blocks will allow the construction of P_1 superbases whose gas-phase basicity can also easily reach (or even exceed) 280 kcal/mol. So, the replacement of only one NH_2 group in $(\text{H}_2\text{N})_3\text{P}=\text{NH}$ with the $[(\text{H}_2\text{N})_2\text{C}=\text{N}]_2\text{C}=\text{N}-$ fragment, yielding **25**, increases the basicity by 30.9 kcal/mol, to 272.6 kcal/mol. Keeping in mind the relatively large basicity-increasing alkylation effect on going from **46** to its methylated analogue **47**, it is evident that the basicity of the singly bistetraalkylguanidinocarbimine-substituted P_1 phosphazene superbase would range between 280 and 290 kcal/mol. The above statement is even more true for the respective P_1 triguani-

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dophosphazenes (derivatives of **26**). Indeed, our present calculations indicate that the gas-phase basicity of the non-alkylated triguanidophosphazene **26** already reaches 296.2 kcal/mol. This could easily be significantly increased by alkylation of the imino nitrogen and the amino groups on the guanidino fragments, resulting in a gas-phase basicity value well beyond 300 kcal/mol! At the same time, various calculations and estimates put the gas-phase basicity of the most widely known and used phosphazene superbase **39b** into a rather narrow range around 285–290 kcal/mol; i.e., it is predicted to be a weaker base than the just-described P₁-triguanidophosphazene.

Another, more traditional^{2,7} way to increase the basicity of phosphazenes is to use the homologization (“battery cell”) principle: to increase the number of (substituent)P=N subunits incorporated in the respective superbase.

According to the most conservative estimates,^{2,3} the transfer from P₁ phosphazenes to P₂ phosphazenes increases the intrinsic basicity of the latter by 13–18 kcal/mol. Taking into account the above statements regarding N-alkylated tmg-substituted P₁ phosphazene superbases (with estimated 275 ≤ GB ≤ 285 kcal/mol) and their bis-guanidocarbimino-substituted analogues, this means that the gas-phase basicity of the novel guanidino- or tmg-substituted P₁ or P₂ phosphazenes is expected to be in the same range as or above the basicity of the **39b** superbase, which is around 290 kcal/mol. Indeed, our calculations show that the replacement of three NH₂ groups with three guanidino groups in the simple model P₂ phosphazene **31** at the phosphorus atom that does not carry the basicity center =NH group produces the superbase **23**, whose basicity is 11.2 kcal/mol higher than that of the starting base. The replacement of the two remaining amino groups at the phosphorus atom carrying the =NH basicity center, yielding **24**, increases the expected basicity of the designed superbase even more significantly — by 14 kcal/mol. This makes the overall basicity increase ca. 25 kcal/mol, whereas the GB of **24** is calculated to be 290 kcal/mol. Keeping in mind a rather realistic further 10–20 kcal/mol basicity increase due to the transfer from the guanidino to the imino or tmg substituents and alkylation of the =NH basicity center, the “magic” basicity range of 300 kcal/mol could be easily reached using this approach, even for the more “traditional” novel P₂ phosphazenes, as it was predicted for the base **26**.

Triguanidinophosphines. Recently, Schmutzler et al. have suggested²³ that the not-yet-synthesized tris-tmg phosphine **49** should possess extraordinary basic properties. Unfortunately, all their attempts to liberate this compound from its HCl salt have failed.

Our calculations show that **48** and **49** are, indeed, expected to be rather strong superbases. The phosphorus basicity center of the former is predicted to be 8 kcal/mol stronger (GB = 258.9 kcal/mol) than the nitrogen center (protonation on the N atom of guanidino group) but 7.6 kcal/mol weaker than the respective **3a** phosphazene.

The modification from **48** to **49** results in a much stronger base, with GB values around 270 kcal/mol, whereas the respective basicities due to protonation on the P atom or the N-imino atom of the tmg group are practically leveled out within the uncertainty limits of the used DFT B3LYP 6-311+G** approach.²² Still, **8a** is, by its basicity, by 6 kcal/mol superior to the phosphine superbase **49**. The latter, in turn, is expected to exceed by its gas-phase basicity the landmark cyclic

phosphatrane superbase N[CH₂CH₂N(CH₃)₃]₃P of Verkade et al.⁶ by more than 12 kcal/mol.²⁷ Even stronger phosphine superbases are expected to be designed by replacement of the tmg groups in **49** by the (dma)₃P=N– groups to give [(dma)₃P=N–]₃P, as suggested by Marchenko et al.⁹ In the present work, the basicity of its simple NH₂ analogue **50** (GB = 275.0 kcal/mol) is calculated to be roughly equal to the predicted basicity of the respective imino base **38** (GB = 273.2 kcal/mol). Our calculations allow us to estimate the gas-phase basicity of [(dma)₃P=N–]₃P at around 280 kcal/mol, which is in reasonable agreement with the above-given GB value for **50**. This encourages us to assume that synthesis and basicity measurements of tris(triguanido)phosphines, {[N(Alk)₂C=N]₂C=N]₃P, having only one phosphorus atom, will verify our principle, leading to the most basic and hindered phosphines to date.

Comparison of the Solution (THF) Basicities with the Calculated Gas-Phase Basicities. For several tmg- and dma-substituted phosphazene bases — **8a**, **8b**, **8c**, **8d**, **28a**, **28b**, and **28c** — the solution-phase pK_a values were correlated with the GB values of the respective NH₂-substituted (containing NH₂ groups instead of dma groups, guanidino groups instead of tmg groups) model bases **3a**, **3b**, **3c**, **3d**, **27a**, **27b**, and **27c**. The correlation

$$\text{GB}(\text{NH}_2) = 196.2 + 2.56 \text{ p}K_a(\text{NMe}_2) \quad (13)$$

$$R = 0.962, \quad \text{SD} = 4.4 \text{ kcal/mol}$$

extends over 34 kcal/mol on the GB scale and over 14 pK_a units. The slope of the correlation 2.56/2.3RT = 1.87 indicates that the substituent effects are strongly attenuated while going from the gas phase into THF.

The correlation (13) improves significantly (*R* = 0.995, SD = 1.8 kcal/mol) when the polarizability effect (which is pronounced in the gas phase, differently from the solution phase) is taken into account by using, instead of eq 13, a two-parameter correlation, which besides the *a* pK_a term includes also a polarizability term *b* σ_α, where *a* and *b* are constants and σ_α is Taft's substituent polarizability, characteristic of the respective imino substituent.²⁹

Conclusions

A new principle for creating nonionic superbases is presented. It is based on attachment of tetraalkylguanidino, 1,3-dimethylimidazolidine-2-imino, or bis(tetraalkylguanidino)carbimino groups to the central tetracoordinated phosphorus atom of the iminophosphorane group using tetramethylguanidine or easily available 1,3-dimethylimidazolidine-2-imine.

Using this principle, several new nonionic superbasic phosphazene bases, tetramethylguanidino-substituted at the P atom, were synthesized. Eight new phenyl-substituted iminophosphoranes were also synthesized. The base strength of these compounds was established in THF solution by means of spectrophotometric titration. The gas-phase basicities of numerous guanidino- and *N',N',N'',N''*-tetramethylguanidino-substituted phosphazenes and their cyclic analogues have been calculated, and the crystal structures of (tmg)₃P=N-*t*-Bu and (tmg)₃P=N-*t*-Bu·HBF₄ have been determined.

The enormous basicity-increasing effect has been experimentally verified in the case of the tetramethylguanidino groups in

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the THF medium: the basicity increase when moving from $(\text{dma})_3\text{P}=\text{N}-t\text{-Bu}$ ($\text{p}K_{\text{a}} = 18.9$) to $(\text{tmg})_3\text{P}=\text{N}-t\text{-Bu}$ ($\text{p}K_{\text{a}} = 29.1$) is almost 10 orders of magnitude. A significantly larger basicity increase (up to 20 powers of 10) is expected (based on the high-level DFT calculations) to accompany the similar transfer in the gas phase between $(\text{dma})_3\text{P}=\text{NH}$ and $(\text{tmg})_3\text{P}=\text{NH}$. A much larger basicity-increasing effect is expected when three methylated triguanide fragments, namely $[(\text{dma})_2\text{C}=\text{N}]_2\text{C}=\text{N}^-$, are attached to a single $\text{P}=\text{NH}$ fragment. The gas-phase basicity (around 300 kcal/mol) of this molecule is predicted to exceed that of the widely used commercial $[(\text{dma})_3\text{P}=\text{N}]_3\text{P}=\text{N}-t\text{-Bu}$ ($t\text{-BuP}_4$) superbases.

The new superbases could be used as auxiliary bases in organic synthesis and as indicators to supplement and significantly extend the basicity scale in THF toward the more basic region. Studies on the synthesis of tris(triguanido)phosphazenes, -phosphines, and -phosphine oxides and application of novel

guanidinophosphorus derivatives as auxiliary bases and ligands in organic synthesis are in progress in our laboratories.

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Supporting Information Available: Synthesis and liberation procedures of phosphazene compounds; the ionic radii of the ions (Table S1); details of the UV-vis spectrophotometric measurement method; X-ray diffraction analysis data of compounds **8c** and **8c**· HBF_4 , in CIF format; full details of quantum chemical calculations (Table S2); full citations of refs 7 and 21; and geometry data of the calculated molecules. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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