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New phosphorus-containing polycycles with a spiroamine group

Abstract

Aim. To synthesize hexahydrospiro[cyclopropane-1,10'-pyrido[1,2-*c*]quinazoline] and 2-λ^5-benzo[*f*][1,4,2]diazaphosphepine derivatives – new N-P containing heterocyclic compounds with the 6-azaspiro[2.5]octane fragment.

Results and discussion. A new analog of the powerful electrophilic reagent – "Alder dimer" – was obtained from the interaction of triflic anhydride and spiro(4-cyclopropane) piperidinyl formamide, and further used to synthesize new *N*'-P^V- and P^{III}-substituted *N*'-phenyl, *N*''-hexahydro(azaspiro)octylformamidinium salts – precursors of acyclic N-phosphorylated diamino carbenes with a spiroamine group. It has been shown that acyclic N-phosphorylated diaminocarbenes are transient species affording various products. The structure of the final product is primarily determined by nature of the phosphorus-bearing substituent, namely a phosphoryl or phosphino-group. *N*-P^V-substituted carbene undergoes a 1,2-phosphorus shift with the formation of (selenophosphoryl)formamidine in a high yield. For *N*-P^{III}-substituted carbene a compatible 1,3-*H* shift also occurs with the formation of an intermediate azomethine ylide converted into a new heterocyclic system – hexahydrospirocyclopropane -1,10'-pyrido[1,2-*c*]quinazoline. Under the action of acid an unexpected further expansion of the 6-member ring occurs with the formation of a diazepine derivative.

Experimental part. The reaction of Alder reagent with N-P^V-seleno phosphoryl arylamides afforded N-phosphorus substituted formamidinium salts, which are easily reduced to P^{III} analogues. In addition to the corresponding formamidines, the new *N*-phosphorylated spiroamine-containing polycyclic system was isolated from the reaction mixture formed by the deprotonation of such salts with a strong non-nucleophilic base.

Conclusions. The Alder reagent approach allows synthesizing precursors of acyclic formamidine carbenes with the spiroamine group. Such carbenes are unstable. By converting these compounds *N*-P^{III}-substituted tetrahydropyrimidine and diazaphosphepine derivatives with the 6-azaspiro[2.5]octane fragment have been obtained for the first time.

***Keywords*:** transient acyclic carbenes; 1,2-phosphorus shift; 6-azaspiro[2.5]octane; diazaphosphepine; N-P bond

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Нові фосфоровмісні поліциклічні сполуки зі спіроаміногрупою

Анотація

Мета. Синтезувати похідні гексагідроспіро[циклопропан-1,10'-піридо[1,2-*c*]хіназоліну] та 2-λ^5-бензо[*f*][1,4,2]діазафосфепіну – нові гетероциклічні N-P-вмісні сполуки із фрагментом 6-азаспіро[2.5]октану.

Результати та їх обговорення. У результаті взаємодії ангідриду трифлатної кислоти з формамідом (спіроциклопропан)піперидину отримано потужний електрофільний реагент – новий аналог «димера Альдера», за допомогою якого синтезовано нові *N*'-P^V- та P^{III}-заміщені солі *N*'-феніл, *N*''-азаспірооктил формамідинію – прекурсори ациклічних *N*-фосфорильованих діамінокарбенів зі спіроаміногрупою. Виявлено, що останні не є стабільними сполуками і зазнають *in situ* перетворень з утворенням різних продуктів, будова яких визначається насамперед типом фосфоровмісного замісника: фосфорильна або фосфіно-групи. *N*-P^V-заміщений карбен зазнає 1,2-фосфорного зсуву з утворенням селенофосфорилформамідину з високим виходом. У *N*-P^{III}-заміщених карбенах відбувається також рівнобіжний 1,3-Н зсув з утворенням проміжного азометин іліду, який циклізується в нову гетероциклічну систему – гексагідроспіро[циклопропан-1,10'-піридо[1,2-*c*]-хіназолін]. Неочікуване подальше розширення 6-членного остова з утворенням похідної діазепіну відбувається під дією кислоти.

Експериментальна частина. Оригінальною реакцією реактиву Альдера з *N*-селенофосфорил ариламідами одержано *N*-фосфорил заміщені формамідинові солі, які легко відновлюються до P^{III}-аналогів. Окрім відповідних формамідинів,

нову N-фосфорильовану спіроаміновмісну поліциклічну систему було виділено з реакційної суміші, що утворюється за депротонування таких солей сильною ненуклеофільною основою.

Висновки. Використання підходу з реактивом Альдера дозволяє синтезувати прекурсори ациклічних формамідинових карбенів зі спіроаміногрупою. Такі карбени не є стійкими. Перетворенням цих сполук уперше отримано *N*-P^{III}-заміщений тетрагідропіримідин та похідні 1,2,4-діазадигідрофосфепіну з фрагментом 6-азаспіро[2.5]октану.

Ключові слова: транзитні ациклічні карбени; 1,2-фосфорний зсув; 6-азаспіро[2.5]октан; діазафосфепін; N-P-зв'язок

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■ Introduction

Since the early 1990s, there was the booster progress in *N*-heterocyclic carbenes chemistry owing to their excellent properties as ligands for transition metals [1, 2]. But today they rate far beyond privileged homogeneous catalysis transformations [3]. Their inherent structural and electronic features make them highly useful in different eminent areas of research, such as organometallic materials [4, 5], metallopharmaceuticals [6, 7] and as organocatalysts [8]. Alongside, carbenes still appear as reactive intermediate species in organic transformations, which could lead to rarely accessible heterocyclic compounds [9].

In our previous works, we presented a new type of acyclic diaminocarbenes: *N*-P^{III}- and P^{V}-substituted diaminocarbenes **A** (X = lone pair or Se) (Figure) [10–12]. It was found that diaminocarbenes **A** (X = lone pair) bearing bulky alkyl groups (R = *t*Bu or Ad) and N(*i*Pr)$_2$ were the most stable (Figure). Both increase and decrease in the size of the dialkylamino group N(R^2)$_2$ made them unstable leading to various transformations. Nevertheless, these P^{III} carbenes were characterized spectroscopically unlike their P^{V} congeners that gave C-phosphorylated formamidines **B** (X = Se) [10, 11]. The carbenes **A** (X = lone pair) featuring N(R^2)$_2$ groups (piperidino, pyrrolidino, azetidino and dimethylamino) were found to be unstable eventually producing a mixture of products. The major product in the mixture appeared to be *N*-P^{III}-substituted tetrahydroquinazolines [12]. Compared to N-heterocyclic carbenes, acyclic diaminocarbenes (ADCs) are known to lack a geometrical rigidity that drives for better σ-donor properties and facilitates in some cases the creation of a chiral environment. However, flexibility of these systems makes them less stable, and the σ-donicity strongly depends on their conformation [13, 14] with both controlled by steric encumbrance of the *N*,*N*'-substituents attached to the C^2 carbon centre. In addition to dimerization, ADCs are disposed to undergo different routes of decomposition. *β*-Fragmentation of stable [*bis*(diisopropyl)amino]carbene was reported by *Alder* [15]. The above-mentioned 1,2-migrations are described for both cyclic azole-based analogs and imidazolylidenes that have other heteroatom centered groups (B, Si, N) attached at the adjacent nitrogens [16–18]. Analogous transformation by C-H bond insertion is less known [19]. An example of cyclization into a novel bicyclic compound by an acid-promoted 1,3-isomerization of a stable aminocarbene into a transient azomethine ylide was reported by *Bertrand* [20]. Moreover, among the intramolecular cyclizations, which are rare ways to larger phosphorus heterocycles, ring-enlargement reactions with the insertion of phosphorous are not common. Among a few examples there is the

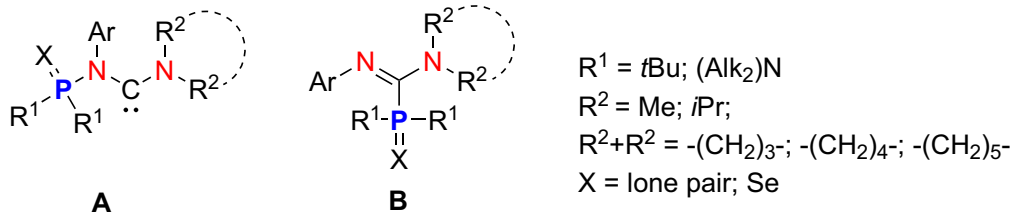

Figure. N-phosphorylated diaminocarbenes and C-phosphorylated formamidines

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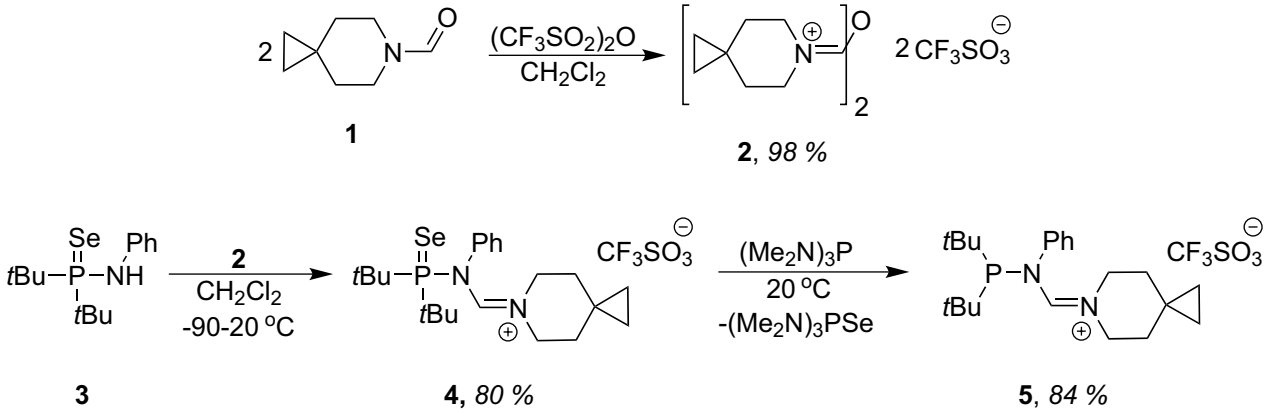


Scheme 1. The synthesis of P^{III} formamidinium salt

insertion of a phosphorus atom into the C-O linkage of oxazolidine that is a key step in the synthesis of α-amino phosphonic acids [21]. When benzylated 1-O-acetyl-D-hexopyranoses reacted with triethyl phosphite and trimethylsilyl trifluoromethanesulfonate as a catalyst the similar phosphorus insertion opened a way to seven-membered nucleoside phostones [22].

We were interested in using the method described above to obtain derivatives of higher complexity amines actually used as a structural fragment in the synthesis of therapeutic agents. With the growth of pandemic agents' activity in the world, the generation of new models of compounds with the biological activity does not lose its relevance. This work focuses on derivatives containing the residue of spirocyclopropyl piperidine – 6-azaspiro[2.5]octane. Namely, spiroamino compounds of this type are associated with the synthesis of the immune checkpoint inhibitor, chemokine receptor antagonists [23, 24]. Astra Zeneca synthesized such derivatives as a potent histamine H3 receptor antagonist [25]. It is believed that the antibacterial activity of DV-7751 correlate with the (*S*)-amino-6-azaspiro[3.4]octane moiety [26].

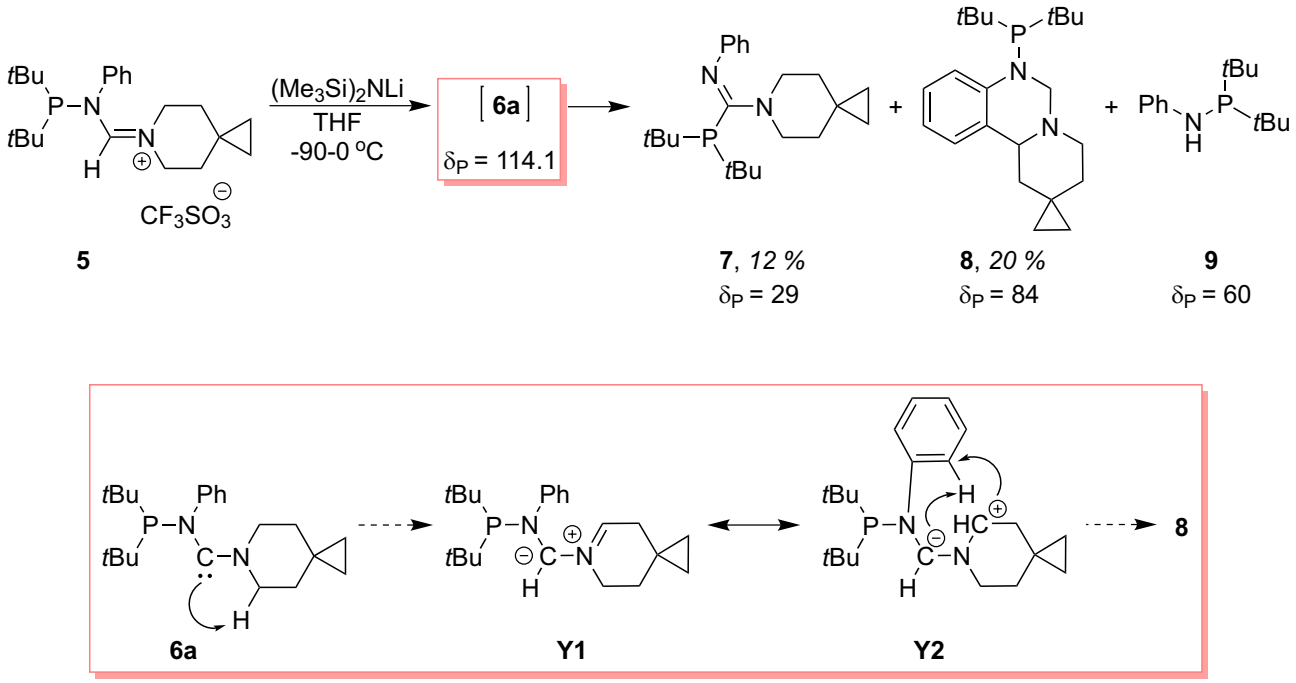
■ Results and discussion

Compound **2** is an analog of the Alder reagent bearing the residue of spirocyclopropyl piperidine. It can be quite easily synthesized from the available starting substances by the interaction of formamide **1** with triflic acid anhydride (Scheme 1) [27]. Mixing the reagents at the temperature range of -90–-70°C in dichloromethane gave a pure compound **2** that gradually precipitated as a colorless crystalline solid. It is well stored in a solid state at +4°C; if necessary, it can be crystallized from acetonitrile.

Previously, we showed that *N*-Aryl phosphinoselenoic amides **3** reacted readily with Alder dimers in a molar ratio of 1:1 giving hydrolytically stable P^{V}-*N*-substituted salts like **4** with a yield of more than 90% [12, 28]. Similarly, formamidinium triflate **4** was prepared in dichloromethane in a good yield (Scheme 1). The selenophosphoryl group of salt **4** was readily reduced when treated with hexamethylphosphorus triamide to give the corresponding *N*-P^{III}-substituted formamidinium salt **5** (Scheme 2). In ^{1}H NMR spectra both compounds had a weak signal at δ_{H} 8–9 ppm, which was distinctive for the N-CH=N– fragment. Equivalent signals as the most downfield doublet for **4** and singlet for P^{III}- **5** were present in their ^{13}C NMR spectra (δ_{C} 155–157 ppm). A distinctive quartet with a typical constant 320 Hz was observed for the CF_3-group.

As noted above, *N*-P^{V}- and P^{III}-substituted formamidinates like **4** and **5** meet the requirements as precursors of carbenes. However, it was found that regardless of the nature of the substituents at the adjacent *N*-atoms after deprotonation of *N*-P^{V}-substituted derivatives like **4**, the reaction mixture contained *C*-selenophosphoryl-formamidines when reaching the room temperature [10, 12]. In some cases, carbene **C** (P^{V}-) (Figure) was recorded using ^{31}P NMR at low temperatures.

As we were interested in the formation of phosphorus heterocycles, we studied directly deprotonation of P^{III}-derivatives. Like in the case of other formamidinium carbenes with cyclic secondary amino groups the formation of **6a** by addition of lithium hexamethyldisilazide to salt **5** was confirmed by ^{31}P NMR (δ_{P} = 114 ppm, -10°C) [12]. The final reaction mixture contained tetrahydroquinazolines **8**, as well as phosphanes **7** and tBu$_2$PNHPh (**9**). The compounds **8** and **7** were isolated, and their structure was confirmed by



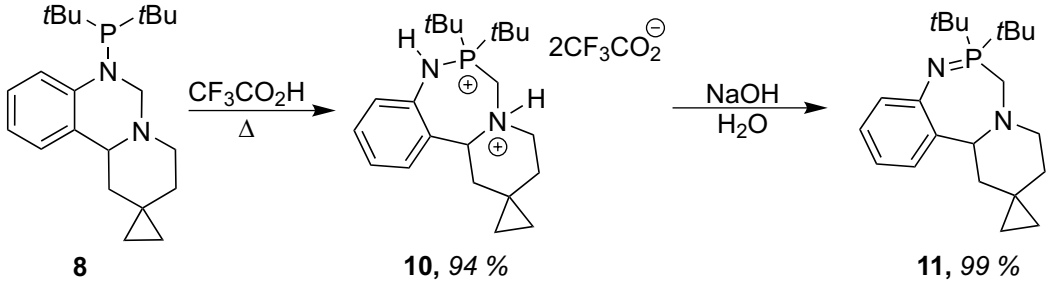
Scheme 2. Deprotonation of formamidinium salt **5**

NMR spectroscopy and mass-spectrometry. Amide **9** was identified by comparing the ^{31}P NMR signal with the tabular value. As seen in Table, the stability of carbene **6** as well as the content of the target cyclic product **8** is quite low compared to the previous results with azetidine (**6b**), pyrrolidine (**6c**) and piperidine (**6d**) [12]. Taking into account the mechanism of this cyclization earlier calculated according to DFT [12], aza-ylide **Y1** formed as an intermediate can be unstable in case of large secondary amines, such as 6-azaspiro[2.5]octane. As a result, the decomposition of carbene to phosphinous amide under the reaction conditions proceeds to a greater extent.

It is well known that amidophosphinous derivatives $(R^1)_2$P-N$(R^2)_2$ are readily hydrolyzed when treating with aqueous acids to give the corresponding phosphinic acids [29]. Similarly to the derivatives of quinazolines containing a pyrrolidine or piperidine fragment, the action of trifluoroacetic acid on tricyclic compound **8** led to the formation of phosphonium compounds **10**, but not to the hydrolysis of the P-N bond [30]. Subsequent addition of an alkali to a solution of such

Table. Properties of carbenes **6**

Compound No.	*t*Bu$_2$PNHPh Yield, %	Yield of **7**, %	Yield of **8**, %	$t_{1/2}$ of carbene **6**
6a	50	22	21	3 days (-4 °C)
6b	25	-	54	4 days (-4 °C)
6c	18	12	60	54 min (20 °C)
6d	30	23	46	75 min (20 °C)



Scheme 3. The ring enlargement reaction of compound **8**

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a salt also smoothly gave phosphazene **11** with a cycle size of one atom larger (Scheme 3). In favor of changes in the structure of these substances spectral data are indicative. Thus, in ^{31}P NMR spectra the signals of compounds **8**–**10**–**11** shifted naturally in a range of δ_P 85–69–42 ppm, in the area of a strong field corresponding to P^V compounds. The most downfield doublet observed in the ^{1}H NMR spectrum of salt **10** apparently corresponded to the ammonium proton and disappeared after the treatment of salt with a base. In ^{13}C NMR spectra of seven-membered cycles **10** and **11**, the signal of the methylene carbon atom of –N-$\underline{CH_2}$-N– group had a greater coupling constant and was shifted by almost 30 ppm to a strong field, reflecting a change in the coordination number of the phosphorus atom and the formation of the C-P bond. The appearance of additional conjugation of double bonds in the diazaphosphepine cycle of **11** was noticeably displayed by the change of chemical shifts of the benzene ring carbon atoms.

Conclusions

New *N*-P^{III}-substituted tetrahydropyrimidine and diazaphosphepine derivatives with the 6-azaspiro[2.5]octane fragment have been obtained as a result of inherent transformations of acyclic formamidinium carbenes.

Experimental part

All procedures with air- and moisture-sensitive compounds were performed under dry argon in flame-dried glassware. Solvents were purified and dried by standard methods. Melting points were determined with an electrothermal capillary melting point apparatus. ^{1}H NMR spectra were recorded with a Bruker Avance DRX 500 (500.13 MHz) or a Varian VXR-300 (299.94 MHz) spectrometer. ^{13}C NMR spectra were recorded with a Bruker Avance DRX 500 (125.75 MHz) spectrometer. ^{31}P NMR spectra were recorded with a Varian VXR-300 (121.4 MHz) spectrometer. Chemical shifts (δ) were given in ppm downfield relative to internal tetramethylsilane (TMS) for ^{1}H and ^{13}C and external 85% H_3PO_4 for ^{31}P. Elemental analyses were performed at the analytical laboratory of the Institute of Organic Chemistry, National Academy of Sciences of Ukraine. Mass spectra were recorded on an Agilent 1200 LCMSD SL instrument (atmospheric pressure chemical ionization (APCI), electrospray ionization (ESI)) or Agilent 7820A gas chromatograph system (electron impact ionization (EI), ionization energy −70 eV).

The synthesis of 6-azaspiro[2.5]octane-6-carbaldehyde (1)

To the solution of 6-azaspiro[2.5]octane (8.9 g, 0.08 mol) in *o*-xylene (30 mL), formic acid (4.0 g, 0.087 mol) was added. The reaction mixture was heated at 170°C for 2 h and another 1 h at 190°C with the distillation of *o*-xylene by the help of a Dean-Stark nozzle. The residue was kept at the reduced pressure (12 mmHg) at 95°C with a condensate detachment, then re-distilled twice in high vacuo (b. p. 60°C/0.05 mmHg) to give aldehyde **1**. Anhydrous compound **1** was obtained by distillation under P_2O_5.

A white solid. Yield – 10.1 g (92%). M. p. 26–28°C (hexane). ^{1}H NMR (500 MHz, $CDCl_3$), δ, ppm: 0.35 (4H, s, CH_2); 1.31–1.38 (4H, m, CH_2); 3.34 (2H, t, J = 5.5 Hz, CH_2); 3.52 (2H, t, J = 5.5 Hz, CH_2); 8.02 (1H, s, CH). ^{13}C NMR (125.7 MHz, $CDCl_3$), δ, ppm: 11.4 (s, CH_2); 17.9 (s, *C*); 34.2 (s, CH_2); 35.8 (s, CH_2); 39.7 (s, CH_2); 45.9 (s, CH_2); 160.59 (s, CH). GC-MS (EI), m/z, peak area: 139, 99.6%.

The synthesis of the Alder dimer 6,6'-(oxybis(methaneyl-6-ylidene))bis(6λ^4-azaspiro[2.5]octane) trifluoromethanesulfonate (2)

To a cooled to -90°C solution of trifluoromethanesulfonic anhydride (3.4 g, 12 mmol) in dichloromethane (30 mL) the solution of formamide **1** (3.5 g, 25 mmol) in dichloromethane (30 mL) was added. The reaction mixture was stirred until the temperature increased to 16°C, and then for 1 h. The precipitate was filtered under argon, washed with dichloromethane (3×20 mL) and dried to give a pure target compound. The analytical sample was obtained by crystallization from acetonitrile.

A white powder. Yield – 6.52 g (98%). M. p. 191–193°C (decomp.). Anal. Calcd. for $C_{18}H_{26}F_6N_2O_7S_2$, %: C 38.57; H 4.68; N 5.00. Found, %: C 38.93; H 4.75; N 5.07. ^{1}H NMR (500 MHz, CD_3CN), δ, ppm: 0.58 (4H, s, 2×CH_2); 1.77 (2H, br. s, CH_2); 1.82 (2H, br. s, CH_2); 4.14 (4H, br. s, 2×CH_2); 9.31 (1H, s, CH). ^{13}C NMR (125.74 MHz, $CDCl_3$), δ, ppm: 11.16 (s, CH_2); 16.07 (s, C); 32.94 (s, CH_2); 33.58 (s, CH_2); 49.72 (s, CH_2); 54.52 (s, CH_2); 120.8 (q, J_{CF} = 320 Hz, CF_3); 158.32 (br. s, CH).

The synthesis of 6-(((di-*tert*-butylphosphoroselenoyl)(phenyl)amino)methylene)-6-azaspiro[2.5]octan-6-ium trifluoromethanesulfonate (4)

To the suspension of Alder dimer **2** (6.5 g, 11.5 mmol) cooled to -90°C in dichloromethane (30 mL) the solution of *P*,*P*-di-*tert*-butyl-

N-phenylphosphinoselenoic amide **3** (3.8 g, 12.0 mmol) in dichloromethane (20 mL) was added. After reaching the room temperature (16°C) the reaction mixture was stirred for 20 min. The solvent was evaporated at reduced pressure. Diethyl ether (50 mL) was added to the oil-like residue, then it was shaken to its solidification. The crystalline product formed was filtered under argon using a reverse rinse filter, washed with diethyl ether (4×20 mL), dried and then dissolved in THF (20 mL). The solid product formed at 2°C was separated by filtration under argon, washed with THF (2×15 mL) to give compound **4**. The mother liquor was evaporated in vacuo, the solid residue was washed with water (4×5 mL) to the neutral pH, the insoluble precipitate was dried in vacuo to give an additional amount of compound **4**.

A white powder. Yield – 5.4 g (80%). M. p. 177–178°C. Anal. Calcd. for $C_{23}H_{36}F_3N_2O_3PSSe$, %: C 47.02; H 6.18; N 4.77. Found, %: C 46.92; H 6.02; N 4.99. ^{1}H NMR (500 MHz, $CDCl_3$), δ, ppm: 0.32 (2H, s, CH_2); 0.41 (2H, s, CH_2); 1.15 (2H, s, CH_2); 1.58 (18H, d, J_{HP} = 17.5 Hz, 6×CH_3); 1.68 (2H, s, CH_2); 2.92 (2H, s, CH_2); 4.01 (2H, s, CH_2); 7.4–7.6 (5H, m, Ph); 8.75 (1H, s, CH). ^{13}C NMR (125.74 MHz, $CDCl_3$), δ, ppm: 11.7 (s, CH_2); 16.5 (s, CH_2); 29.2 (s, CH_3); 34.2 (s, CH_2); 35.8 (s, CH_2); 45.0 (d, J_{CP} = 28 Hz, $\underline{C}(CH_3)_3$); 49.1 (s, CH_2); 59.3 (s, CH_2); 120.9 (q, J_{CF} = 320 Hz, CF_3); 129.8 (s, CH); 130.0 (s, CH); 130.1 (s, CH); 136.6 (s, *C*); 155.4 (d, J_{CP} = 9 Hz, CH). ^{31}P NMR (202.4 MHz, $CDCl_3$), δ, ppm: 141.4 (J_{PSe} = 832 Hz). LC-MS (ESI), *m/z*: 439 $[M–CF_3SO_3+1]^+$; 149 $[CF_3CO_3]^-$; 316 $[M\text{-}124]^-$.

The synthesis of 6-(((di-*tert*-butylphosphanyl)(phenyl)amino)methylene)-6-azaspiro[2.5]octan-6-ium trifluoromethanesulfonate (5)

To the suspension of compound **4** (4.0 g, 6.8 mmol) in dichloromethane (15 mL) at 20°C, hexamethylphosphorous triamide (1.2 g, 7.4 mmol) was added dropwise with stirring. In 30 min, the solvent was evaporated to dryness at reduced pressure. A dry diethyl ether (30 mL) was added to the residue. The flask was shaken until a crystalline solid was formed. The solid was collected by filtration under argon, washed with diethyl ether (4×20 mL), and dried to constant weight in vacuo (0.05 Torr).

A white powder. Yield – 2.9 g (84%). M. p. 93–94°C. Anal. Calcd. for $C_{23}H_{36}F_3N_2O_3PS$, %: N 5.51; P 6.09. Found, %: N 5.17; P 5.93. ^{1}H NMR (300 MHz, $CDCl_3$), δ, ppm: 0.31 (2H, s, CH_2); 0.40 (2H, s, CH_2); 1.21 (2H, s, CH_2); 1.34 (18H, d, J_{HP} = 13.2 Hz, 6×CH_3); 1.65 (2H, t, J_{HH} = 5.4 Hz, CH_2); 2.98 (2H, br. t, J_{HH} = 5.6 Hz, CH_2); 4.0 (2H, br. s, CH_2); 7.3-7.5 (5H, m, Ph); 8.04 (1H, br. s, CH). ^{13}C NMR (125.7 MHz, $CDCl_3$), δ, ppm: 11.6 (s, CH_2); 16.4 (s, CH_2); 29.24 (d, J_{CP} = 18 Hz, *C*); 33.96 (s, CH_2); 35.1 (s, CH_2); 36.9 (d, J_{CP} = 35 Hz, *C*); 48.0 (s, CH_2); 56.7 (s, CH_2); 120.9 (q, J = 320 Hz, CF_3); 126.0 (s, CH); 128.6 (s, CH); 130.5 (s, CH); 144.2 (s, *C*); 156.8 (s, CH). ^{31}P NMR (202.4 MHz, $CDCl_3$), δ, ppm: 131.5.

The procedure for the synthesis of compounds 7 and 8.

To the solution of salt **5** (2.9 g, 5.8 mmol) in THF (20 mL) at -90°C the solution of lithium hexamethyldisilazide (930 mg, 5.6 mmol) in THF (20 mL) was added dropwise over 5 min. After reaching -60°C, the reaction mixture was stirred for another 10 min, then kept stirring at 0°C for 10 days (or at -4°C for 13 days). The solvent was evaporated in vacuo, the solid residue was extracted with pentane (50 mL), the precipitate was filtered off under argon using the reverse rinse filter, washed with pentane (3×20 mL). The filtrate was evaporated in vacuo, the residue was purified by fractionation at reduced pressure. Amidophosphonite **9** (1.27 g; b. p. 60–110°C/0.05 mmHg) was obtained in the first fraction. The second fraction (b. p. 150–160°C/0.05 mmHg) contained mixture of products **7** and **8** (930 mg). This mixture was recrystallized from pentane (2.5 mL), the precipitate formed at -18°C was collected to give compound **8** (400 mg, 20%; m. p. 96–97°C). The mother liquor was concentrated at reduced pressure to 1/4 of volume, in 24 h at -18°C the precipitated compound **7** (280 mg, 12%; m. p. 110–112°C) was collected.

[(6-Aza-spiro[2.5]oct-6-yl)-(di-tert-butyl-phosphanyl)-methylene]-phenyl-amine (**7**)

Yellowish crystals. Yield – 0.28 g (12%). M. p. 110–112°C (hexane). Anal. Calcd. for $C_{22}H_{35}N_2P$, %: C 73.71; N 7.81. Found, %: C 73.66; N 7.74. ^{1}H NMR (300 MHz, $CDCl_3$), δ, ppm: 0.25 (4H, s, 2×CH_2); 1.26 (4H, br. s, 2×CH_2); 1.33 (18H, d, J_{PH} = 12 Hz, 6×CH_3); 3.30 (4H, br. s, 2×CH_2); 6.72 (2H, d, J_{HH} = 8 Hz, Ph); 6.88 (1H, t, J_{HH} = 8 Hz, Ph); 7.25 (1H, t, J_{HH} = 8 Hz, Ph); 7.26 (1H, t, J_{HH} = 8 Hz, Ph). ^{13}C NMR (125.7 MHz, $CDCl_3$), δ, ppm: 11.3 (s, CH_2); 17.5 (s, CH_2); 30.14 (d, J_{CP} = 14 Hz, $\underline{C}(CH_3)_3$); 33.15 (d, J_{CP} = 20 Hz, *C*); 35.0 (s, CH_2); 49.25 (d, J_{CP} = 16 Hz, C); 120.0 (s, CH, Ph); 120.6 (s, CH, Ph); 128.7 (s, CH, Ph); 163.15 (d, J_{CP} = 10 Hz, C-P). ^{31}P NMR (81 MHz, $CDCl_3$), δ, ppm: 29.5. LC-MS (ESI), *m/z*, peak area: 359.2 $[M+H]^+$, 94%.

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5'-(Di-tert-butylphosphino)-5',6',8',9',11',11a'-hexahydrospiro[cyclopropane-1,10'-pyrido[1,2-c]quinazoline] (**8**)

A white solid. Yield – 0.2 g (20%). M. p. 96–97°C. Anal. Calcd. for $C_{22}H_{35}N_2P$, %: C 73.71; H 9.84; N 7.81. Found, %: C 73.70; H 9.78; N 7.75. ^{1}H NMR (300 MHz, $CDCl_3$), δ, ppm: 0.36-0.41 (3H, m, CH_2); 0.86 (1H, d, J_{HH} = 12.6 Hz, CH_2); 1.30 (9H, d, J_{HP} = 12.3 Hz, 3×CH_3); 1.31 (9H, d, J_{HP} = 12.6 Hz, 3×CH_3); 1.92 (1H, t, J_{HH} = 12 Hz, CH_2); 2.16 (1H, t, J_{HH} = 12 Hz, CH_2); 2.34 (1H, t, J_{HH} = 11 Hz, CH_2); 2.87 (1H, d, J_{HH} = 10 Hz, CH_2); 3.53 (1H, d, J_{HH} = 10.5 Hz, CH_2); 3.89 (1H, d, J_{HH} = 10.5 Hz, CH_2); 4.36 (1H, d, J_{HH} = 10.5 Hz, CH_2); 6.75 (1H, t, J_{HH} = 7.5 Hz, Ph); 6.94 (1H, d, J_{HH} = 7.5 Hz, Ph); 7.07 (1H, t, J_{HH} = 7.5 Hz, Ph); 7.66 (1H, t, J_{HH} = 7.0 Hz, Ph). ^{13}C NMR (125.7 MHz, $CDCl_3$), δ, ppm: 11.2 (s, CH_2); 12.9 (s, CH_2); 18.3 (s, *C*); 29.5 (d, J_{CP} = 16 Hz, *C*); 30.3 (d, J_{CP} = 18 Hz, *C*); 34.85 (s, CH_2); 35.7 (d, J_{CP} = 24 Hz, *C*); 37.04 (d, J_{CP} = 30 Hz, *C*); 41.8 (s, CH_2); 51.8 (s, CH_2); 62.3 (s, CH_2); 70.1 (d, J_{CP} = 10 Hz, *C*); 118.6 (s, CH); 119.2 (d, J_{CP} = 30 Hz, CH); 125.2 (s, CH); 126.2 (s, CH); 126.77 (d, J_{CP} = 4 Hz, *C*); 147.7 (d, J_{CP} = 23 Hz, *C*). ^{31}P NMR (81 MHz, $CDCl_3$), δ, ppm: 84.9. LC-MS (ESI), *m/z*, peak area: 359.2 $[M+H]^+$, 97%.

The synthesis of 6,6-di-*tert*-butyl-5,6,7,8,9,10,12,12a-octahydrospiro[benzo[*f*]pyrido[1,2-*d*][1,4,2]diazaphosphepine-11,1'-cyclopropane]-6,8-diium *bis*(2,2,2-trifluoro acetate) (**10**)

The mixture of **8** (200 mg, 0.56 mmol) and trifluoroacetic acid (2 g, 4.4 mmol, at least 2.5 equivalents) was refluxed at 95–100°C for 1 h. The mixture was concentrated at reduced pressure, the residue was dissolved in Et_2O (5 mL) and kept at -18°C until the residue solidifies, the solid product was collected, washed with Et_2O (2×2 mL) and dried in vacuo.

A white solid. Yield – 0.300 g (94%). M. p. 126–127°C. ^{1}H NMR (500 MHz, $CDCl_3$), δ, ppm: 0.32 + 0.35 (4H, 2×br. s, CH_2); 0.75 (1H, d, J = 13.5 Hz, CH_2); 0.86 (1H, d, J = 13 Hz, CH_2); 1.20 (9H, d, J_{HP} = 14.5 Hz, 3×CH_3); 1.62 (9H, d, J = 15 Hz, 3×CH_3); 2.06-2.11 (2H, m, CH_2); 2.896 (1H, t, J = 11 Hz, CH_2); 3.05 (1H, d, J = 11 Hz, CH_2); 3.64–3.76 (3H, m, CH + CH_2); 7.00 + 7.046 (2H, d + t, J = 7.5 Hz + J = 7.5 Hz, ArH); 7.12 (1H, t, J = 7.5 Hz, ArH); 7.39 (1H, d, J = 8.0 Hz, ArH); 7.72 (1H, d, J = 8.0 Hz, NH). ^{13}C NMR (125.7 MHz, $CDCl_3$), δ, ppm: 10.8 (CH_2); 12.5 (CH_2); 18.0 (*C*); 26.97 (CH_3); 27.9 (CH_3); 35.0 (CH_2); 35.8 (d, $^1J_{CP}$ = 46.5 Hz, *C*); 38.5 (d, $^1J_{CP}$ = 31 Hz, *C*); 45.0 (d, $^1J_{CP}$ = 69 Hz, CH_2); 46.9 (CH_2); 57.2 (d, $^3J_{CP}$ = 11 Hz, CH_2); 71.3 (CH); 116.0 (q, $^1J_{CF}$ = 290.5 Hz); 125.5 (CH); 126.6 (d, $^4J_{CP}$= 6.3 Hz, CH); 128.5 (CH); 130.8 (CH); 132.9 (*C*); 136.9 (d, $^2J_{CP}$= 5 Hz, *C*); 160.4 (d, $^1J_{CF}$ = 3.8 Hz). ^{31}P NMR (80.9 MHz, $CDCl_3$), δ, ppm: 69.5. LC-MS (ESI), *m/z*: 359.2 $[M–CF_3CO_2+1]^+$; 113 $[CF_3CO_2]^-$.

The synthesis of 6,6-di-*tert*-butyl-9,10,12,12a-tetrahydro-7*H*-6λ^5-spiro[benzo[*f*]pyrido[1,2-*d*] [1,4,2]diazaphosphepine-11,1'-cyclopropane] (**11**)

To the solution of salt **10** (280 mg, 0.9 mmol) in H_2O (3 mL) the solution of NaOH (500 mg) in H_2O (1 mL) was added. The mixture was heated at 80°C with stirring for 1 h. Then after cooling benzene (2×4 mL) was added, the organic phase was collected, concentrated under vacuum, dried and distilled (180°C/0.05 mmHg) to give **11** as a mushy solid recrystallized from pentane (2.5 mL).

A beige solid. Yield – 0.150 g (99%). M. p. 102–103°C (pentane). Anal. Calcd. for $C_{22}H_{35}N_2P$, %: C 73.71; H 9.84; N 7.81. Found, %: C 73.67; H 9.97; N 7.75. ^{1}H NMR (500 MHz, $CDCl_3$), δ, ppm: 0.29-0.33 (4H, m, CH_2); 0.76 + 0.825 (2H, d + d, J = 13.5 Hz, J = 15 Hz, CH_2); 1.11 (9H, d, J_{PH} = 12.5 Hz, 3×CH_3); 1.44 (9H, d, J_{PH} = 13.5 Hz, 3×CH_3); 2.06–2.11 (1H, m, CH_2); 2.24 (1H, t, J = 9.5 Hz, CH_2); 2.76 (1H, t, J = 11.0 Hz, CH_2); 2.92 (1H, d, J = 12.0 Hz, CH_2); 3.11 (1H, dd, J_1 = 15.0 Hz, J_2 = 6.5 Hz, CH); 3.44 (1H, d, J = 13.0 Hz, CH_2); 3.61 (1H, d, J = 10.5 Hz, CH_2); 6.58-6.60 (1H, m, ArH); 6.83 (1H, d, J = 8.0 Hz, ArH); 6.92 (2H, br. s, ArH). ^{13}C NMR (125.7 MHz, $CDCl_3$), δ, ppm: 10.9 (CH_2); 12.7 (CH_2); 18.2 (*C*); 27.5 (CH_3); 28.2 (CH_3); 35.2 (d, $^1J_{CP}$= 70 Hz, *C*), 35.4 (CH_2), 38.56 (d, $^1J_{CP}$= 47 Hz, *C*); 46.3 (CH_2); 46.56 (d, $^1J_{CP}$= 50 Hz, CH_2); 57.7 (d, $^2J_{CP}$ = 11 Hz, CH_2); 71.0 (CH); 117.4 (d, $^4J_{CP}$ = 2.5 Hz, CH); 126.9 (CH); 128.55 (d, $^3J_{CP}$= 15 Hz, CH); 129.4 (d, $^4J_{CP}$= 2.5 Hz, CH); 133.4 (d, $^3J_{CP}$= 5 Hz, *C*); 153.5 (d, $^2J_{CP}$= 5 Hz, *C*). ^{31}P NMR (80.9 MHz, $CDCl_3$), δ, ppm: -41.7. LC-MS (ESI), *m/z*: 360.1 $[M+2]^+$.

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