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A New Class of Chiral Phosphazene Bases: Synthesis and Characterization

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Chiral examples of phosphazene bases **2a–c** were synthesized by treatment of (*S*)-2-(dialkylaminomethyl)pyrrolidine **1a–c**, derived from 5-oxo-(*S*)-proline, with phosphorus pentachloride and subsequent addition of gaseous ammonia. The phosphazenes **2a–c** were isolated as HBF_4 salts in high yields and fully characterized by ^1H, ^{13}C and ^{31}P NMR spectroscopy, various 1D and 2D NMR experiments and mass spectrometry (EI). The molecular structure and the absolute configuration of the salts **2a–c**·HBF_4 were determined by X-ray analysis. DFT calculations indicate that **2a** is more basic than the Schwesinger base $\mathbf{P_1}$ by approximately nine pK_a units.

Introduction

Uncharged organic bases have been found to be efficient and irreplaceable reagents in base-mediated transformations.[1] Several different families of strong neutral bases, phosphazenes,[2] guanidines,[3] amidines,[4] Proton-Sponges® [1,8-bis(dimethylamino)naphthalenes][5] and proazaphosphatranes[6] have emerged. The phosphazene bases developed by Schwesinger belong to the family of very strong and non-metallated organic bases.[7] In acetonitrile these triaminoiminophosphoranes show extreme basicity up to pK_{BH+} values of 50 and have been used in various selective deprotonation reactions.[2b,8] Schwesinger-type bases have a general structure of $(R_2N)_3P{=}N{-}R$ and their basicity strength increases with the number of phosphazene units. Thus, the high basicity, or rather the lower nucleophilicity, is based on the increased steric hindrance and the participation of various donors to the conjugation in the cation structure. Today, many of these bases are commercially available and offered as monomeric (P_1), dimeric (P_2) and tetrameric (P_4) reagents (Figure 1).

Furthermore, phosphazene bases have broad applications in organic synthesis and can be used for Michael addition,[9] alkylation,[10] silylation[11] and heterocumulene[12] reactions. Polyphosphazenes of the type $[(RO)_2P{=}N]$ are one of the most studied macromolecules due to both academic and industrial interest.[13] The development of new synthetic methods for polyphosphazene units has lead to an increased activity in this field.[14] Applications of Schwesinger bases in asymmetric synthesis are limited.[15] For instance, the catalytic enantioselective synthesis of α-amino acid derivatives by using BEMP (2-*tert*-butylimino-2-diethylamino-1,3-dimethylperhydro-1,3,2-diazaphosphorine) and a quaternary ammonium salt catalyst has been reported by O'Donnell.[16] In 1999, the first chiral iminophosphoranes of the type $(R_2N)_3P{=}N{-}R$ with a stereogenic phosphorus centre were reported.[17]

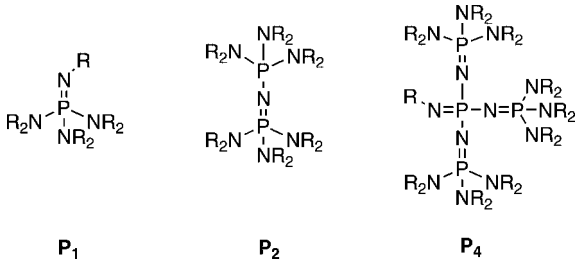

Figure 1. Phosphazene bases.

Our ongoing research is devoted to the development of chiral organic bases containing a (*S*)-2-(dialkylaminomethyl)pyrrolidine unit and to their use in asymmetric synthesis. Based on our previous studies on the preparation and synthetic utility of chiral guanidines it is the aim of this article to explore a new class of phosphazene bases starting from chiral 1,2-diamines.

Results and Discussion

The synthesis of enantiomerically pure 1,2-diamines such as **1a–c** follows a route described by Amedjkouh,[19] starting from the commercially available 5-oxo-(*S*)-proline by formation of a diastereomerically pure oxazolidinone deriva-

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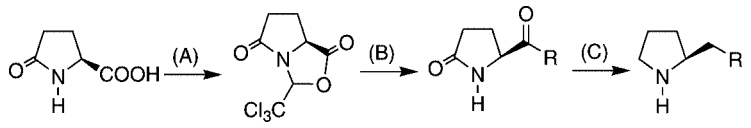
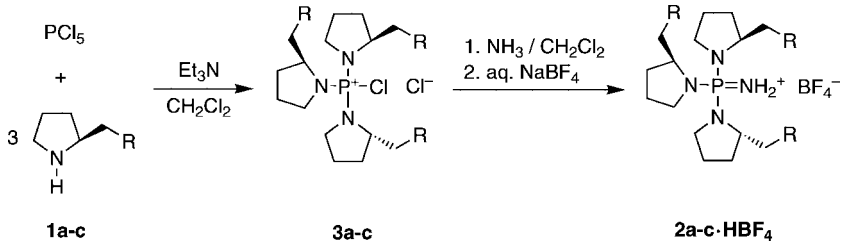


Scheme 1. Formation of the 1,2-diamines **1a**–**c**; **1a**: R = pyrrolidin-1-yl, **1b**: R = morpholin-4-yl and **1c**: R = piperidin-1-yl.



Scheme 2. Synthesis of the HBF_4 salts of the chiral phosphazenes **2a**–**c** (for R see Scheme 1).

tive (A). Opening of the oxazolidinone ring with the corresponding secondary amine (B) and subsequent reduction of the amide groups (C) provides the chiral 1,2-diamines **1a**–**c** (Scheme 1). For the formation of the chiral 1,2-diamines, we obtained similar results for **1a** and **1c** as in the original procedure and also applied this concept in order to prepare **1b** in good yield.

The syntheses of chiral phosphazenes **2a**–**c** were accomplished as depicted in Scheme 2, according to Schwesinger's procedure.[2b] One-pot reactions of three equivalents of **1a**–**c** with PCl_5 in dichloromethane and triethylamine at –50 °C gave the chlorophosphonium salts **3**, which were used without further purification. Subsequently, compounds **3** were converted into the chiral phosphazenes **2a**–**c** by saturation of the solution with NH_3 gas. After filtration, to remove ammonium chloride, we decided to purify the viscous crude products **2a**–**c** by formation of their tetrafluoroborate salts. Treatment of the phosphazene bases **2a**–**c** with aqueous $NaBF_4$ solution afforded the tetrafluoroborate salts **2a**–**c**·HBF_4 as white solids in moderate to good yields (Table 1). Due to their improved manageability the resulting salts **2a**–**c**·HBF_4 were isolated and fully characterized (Scheme 2).

Table 1. Prepared HBF_4 salts of **2a**–**c**.

HBF_4 salts	1,2-Diamine	R	Yield [%]	$[\alpha]_D^{rt}$
2a	**1a**	pyrrolidin-1-yl	87.4	–17.97
2b	**1b**	morpholin-4-yl	53.0	–21.88
2c	**1c**	piperidin-1-yl	87.4	–14.55

In order to show that the phosphazene bases **2a**–**c** are stable under aqueous conditions, we synthesized the corresponding phosphoric acid triamide of **2a** and compared the ^{31}P NMR spectroscopy data with those of **2a**·HBF_4 (δ = 29.8 ppm). The phosphoric acid triamide of **2a** showed a ^{31}P NMR resonance at δ = 19.5 ppm in chloroform solution. This value compares well with results reported by Hoeg-Jensen et al. for the ^{31}P NMR resonance of the P=O group in tripyrrolidinophosphane oxide (δ = 14.9 ppm).[20] Based upon these results we conclude that hydrolysis of the phosphazene bases **2a**–**c** does not occur during aqueous work up.

Release of the free bases **2a**–**c** were conveniently achieved by treatment of **2a**–**c**·HBF_4 with KOMe in anhydrous MeOH[2b] followed by distillation in high vacuum. The resulting phosphazene bases **2a**–**c** are highly viscous.

The molecular structures of **2a**–**c**·HBF_4 in solution were established from their NMR (^1H, ^{13}C, ^{31}P, DEPT 135, HMQC, HMBC and EXSY) spectroscopic data. As a consequence of the chirality at the C2 stereo center, the geminal protons of the methylene groups are anisochronous and the ^1H spectra of **2a**–**c**·HBF_4 show multiplets in the range 1.40 to 3.90 ppm. The ^{13}C NMR spectra of **2a**–**c**·HBF_4 display the required number of signals for one ligand unit, thereby indicating that all three ligands have the same chemical environment and thus, the HBF_4 salts of **2a**–**c** have time-averaged C_3 symmetry in solution (Figure 2). Furthermore, the signals for methylene carbons C3, C4, C5 and C6 in **2a**·HBF_4 split into two equivalent singlets due to coupling with the phosphorus atom. The coupling constant (^2J) between P and C2 is 7.8 Hz.

The ^{31}P NMR spectrum of **2a**·HBF_4 shows two sharp signals at δ = 29.8 ppm (major) and 32.7 ppm (minor) with a 91:9 intensity ratio, indicating two detectable species of **2a**·HBF_4 in chloroform solution (Figure 3). ^{31}P-^{31}P EXSY NMR was recorded for **2a**·HBF_4 in order to determine a change in conformation between these species. No characteristic cross peaks appeared in the corresponding part of the EXSY NMR spectrum. This observation can be explained by the independent existence of both species in solution. In addition to the standard 2D experiments, the proton resonances of the major product can be assigned using ^1H-^{31}P HMBC NMR due to the corresponding phosphorus atom, whereas the proton resonances of the major product overlay those of the by-product.

The experiments performed allow us to conclude that both species of **2a**·HBF_4 have the same chemical environment. However, in solution the additional proton is at dif-

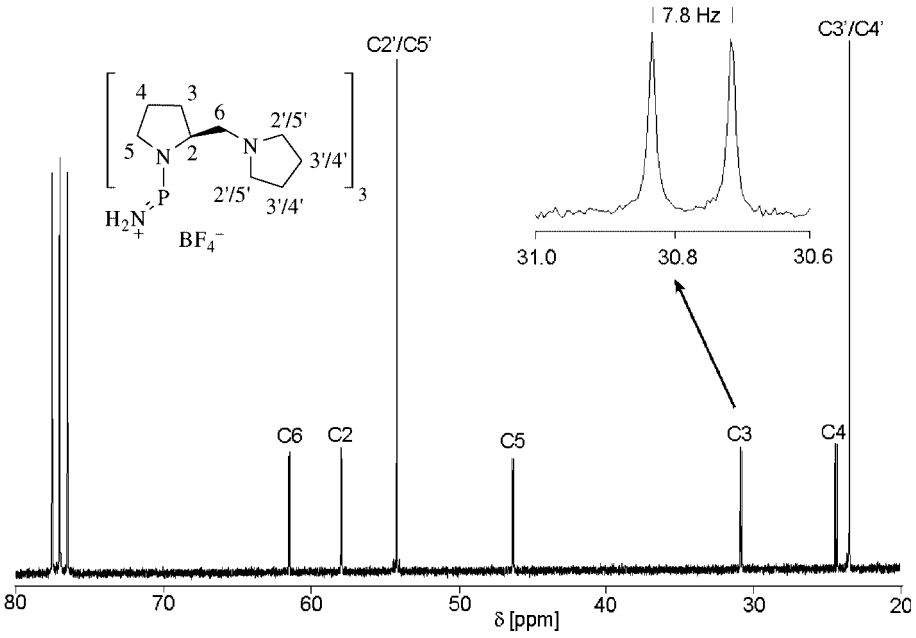


Figure 2. ^{13}C NMR spectrum of **2a**·HBF_4 measured at 62.9 MHz in $CDCl_3$ at room temperature.

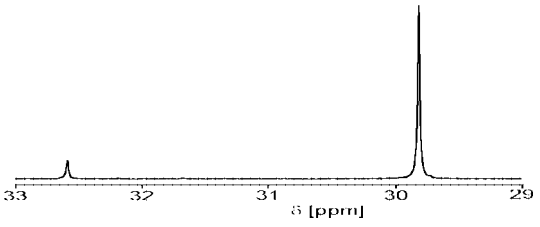


Figure 3. ^{31}P NMR spectrum of **2a**·HBF_4 measured in $CDCl_3$ at room temperature.

ferent positions with respect to the phosphorus atom in solution (Figure 3). In the ^{31}P NMR spectra of the HBF_4 salt of **2b** and **2c**, a sharp major signal was also observed at δ = 29.5 ppm and δ = 30.2 ppm with intensity ratios of 90:10 and 96:4, respectively.

The molecular weights and formulae of the prepared chiral phosphazenium salts **2a**–**c**·HBF_4 were determined by mass spectroscopy as well as by elemental analysis. The mass spectra of **2a**–**c**·HBF_4 revealed molecular peaks at the *m*/*z* value corresponding to $[M-BF_4]^+$ and indicated the loss of the tetrafluoroborate counterion. The base peaks at the *m*/*z* = 84 [**2a**·HBF_4], 100 [**2b**·HBF_4] and 98 [**2c**·HBF_4] result from an α-cleavage relative to the side chain.

Single-crystal X-ray analysis of **2a**–**c**·HBF_4 was performed in order to confirm its molecular structure and in particular to assign the absolute configurations of the three chiral carbon atoms C(1), C(2) and C(3) present in the molecule (**2a**·HBF_4: Figure 4, Table 2. For the X-ray structures of **2b**–**c**·HBF_4 cf. paragraph "Crystal Structure Determination").

Table 2. Selected bond lengths [Å] and bond angles [°] for **2a**·HBF_4.

Bond lengths		Bond angles	
P–N(1)	1.597(2)	N(1)–P–N(2)	104.77(13)
P–N(2)	1.617(2)	N(1)–P–N(3)	113.76(13)
P–N(3)	1.628(2)	N(1)–P–N(4)	111.78(13)
P–N(4)	1.637(2)	N(2)–P–N(3)	111.09(12)
C(2)–N(2)	1.494(3)	N(2)–P–N(4)	112.77(12)
C(1)–N(3)	1.470(3)	N(3)–P–N(4)	102.93(12)

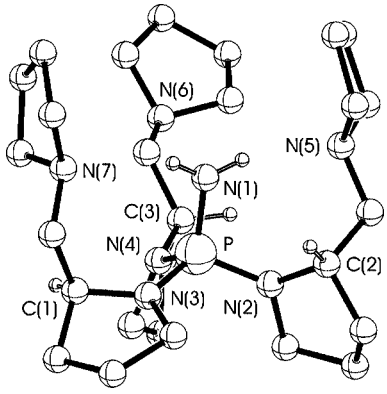
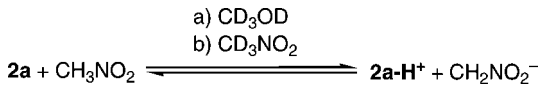


Figure 4. X-ray crystal structure of **2a**·HBF_4, the tetrafluoroborate group and the non-relevant hydrogen atoms are omitted for clarity.

As shown in Figure 4, the X-ray analysis of **2a**·HBF_4 confirms the structural properties and gives evidence for the expected (*S*)-configuration of the carbon atoms C(1), C(2) and C(3). The local symmetry of the arrangement of the three 1,2-diamine units around the phosphorus tends to be C_3. Compared to the situation in solution (benzene, room temperature), in the ^1H and ^{13}C NMR spectra of **2a**–

c·HBF_4 only one set of signals is present for the major compound, in which the possible conformers most likely coexist. The interconversion of these conformers is too fast for the NMR timescale and thus, in all recorded ^1H and ^{13}C NMR spectra only averaged signals were observed. The upper part of the crystal structure forms a pocket similar to an enzyme consisting of the four nitrogen atoms N(7), N(5), N(6) and N(1). In addition to its high basicity, the phosphazene skeleton most likely has the possibility to complex metals. Comparable results were also observed for the compounds **2b**·HBF_4 and **2c**·HBF_4.

Finally, we estimated the pK_a values or rather the relative basicities of the new phosphazene bases **2a**–**c** by using NMR tube experiments (^1H, ^{13}C, HSQC-DEPT). The reaction between **2a** and nitromethane in benzene formed an equilibrium mixture that could be quenched with deuterated methanol to confirm the formation of the nitromethane anion (Scheme 3, a).



Scheme 3. Equilibrium between the phosphazene **2a** and nitromethane.

The ^{13}C NMR spectrum displays an overlapped triplet at δ = 61.5 ppm with a coupling constant $^1J_{CD}$ = 22 Hz for CH_2DNO_2 and quintet at δ = 61.3 ppm with a coupling constant $^1J_{CD}$ = 22 Hz for CHD_2NO_2. The ^1H NMR spectrum gave the corresponding triplet at δ = 3.613 ppm ($^2J_{HD}$ = 1.9 Hz), overlapped by a quintet at δ = 3.600 ppm ($^2J_{HD}$ = 2.0 Hz), indicating the presence of CH_2DNO_2 and CHD_2NO_2. A HSQC-DEPT NMR experiment performed at 30 °C on the quenched equilibrium mixture confirmed our assignment of the ^1H and ^{13}C NMR signals by the presence of the expected peak pattern. Additionally, we performed a second NMR measurement to support the methanol quenching experiment by using CD_3NO_2 as the deuterium source (Scheme 3, b). Upon treatment of the benzene solution with an excess of deuterated nitromethane, both ^1H and ^{13}C NMR spectra provided the aforementioned overlapping peak pattern.

To further quantify the pK_a value of **2a**, we calculated the free energy change for the following reaction in the gas phase:

$$\mathbf{2a} + \mathbf{P_1}\cdot H^+ \rightarrow \mathbf{2a}\cdot H^+ + \mathbf{P_1}$$

These calculations at the B98/G3MP2Large//B3LYP/6-31+G(d) level of theory [for computational details see the Supporting Information, **P1** in his case: *tert*-butylimino-tripyrrolidinophosphorane] revealed that the reaction is exergonic with $\Delta_r G$ = –50.7 kJ mol^{-1}. Using the relation $\Delta pK_a = \Delta_r G/[RT\cdot\ln 10]$ with T = 298.15 K, compound **2a** is 8.9 pK_a units more basic than $\mathbf{P_1}$.

We are intentionally not reporting DFT calculated absolute pK_a values at this point due to the fact that for reliable calculations, one has to apply a more sophisticated theoretical method which are not (yet) computationally feasible for systems as large as those considered in this study.[26,27] As a result of fortuitous error cancellations, *relative* pK_a calculations, also at lower levels such as those presented here, are usually quite reliable.[27]

The NMR experiments and DFT calculations clearly indicate that the corresponding protonated form of **2a** has a pK_a value of at least 28 in acetonitrile, since that represents the pK_a value of nitromethane in acetonitrile.[2b] In comparison with the aforementioned commercially available $\mathbf{P_1}$ bases ($^{MeCN}pK_{BH}+$ = 26.5–28.4),[2b,18] the chiral phosphazene base **2a** should have a $^{MeCN}pK_{BH}+$ value of approximately 35–37.

Conclusion

In order to produce chiral phosphazenes **2a**–**c** we have developed a synthesis for new phosphazene bases possessing three enantiomerically pure 1,2-diamines moieties (*S*)-2-(dialkylaminomethyl)pyrrolidines **1a**–**c**. The latter were synthesized in few steps starting from 5-oxo-(*S*)-proline. After formation of the chiral 1,2-diamines **1a**–**c**, treatment with PCl_5 followed by the addition of gaseous NH_3 afforded **2a**–**c**, which were isolated as **2a**–**c**·HBF_4 salts in high yields. The molecular structures of **2a**–**c**·HBF_4 in solution were characterized using correlated 2D NMR techniques and the expected (*S*)-configuration of the three chiral centers was confirmed by X-ray analysis.

The successful synthesis of the phosphazenes **2a**–**c** provides a new type of chiral base, which will certainly be very valuable for asymmetric synthesis.

Motivated by our deprotonation experiments and DFT calculations, we are currently seeking to extend the chiral phosphazene chemistry by investigating its application for bases as enantioselective deprotonation reagents.

Experimental Section

General Remarks: All manipulations were carried out in an argon atmosphere using standard Schlenk techniques. NMR spectra were recorded on a Bruker AC 250 MHz and AC 400 MHz using the residual solvent resonance as an internal standard. $CDCl_3$ (δ_H = 7.24, δ_C = 77.0 ppm) and benzene (δ_H = 7.15, δ_C = 128.0 ppm) were used as solvents. The geminal protons of the CH_2 groups were listed as centered multiplets, δ = *X*–*Y* ppm. Optical rotations were recorded using a Polartronic E and are reported as $[\alpha]_D^{rt}$ values (*c* in g per 100 mL of solvent). Elemental analyses were conducted by the microanalytical service in our department. IR spectra were recorded using an ATR–BIORAD FTS-25 spectrometer. Mass spectra were recorded using a Finnigan MAT SAQ 710 (EI) spectrometer. All compounds were fully characterized with microanalytical data (±0.4%). Anhydrous CH_2Cl_2, PCl_5, Et_3N and KOMe solutions were commercially available and used without further purification. Chiral 1,2-diamines **1a**–**c** were prepared as described in the literature.[19]

General Procedure for the Synthesis of 2a–c·HBF$_4$: 0.68 g (3.25 mmol) of PCl_5 was dispersed in anhydrous CH_2Cl_2 (20 mL) in an argon atmosphere. To this suspension 1.5 g (9.75 mmol) of

1a and then 0.99 g (9.75 mmol) of Et_3N were added at –50 °C. Et_3N was used to eliminate the evolving HCl. The mixture was stirred at –50 °C for 1 h and then the temperature was allowed to rise to room temperature. Subsequently, the mixture was set aside overnight. After cooling to –10 °C, the mixture was saturated with NH_3 (25 min.) and stirred for 1 h. Precipitated NH_4Cl was filtered off and the filtrate washed with CH_2Cl_2 and the solvent removed at reduced pressure. The brown oily crude product was dissolved in water (10 mL) and 0.39 g (3.58 mmol) of aqueous $NaBF_4$ solution was added. In the case of chiral diamine **1a**, the precipitated residue was filtered off and dried under high vacuum to give the phosphazene HBF_4 salt. In the cases of **1b** and **1c**, the resulting solution was extracted with CH_2Cl_2 (3 × 20 mL), the solvents were removed under vacuum and the crude residue was stirred in diethyl ether to afford the phosphazene HBF_4 salts as white solids.

General Procedure for the Liberation of the Phosphazene Bases from HBF_4 Salts with KOMe:[2b] To a stirred solution of 1.0 g (1 equiv.) of **2a**–**c**·HBF_4 in anhydrous MeOH (5 mL) a commercially available KOMe (1 equiv.) solution was added. After stirring for 2 h, the precipitated KBF_4 was filtered, the filtrate washed with anhydrous MeOH and concentrated under vacuum. The crude residue was purified by distillation in high vacuum to afford the free bases **2a**–**c** as highly viscous oils.

Tris[2-(pyrrolidin-1-ylmethyl)pyrrolidin-1-yl]phosphazenium Tetrafluoroborate (2a·HBF_4): Yield 87.4%, m. p. = 126 °C. ^{1}H NMR (250 MHz, $CDCl_3$, room temp.): δ = 3.74 (m, 1 H, CH), 3.22 (m, 2 H, CH_2), 2.68–2.32 (m, 2 H, CH_2), 2.61–2.32 (m, 4 H, 2 × CH_2), 2.00–1.81 (m, 2 H, CH_2), 1.98 (m, 2 H, CH_2), 1.75 (m, 4 H, 2 × CH_2) ppm, NH protons not detected at room temperature. ^{13}C NMR (62.5 MHz, $CDCl_3$, room temp.): δ = 61.4 (CH_2), 57.9 (CH), 54.2 (2 × CH_2), 46.3 (CH_2), 30.8 (CH_2), 24.4 (CH_2), 23.5 (2 × CH_2) ppm. ^{31}P NMR (162 MHz, $CDCl_3$, room temp.): δ = 29.8 ppm. IR (KBr): $\tilde{\nu}$ = 3277 (NH), 2966–2788 (CH), 1460, 1362, 1341, 1263, 1213, 1147, 1121, 1092, 1054, 877 cm^{-1}. MS (DEI): *m*/*z* (%) = 506 (10) $[M-HBF_4]^+$, 84 (100) $[M-C_{22}H_{43}N_6P]^+$. $C_{27}H_{53}N_7PBF_4$ (593.54): calcd. C 54.64, H 9.00, N 16.52; found C 54.40, H 8.84, N 16.47. $[\alpha]_D^{20}$ = –17.97 (*c* = 2.56, CH_2Cl_2).

Tris[2-(pyrrolidin-1-yl-methyl)pyrrolidin-1-yl]phosphazene (2a): ^{1}H NMR (250 MHz, [D_6]benzene, room temp.): δ = 4.05 (m, 1 H, CH), 3.26–2.92 (m, 2 H, CH_2), 2.65–2.47 (m, 2 H, CH_2), 2.52 (m, 4 H, 2 × CH_2), 1.99–1.86 (m, 2 H, CH_2), 1.69 (m, 2 H, CH_2), 1.58 (m, 4 H, 2 × CH_2) 0.50 (s, 1 H, NH) ppm. ^{13}C NMR (62.5 MHz, [D_6]-benzene, room temp.): δ = 61.5 (CH_2), 57.7 (CH), 54.8 (2 × CH_2), 46.6 (CH_2), 29.9 (CH_2), 25.3 (CH_2), 24.0 (2 × CH_2) ppm. ^{31}P NMR (162 MHz, [D_6]benzene, room temp.): δ = 34.0 ppm. $C_{27}H_{52}N_7P$ (505.74): calcd. C 64.12, H 10.36, N 19.39; found C 63.87, H 10.52, N 19.30.

Tris[2-(morpholin-4-ylmethyl)pyrrolidin-1-yl]phosphazenium Tetrafluoroborate (2b·HBF_4): Yield 36.4%, m. p. = 145 °C. ^{1}H NMR (250 MHz, $CDCl_3$, room temp.): δ = 3.87 (m, 1 H, CH), 3.69 (m, 4 H, 2 × CH_2), 3.23 (m, 2 H, CH_2), 2.63–2.52 (m, 4 H, 2 × CH_2), 2.58–2.23 (m, 2 H, CH_2), 2.04–1.86 (m, 2 H, CH_2), 1.96 (m, 2 H, CH_2) ppm, NH protons not detected at room temperature. ^{13}C NMR (62.5 MHz, $CDCl_3$, room temp.): δ = 66.6 (2 × CH_2), 63.8 (CH_2), 56.0 (CH), 54.0 (2 × CH_2), 46.3 (CH_2), 30.6 (CH_2), 24.3 (CH_2) ppm. ^{31}P NMR (162 MHz, $CDCl_3$, room temp.): δ = 29.5 ppm. IR (KBr): $\tilde{\nu}$ = 3352 (NH), 2959–2849 (CH), 1458, 1309, 1276, 1210, 1118 (COC), 1053 (COC), 995 cm^{-1}. MS (DEI): *m*/*z* (%) = 553 (7) $[M-HBF_4]^+$, 100 (100) $[M-C_{22}H_{43}N_6O_2P]^+$. $C_{27}H_{53}N_7O_3PBF_4$ (641.54): calcd. C 50.55, H 8.33, N 15.28; found C 50.18, H 8.32, N 15.14. $[\alpha]_D^{20}$ = –21.88 (*c* = 2.59, CH_2Cl_2).

Tris[2-(morpholin-4-ylmethyl)pyrrolidin-1-yl]phosphazene (2b): ^{1}H NMR (250 MHz, [D_6]benzene, room temp.): δ = 4.14 (m, 1 H, CH), 3.71 (m, 4 H, 2 × CH_2), 3.12–2.97 (m, 2 H, CH_2), 2.66–2.19 (m, 2 H, CH_2), 2.55–2.41 (m, 4 H, 2 × CH_2), 1.97 (m, 2 H, CH_2), 1.77 (m, 2 H, CH_2), 0.70 (s, 1 H, NH) ppm. ^{13}C NMR (62.5 MHz, [D_6]-benzene, room temp.): δ = 67.2 (2 × CH_2), 64.0 (CH_2), 56.0 (CH), 54.9 (2 × CH_2), 46.4 (CH_2), 29.9 (CH_2), 25.2 (CH_2) ppm. ^{31}P NMR (162 MHz, [D_6]benzene, room temp.): δ = 34.4 ppm. $C_{27}H_{52}N_7O_3P$ (553.73): calcd. C 58.57, H 9.47, N 17.71; found C 58.17, H 9.58, N 17.27.

Tris[2-(piperidin-1-ylmethyl)pyrrolidin-1-yl]phosphazenium Tetrafluoroborate (2c·HBF_4): Yield 87.4%, m. p. = 164 °C. ^{1}H NMR (400 MHz, $CDCl_3$, room temp.): δ = 7.51 (s, 2 H, NH), 3.78 (m, 1 H, CH), 3.28–3.19 (m, 2 H, CH_2), 2.49–2.38 (m, 4 H, 2 × CH_2), 2.47–2.14 (m, 2 H, CH_2), 2.00–1.80 (m, 2 H, CH_2), 2.00–1.93 (m, 2 H, CH_2), 1.54 (m, 4 H, 2 × CH_2), 1.49 (m, 2 H, CH_2) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, room temp.): δ = 64.4 (CH_2), 56.4 (CH), 55.1 (2 × CH_2), 46.1 (CH_2), 30.7 (CH_2), 25.8 (2 × CH_2), 24.4 (CH_2), 24.0 (CH_2) ppm. ^{31}P NMR (162 MHz, $CDCl_3$, room temp.): δ = 30.2 ppm. IR (KBr): $\tilde{\nu}$ = 3375 (NH), 2934–2815 (CH), 1451, 1389, 1282, 1203, 1128, 1092, 1050 cm^{-1}. MS (DEI): *m*/*z* (%) = 547 (5) $[M-HBF_4]^+$, 98 (100) $[M-C_{24}H_{47}N_6P]^+$. $C_{30}H_{59}BF_4N_7P$ (635.46): calcd. C 56.69, H 9.36, N 15.43; found C 56.70, H 9.66, N 14.97. $[\alpha]_D^{20}$ = –14.55 (*c* = 2.61, CH_2Cl_2).

Tris[2-(piperidin-1-ylmethyl)pyrrolidin-1-yl]phosphazene (2c): ^{1}H NMR (400 MHz, [D_6]benzene, room temp.): δ = 4.13 (m, 1 H, CH), 3.30–2.98 (m, 2 H, CH_2), 2.63–2.18 (m, 2 H, CH_2), 2.57–2.36 (m, 4 H, 2 × CH_2), 1.98–1.88 (m, 2 H, CH_2), 1.72 (m, 2 × 4 H, CH_2), 1.51 (m, 2 H, CH_2), 1.31 (m, 2 H, CH_2), 0.62 (s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, [D_6]benzene, room temp.): δ = 64.5 (CH_2), 56.6 (CH), 55.8 (2 × CH_2), 46.6 (CH_2), 30.0 (CH_2), 25.8 (2 × CH_2), 25.3 (CH_2), 25.0 (CH_2) ppm. ^{31}P NMR (162 MHz, [D_6]benzene, room temp.): δ = 34.3 ppm. $C_{30}H_{58}N_7P$ (547.82): calcd. C 65.78, H 10.67, N 17.90; found C 65.53, H 10.40, N 17.72.

NMR Tube Experiments

2a (0.833 mmol) was dissolved in anhydrous deuterated benzene (0.5 mL) and nitromethane (50 μL, 0.917 mmol) was added with a syringe. The solution was left to stand for at least 24 h to allow for equilibration (yellow solution). Finally, an excess of deuterated methanol (200 μL, nitromethane) was added and the NMR experiments were performed.

Crystal Structure Determination

The intensity data for the compounds was collected using a Nonius Kappa CCD diffractometer, using graphite-monochromated Mo-K_α radiation. Data were corrected for Lorentz and polarization effects, but not for absorption effects.[21,22]

The structures were solved by direct methods (SHELXS[23]) and refined by full-matrix least-squares techniques against F_o^2 (SHELXL-97[24]). For the amine groups of **2a**·HBF_4, **2b**·HBF_4 and **2c**·HBF_4, the hydrogen atoms were located by difference Fourier synthesis and refined isotropically. All other hydrogen atoms were included at calculated positions with fixed thermal parameters. All non-hydrogen atoms were refined anisotropically.[24] XP (SIEMENS Analytical X-ray Instruments, Inc.) was used for structure representations.

Crystal Data for 2a·HBF_4:[25] $[C_{27}H_{53}N_7P]^+$ $[BF_4]^-$, M_r = 593.54 gmol^{-1}, colorless prism, size 0.04 × 0.04 × 0.04 mm^3, orthorhombic, space group $P2_12_12_1$, *a* = 9.4780(2), *b* = 12.9628(2), *c* = 25.4777(6) Å, *V* = 3130.23(11) Å^3, *T* = –90 °C, *Z* = 4, $\rho_{calcd.}$ = 1.259 gcm^{-3}, μ (Mo-K_α) = 1.41 cm^{-1}, *F*(000) = 1280, 20441 reflec-

tions in h(–12/10), k(–15/16), l(–31/33), measured in the range 2.24° ≤ Θ ≤ 27.50°, completeness Θ_{max} = 99.7%, 7170 independent reflections, R_{int} = 0.045, 5742 reflections with $F_o > 4\sigma(F_o)$, 367 parameters, 0 restraints, R_{1obs} = 0.057, wR_{2obs} = 0.142, R_{1all} = 0.077, wR_{2all} = 0.156, GOOF = 1.025, Flack parameter 0.05(11), largest difference peak and hole: 0.605/–0.445 e·Å^{-3}.

Crystal Data for 2b·(HBF$_4$):[25] $[C_{27}H_{53}N_7O_3P]^+$ $[BF_4]^-$, M_r = 641.54 gmol^{-1}, colorless prism, size 0.06×0.05×0.05 mm^3, monoclinic, space group $P2_1$, a = 10.4725(3), b = 11.1231(5), c = 14.9360(7) Å, β = 104.598(3)°, V = 1683.68(12) Å^3, T = –90 °C, Z = 2, $\rho_{calcd.}$ = 1.265 g cm^{-3}, μ (Mo-K_α) = 1.43 cm^{-1}, F(000) = 688, 11509 reflections in h(–13/13), k(–13/14), l(–19/15), measured in the range 3.85° ≤ Θ ≤ 27.49°, completeness Θ_{max} = 98.7%, 7187 independent reflections, R_{int} = 0.063, 6059 reflections with $F_o > 4\sigma(F_o)$, 386 parameters, 1 restraints, R_{1obs} = 0.066, wR_{2obs} = 0.172, R_{1all} = 0.081, wR_{2all} = 0.186, GOOF = 1.028, Flack parameter 0.12(12), largest difference peak and hole: 0.522/–0.622 e·Å^{-3}.

Crystal Data for 2c·(HBF$_4$):[25] $[C_{30}H_{59}N_7P]^+$ $[BF_4]^-\cdot H_2O$, M_r = 653.64 gmol^{-1}, colorless prism, size 0.06×0.06×0.04 mm^3, orthorhombic, space group $C222_1$, a = 10.3975(4), b = 17.9047(6), c = 38.3944(12) Å, V = 7147.7(4) Å^3, T = –90 °C, Z = 8, $\rho_{calcd.}$ = 1.215 g cm^{-3}, μ (Mo-K_α) = 1.32 cm^{-1}, F(000) = 2832, 17100 reflections in h(–13/13), k(–23/23), l(–49/46), measured in the range 2.27° ≤ Θ ≤ 27.51°, completeness Θ_{max} = 98%, 7763 independent reflections, R_{int} = 0.057, 6099 reflections with $F_o > 4\sigma(F_o)$, 404 parameters, 0 restraints, R_{1obs} = 0.066, wR_{2obs} = 0.153, R_{1all} = 0.090, wR_{2all} = 0.167, GOOF = 1.046, Flack parameter –0.03(13), largest difference peak and hole: 0.479/–0.347 e·Å^{-3}.

Supporting Information (see footnote on the first page of this article): Computational details, absolute energies and Cartesian coordinates of the calculated structures.

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[1] a) *Encyclopedia of Reagents for Organic Synthesis* (Eds.: L. A. Paquette); John Wiley & Sons: Chichester, **1995**; b) R. Schwesinger, *Nachr. Chem. Tech. Lab.* **1990**, *38*, 1214–1225.

[2] a) R. Schwesinger, C. Hasenfratz, H. Schlemper, L. Walz, E. M. Peters, K. Peters, H. G. von Schnering, *Angew. Chem.* **1993**, *105*, 1420–1422; b) R. Schwesinger, H. Schlemper, C. Hasenfratz, J. Willaredt, T. Dambacher, T. Breuer, C. Ottaway, M. Fletschinger, J. Boele, H. Fritz, D. Putzas, H. W. Rotter, F. G. Bordwell, A. Satish, G.-Z. Ji, E.-M. Peters, H. G. von Schnering, G. Walz, *Liebigs Ann.* **1996**, 1055–1081.

[3] a) U. Köhn, W. Günther, H. Görls, E. Anders, *Tetrahedron: Asymmetry* **2004**, *15*, 1419–1426; b) D. H. R. Barton, J. D. Elliott, S. D. Gero, *J. Chem. Soc., Perkin Trans. 1* **1982**, 2085–2090; c) M. Costa, G. P. Chiusoli, D. Taffurelli, G. Dalmonego, *J. Chem. Soc., Perkin Trans. 1* **1998**, 1541–1546; d) K. T. Leffek, P. Pruszynski, K. Thanapaalasingham, *Can. J. Chem.* **1989**, *67*, 590–595; e) T. Ishikawa, T. Isobe, *Chem. Eur. J.* **2002**, *8*, 552–557; f) R. Chinchilla, C. Najera, P. Sanchez-Agullo, *Tetrahedron: Asymmetry* **1994**, *5*, 1393–1402.

[4] a) H. Oediger, F. Moeller, K. Eiter, *Synthesis* **1972**, 591–598; b) F. Heinzer, M. Soukup, A. Eschenmoser, *Helv. Chim. Acta* **1978**, *61*, 4851–4874; c) Y. Yamamoto, S. Kojima, *The Chemistry of Amidines and Imidates* (Eds.: S. Patai, Z. Rappoport); John Wiley & Sons Inc.: NewYork, **1991**; vol. 2, 485–526.

[5] a) C. Cox, H. Wack, T. Lectka, *Angew. Chem. Int. Ed.* **1999**, *38*, 798–800; b) I. Koppel, J. Koppel, V. Pihl, *Org. React.* **1987**, *24*, 387–398; c) R. W. Alder, M. R. Bryce, N. C. Goode, N. Miller, J. Owen, *J. Chem. Soc., Perkin Trans. 1* **1981**, 2840–2847; d) V. Raab, K. Harms, J. Sundermeyer, B. Kovacevic, Z. B. Maksic, *J. Org. Chem.* **2003**, *68*, 8790–8797; e) J. Sundermeyer, V. Raab, in: *Ger. Offen.* (BASF AG, Germany). De, **2003**, p. 14 pp.

[6] a) J. G. Verkade, P. B. Kisanga, *Aldrichimica Acta* **2004**, *37*, 3–14; b) J. G. Verkade, P. B. Kisanga, *Tetrahedron* **2003**, *59*, 7819–7858; c) J. G. Verkade, *Coord. Chem. Rev.* **1994**, *137*, 233–295; d) J. G. Verkade, *Acc. Chem. Res.* **1993**, *26*, 483–489; e) J. Tang, J. Dopke, J. G. Verkade, *J. Am. Chem. Soc.* **1993**, *115*, 5015–5020.

[7] a) R. Schwesinger, J. Willaredt, H. Schlemper, M. Keller, D. Schmitt, H. Fritz, *Chem. Ber.* **1994**, *127*, 2435–2454; b) R. Schwesinger, *Chimia* **1985**, *39*, 269–272; c) R. Schwesinger, H. Schlemper, *Angew. Chem.* **1987**, *99*, 1212–1214.

[8] a) G. A. Kraus, N. Zhang, J. G. Verkade, M. Nagarajan, P. B. Kisanga, *Org. Lett.* **2000**, *2*, 2409–2410; b) I. Leito, T. Rodima, I. A. Koppel, R. Schwesinger, V. M. Vlasov, *J. Org. Chem.* **1997**, *62*, 8479–8483; c) H. Schlaad, H. Kukula, J. Rudloff, I. Below, *Macromolecules* **2001**, *34*, 4302–4304; d) T. Pietzonka, D. Seebach, *Angew. Chem.* **1992**, *104*, 1543–1545; e) T. Pietzonka, D. Seebach, *Chem. Ber.* **1991**, *124*, 1837–1843.

[9] a) C. Paulitz, W. Steglich, *J. Org. Chem.* **1997**, *62*, 8474–8478; b) M. J. O'Donnell, *Aldrichimica Acta* **2001**, *34*, 3–15; c) E. Dominguez, M. J. O'Donnell, W. L. Scott, *Tet. Lett.* **1998**, *39*, 2167–2170; d) H. Richter, T. Walk, A. Hoeltzel, G. Jung, *J. Org. Chem.* **1999**, *64*, 1362–1365; e) E. Dominguez, M. J. O'Donnell, W. L. Scott, *Tet. Lett.* **1998**, *39*, 2167–2170; f) H. Richter, T. Walk, A. Hoeltzel, G. Jung, *J. Org. Chem.* **1999**, *64*, 1362–1365.

[10] a) S. Knapp, V. K. Gore, *Org. Lett.* **2000**, *2*, 1391–1393; b) X. Du, R. W. Armstrong, *J. Org. Chem.* **1997**, *62*, 5678–5679; c) W. McComas, L. Chen, K. Kim, *Tet. Lett.* **2000**, *41*, 3573–3576; d) J. Habermann, S. V. Ley, J. S. Scott, *J. Chem. Soc., Perkin Trans. 1* **1999**, 1253–1256; e) M. Caldarelli, J. Habermann, S. V. Ley, *J. Chem. Soc., Perkin Trans. 1* **1999**, 107–110; f) I. R. Baxendale, A.-L. Lee, S. V. Ley, *J. Chem. Soc., Perkin Trans. 1* **2002**, 1850–1857; g) S. V. Ley, A. Massi, *J. Chem. Soc., Perkin Trans. 1* **2000**, 3645–3654.

[11] G. Lutz, D. Hunkler, G. Rihs, H. Prinzbach, *Angew. Chem.* **1989**, *101*, 307–309.

[12] T. L. Graybill, S. Thomas, M. A. Wang, *Tet. Lett.* **2002**, *43*, 5305–5309.

[13] a) M. Gleria, R. De Jaeger, *Top. Curr. Chem.* **2005**, *250*, 165–251; b) M. Gleria, R. De Jaeger (Eds.), *Phosphazenes: A Worldwide Insight*, Nova Science Publishers, New York **2004**; c) M. Gleria, R. De Jaeger, *J. Inorg. Organomet. Polym.* **2001**, *11*, 1–45.

[14] a) G. A. Carriedo, F. J. G. Alonso, C. D. Valenzuela, M. L. Valenzuela, *Macromolecules* **2005**, *38*, 3255–3262; b) G. A. Carriedo, J. I. Fidalgo, F. J. G. Alonso, A. P. Soto, C. D. Valenzuela, M. L. Valenzuela, *Macromolecules* **2004**, *37*, 9431–9437; c) G. A. Carriedo, F. J. G. Alonso, P. Gomez-Elipe, J. I. Fidalgo, J. L. G. Alvarez, A. Presa-Soto, *Chem. Eur. J.* **2003**, *9*, 3833–3836; d) G. A. Carriedo, F. J. G. Alonso, A. Presa-soto, *Eur. J. Inorg. Chem.* **2003**, 4341–4346.

[15] a) A. Solladie-Cavallo, M. Roje, R. Welter, V. Sunjic, *J. Org. Chem.* **2004**, *69*, 1409–1412; b) A. Solladie-Cavallo, B. Crescenzi, *Synlett* **2000**, 327–330; c) A. Solladie-Cavallo, M. Roje, T. Isarno, V. Sunjic, V. Vinkovic, *Eur. J. Org. Chem.* **2000**, 1077–1080.

[16] M. J. O'Donnell, F. Delgado, C. Hostettler, R. Schwesinger, *Tet. Lett.* **1998**, *39*, 8775–8778 and cited references.

[17] J. M. Brunel, O. Legrand, S. Reymond, G. Buono, *J. Am. Chem. Soc.* **1999**, *121*, 5807–5808.

[18] http://www.sigmaaldrich.com/area_of_Interest/Chemistry/Chemical_Synthesis/Pro-duct_Highlights/Phophazenes.html.

[19] M. Amedjkouh, P. Ahlberg, *Tetrahedron: Asymmetry* **2002**, *13*, 2229–2234.
[20] T. Hoeg-Jensen, C. E. Olsen, A. Holm, *J. Org. Chem.* **1994**, *59*, 1257–1263.
[21] COLLECT, Data Collection Software; Nonius B. V., Netherlands, **1998**.
[22] Z. Otwinowski, W. Minor, "Processing of X-ray Diffraction Data Collected, in: *Oscillation Mode*", in *Methods in Enzymology*, vol. 276, Macromolecular Crystallography, Part A, (Eds.: C. W. Carter, R. M. Sweet), pp. 307–326, Academic Press **1997**.
[23] G. M. Sheldrick, *Acta Crystallogr., Sect. A* **1990**, *46*, 467–473.
[24] G. M. Sheldrick, SHELXL-97 (Release 97–2), University of Göttingen, Germany, **1997**.
[25] CCDC-283728 (for **2a**·HBF_4), -283729 (for **2b**·HBF_4), and -283730 (for **2c**·HBF_4) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
[26] M. D. Liptak, K. C. Gross, P. G. Seybold, S. Feldgus, G. C. Shields, *J. Am. Chem. Soc.* **2002**, *124*, 6421–6427.
[27] D. Gao, P. Svoronos, P. K. Wong, D. Maddalena, J. Hwang, H. Walker, *J. Phys. Chem. A* **2005**, *109*, 10776–10785.

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