

# Hetero-Diels-Alder reactions of *N*-phosphoryltrihaloacetimidoyl chlorides with 1,3-butadienes

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**Dedicated to Prof. Pawel Kafarski to honor the achievements within his career**

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## Abstract

Hetero-Diels-Alder reactions of *N*-phosphoryltrihaloacetimidoyl chlorides with 1,3-butadienes led to new 2-chloro-2-trihalomethyl substituted tetrahydropyridine adducts. Cycloadducts with CF<sub>3</sub> group undergo thermal or acid catalyzed dehydrochlorination affording respective dihydropyridines and subsequent aromatization to form 2-trifluoromethylpyridines. Trichloromethyl analogs under similar conditions undergo aromatization accompanied by unusual reduction of CCl<sub>3</sub> group to form respective 2-dichloromethyl substituted pyridines.

**Keywords:** Aza-Diels-Alder reaction, imidoyl chlorides, tetrahydropyridines, dihydropyridines, pyridines

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## Introduction

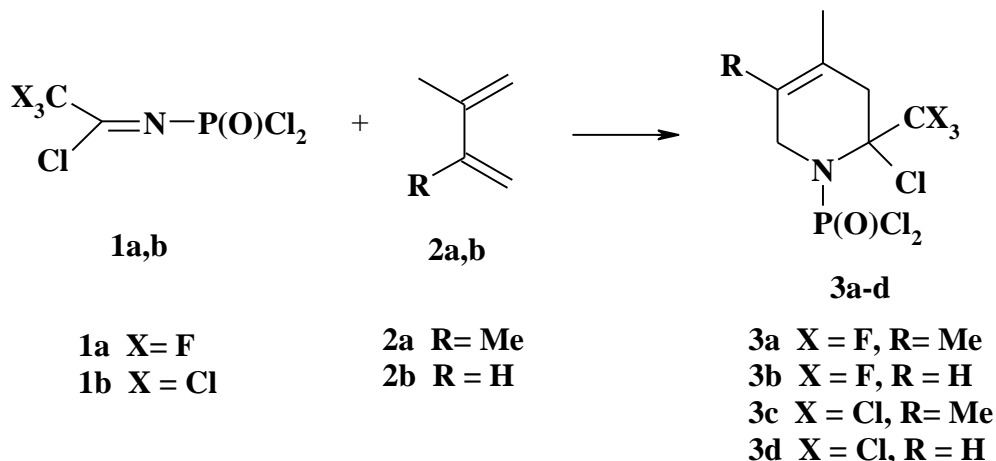
Imidoyl chlorides combine the properties of acid chlorides and azomethynes. They are reactive and versatile chemical agents and have found wide application in organic synthesis and in the study of chemical reactivity.<sup>1</sup> Trihaloacetimidoyl chlorides are regarded as new promising building blocks for regioselective introduction of (poly)haloalkyl groups into acyclic or heterocyclic compounds.<sup>2</sup> Cycloaddition across C=N bond of trihaloacetimidoyl chlorides would offer additional opportunities connected with the possibility to introduce regioselectively trihalomethyl group into a molecule and further transformations of primary products via chlorine atom participation. Replacement of hydrocarbon groups in molecules with their fluorinated analogs imparts a variety of useful properties to certain medicines, including enhanced binding interactions and metabolic stability.<sup>3</sup> As a result, fluorine containing compounds are becoming increasingly important in both agrochemistry and medicine.<sup>4</sup> On the other hand polychloroalkyl

derivatives reveals as a rule greater herbicidal and fungicidal activity than their fluorinated counterparts.<sup>5</sup> In the pyridine and dihydropyridine series a number of compounds bearing polyfluoro- and/or polychlorohaloalkyl substituents was found to possess useful pharmacological properties.<sup>6</sup> At the same time the use of imidoyl chlorides for construction of heterocyclic ring by means of hetero-Diels-Alder reactions with 1,3-dienes remains almost unexplored.<sup>7</sup>

Now we report on a novel approach for hydrogenated  $\alpha$ -polyhalomethyl containing pyridines and respective pyridines based on cycloaddition reactions of *N*-phosphoryltrihaloacetimidoyl chlorides with 1,3-butadienes.

## Results and Discussion

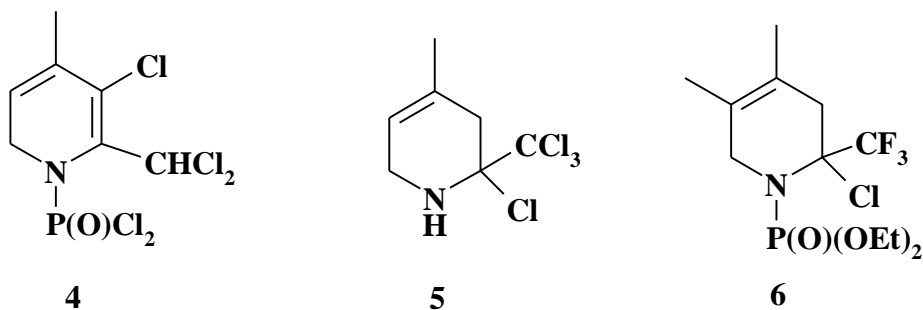
We have found that *N*-dichlorophosphoryltrihaloacetimidoyl chlorides **1a,b** readily react with 1,3-dienes **2a,b** under mild conditions to afford functionalized tetrahydropyridines **3a-d** (Scheme 1). Remarkably, the reaction with non-symmetrical diene **2b** proceeds regioselectively with the formation of 4-methyl substituted isomers **3b,d**.



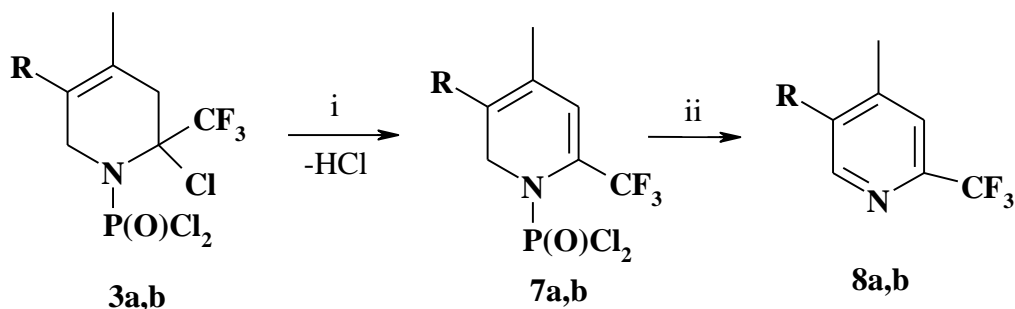
### Scheme 1

Cycloaddition is favored by electron-withdrawing substituents X in imine **1** ( $\text{CF}_3 > \text{CCl}_3$ ) and electron releasing substituents R in diene **2** ( $\text{Me} > \text{H}$ ). Thus, reaction of **1a** with **2** easily proceeds at room temperature and with exothermic effect (in case of **2a**), while trichloro analog **1b** reacts with **2a** only at heating (ether, 5 hrs). For the completion of reaction of **1b** and **2b** boiling in benzene is necessary. Under these conditions in addition to **3d**, 50%, 5-chloro-6-dichloromethyl-1-dichlorophosphoryl-4-methyl-1,2-dihydropyridine **4**, 12%, and 2-chloro-4-methyl-2-trichloromethyl-1,2,3,6-tetrahydropyridine **5**, 3%, were isolated by column chromatography. Replacing the dichlorophosphoryl group at nitrogen atom in **1a** with less electron-withdrawing  $(\text{EtO})_2\text{P}(\text{O})$  substituent ( $\sigma_I$  0.65 and 0.35, respectively),<sup>8</sup> essentially retards

its reactivity toward **2**. The reaction of respective imidoyl chloride,  $\text{CF}_3\text{C}(\text{Cl})=\text{NP}(\text{O})(\text{OEt})_2$ , with diene **2a** proceeds only at prolonged heating in benzene; cycloaddition under these conditions is accompanied by other processes leading to a complex mixture. As a result, cycloaddition product **6** was not isolated and detected only spectrally ( $\delta_{\text{F}} -63.7$  ppm,  $\delta_{\text{P}} 8.3$  ppm).



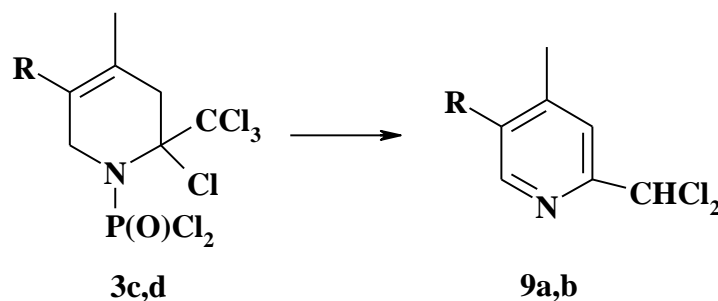
Tetrahydropyridines **3c,d** bearing trichloromethyl group are relatively stable crystalline compounds and can be kept at room temperature for several months. At the same time their trifluoro analogs **3a,b** upon distillation in vacuum eliminate hydrogen chloride to afford dihydropyridines **7a,b** (Scheme 2).



**Scheme 2.** Reagents and conditions: i)  $\Delta$  or  $\text{CF}_3\text{COOD}$ ; ii) aq HCl-dioxane or  $\Delta$ .

Slow transformation **3a**→**7a** occurs even at room temperature. Nitrogen bases (DBU, DABCO,  $\text{Et}_3\text{N}$ ) or carboxylic acid additives favor the reaction. Thus, in solutions of  $\text{CF}_3\text{COOD}$  the elimination of HCl from **3a,b** is completed within 24 hrs at room temperature. The same is true for  $\text{CF}_3\text{COOH}$  or AcOH solutions but in these cases the formation of **7** is complicated by their partial transformation into respective pyridines **8**. Dihydropyridines **7** are oily rather unstable compounds, easily soluble in organic solvents. Even at room temperatures they are gradually (~4 weeks) converted into resinous-like hardly soluble substances. Upon thermal distillation or heating in aq HCl-dioxane compounds **7** undergo aromatization to afford 2-trifluoromethyl substituted pyridines **8** in 63-81% yields.

The behavior of 2-trichloromethyl tetrahydropyridines **3c,d** is quite different from that of their trifluoromethyl analogs. Upon distillation in vacuum, heating in aq HCl-dioxane solution, or on treatment with CF<sub>3</sub>COOH, they give 2-dichloromethyl pyridines **9** (Scheme 3) rather than expected pyridines with trichloromethyl group.



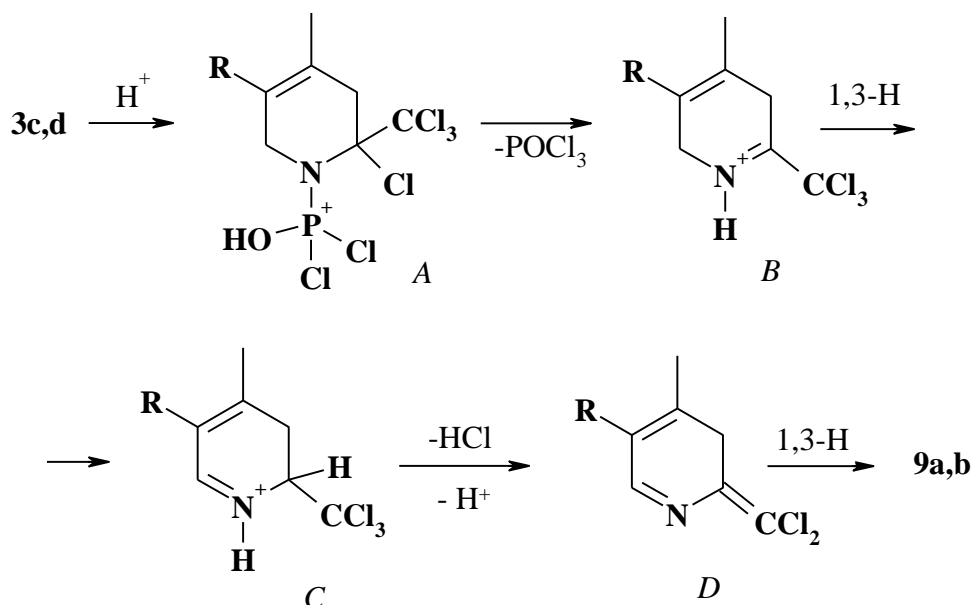
### Scheme 3

Reduction of trichloromethyl group during conversion of tetrahydropyridines **3c,d** to respective pyridines **9a,b** is quite unexpected. The following peculiarities are characteristic of this unusual transformation: 1) the reaction is promoted by acids; 2) the intermediate dihydropyridines analogous to **7** (Scheme 2) were not detected in the course reaction; 3) the performance of the reaction in CF<sub>3</sub>COOH does not lead to incorporation of the of deuterium into dichloromethyl group of **9**. Hydrophosphoryl compounds were reported to convert activated trichloromethyl group into dichloromethyl one.<sup>9</sup> In view of these data we first regarded the possibility of reduction of CCl<sub>3</sub> group with the participation of Cl<sub>2</sub>POH, that could be in principle generated from **3c,d**. However, our attempts to execute reduction of trichloromethyl group of model 4,5-dimethyl-2-(trichloromethyl)pyridine<sup>10</sup> by reacting it with diethylphosphonate, (EtO)<sub>2</sub>P(O)H, under different conditions, failed.

Taking into account the above observations the following pathway of reaction should be outlined (Scheme 4).

Generation of positive charge at phosphorus atom in intermediate *A* promotes the rupture of P-N bond and facilitates the elimination of POCl<sub>3</sub>. Release of sterical strains caused by voluminous 1,2-substituents in *A* also favours transformation *A*→*B*. The greater sterical volume of trichloromethyl group as compared with trifluoromethyl one is likely one of the reasons accounting for distinctions in behavior of tetrahydropyridines **3a,b** and **3c,d**. Electron-withdrawing CCl<sub>3</sub> group and positive charge on nitrogen atom obviously promotes 1,3-proton shift (*B*→*C*) in C-N=C triad;<sup>2c,11</sup> moreover, in azaallylic triad proton tends to migrate to the carbon atom bearing more electron-withdrawing substituent.<sup>11,12</sup> Finally, elimination of hydrogen chloride in *C*, favored by the presence of onium center, and subsequent aromatization of intermediate *D* by means of prototropic shift affords dichloromethylpyridines **9**. It is worthwhile to note that according to proposed scheme hydrogen of CHCl<sub>2</sub> groups comes from hydrogenated

pyridine ring rather than from outer source, accounting for the absence of H-D exchange in the cause of  $\text{CCl}_3 \rightarrow \text{CHCl}_2$  conversion.



**Scheme 4**

The spectral and analytical data of compounds obtained are in complete agreement with their structure. The hydrogenated trifluoromethylpyridines **3a,b**, **7a,b**, and pyridines **8a,b** give clearly distinguishable  $^{19}\text{F}$  NMR characteristics ( $\delta_{\text{F}} -75.8 \div -77.4$  ppm,  $-63.2 \div -63.3$  ppm, and  $-67.4 \div -68.8$  ppm, respectively) that allow easy monitoring of the process and identification of the products in the reaction mixture. The regiochemistry of cycloaddition with non-symmetrical diene **2b** was unambiguously confirmed by  $^1\text{H}$  NMR spectra of pyridines **8b**, **9b** in which characteristic splitting of the 6-H signals was observed:  $\delta$  8.4–8.6 ppm,  $^3J_{\text{H}_6\text{H}_5}$  5 Hz.

## Conclusions

In summary, based on hetero Diels-Alder reactions of *N*-phosphoryltrihaloacetimidoyl chlorides with 1,3-butadienes, we have developed a simple and efficient synthesis of functionalized 2-trihalomethyl tetrahydropyridines, 2-trifluoromethyl dihydropyridines, and pyridines bearing  $\text{CHCl}_2$  or  $\text{CF}_3$  group in  $\alpha$ -position.

## Experimental Section

**General.** IR spectra were obtained with an UR-20 instrument.  $^1\text{H}$ ,  $^{13}\text{C}$  NMR spectra were recorded on Bruker Avance DRX 500 instrument operating at 500.07 and 125.76 MHz, respectively,  $^{19}\text{F}$  NMR and  $^{31}\text{P}$  NMR spectra – on Gemini 200 Varian instrument operating at 188.14 and 80.95 MHz respectively. Chemical shifts are reported relative to TMS ( $^1\text{H}$ ,  $^{13}\text{C}$ ), and  $\text{CFCl}_3$  ( $^{19}\text{F}$ ) as the internal standards or relative to external 85%  $\text{H}_3\text{PO}_4$  ( $^{31}\text{P}$ ). APCI MS spectra were recorded using Agilent 1100 instrument. Melting points are uncorrected. Solvents were dried before use according to standard methods. All reactions were carried out under argon atmosphere.

**2-Chloro-1-dichlorophosphoryl-4,5-dimethyl-2-(trifluoromethyl)-1,2,3,6-tetrahydro-pyridine (3a).** A solution of the 2,3-dimethylbutadiene **2a** (1.2 g, 15 mmol) in 5 mL of diethyl ether was added to a stirred solution of imidoyl chloride **1a**<sup>13</sup> (2.48 g, 10 mmol) in 10 mL of diethyl ether. After stirring at room temperature for 5 hrs the reaction mixture was evaporated in vacuum at 40-50 °C to afford compound **3a**. Yield: 2.67 g (81%), white solid; mp 81-83°C (hexane).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  = 1.88 (s, 6H, 4,5-Me<sub>2</sub>), 2.82 (m, 2H, CCH<sub>2</sub>), 3.68 (dd,  $^2J_{\text{HH}} = 13$  Hz,  $^3J_{\text{HP}} = 14$  Hz, 1H, NCH<sub>A</sub>), 3.92 (dd,  $^2J_{\text{HH}} = 13$  Hz,  $^3J_{\text{HP}} = 15$  Hz, 1H, NCH<sub>B</sub>).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  = 17.05, 18.60 (4-Me, 5-Me), 42.29 (d,  $^3J_{\text{CP}} = 6$  Hz, 3-C), 50.77 (d,  $^2J_{\text{CP}} = 4$  Hz, 6-C), 81.78 (q,  $^2J_{\text{CF}} = 33$  Hz, 2-C), 122.50 (q,  $^1J_{\text{CF}} = 285$  Hz, CF<sub>3</sub>) 126.62 (4-C), 126.75 (d,  $J_{\text{CP}} = 3$  Hz) (5-C).  $^{19}\text{F}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  = -75.75 s.  $^{31}\text{P}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  = 14.0 (dd,  $^3J_{\text{PH}_A} = 13$  Hz,  $^3J_{\text{PH}_B} = 15$  Hz). Anal. Calcd for C<sub>8</sub>H<sub>10</sub>Cl<sub>3</sub>F<sub>3</sub>NOP: C 29.07; H 3.05; Cl 32.18; P 9.37. Found: C 28.89; H 3.09; Cl 31.87; P 9.32.

**2-Chloro-1-dichlorophosphoryl-4-methyl-2-(trifluoromethyl)-1,2,3,6-tetrahydropyridine (3b)** was synthesized analogously to **3a** by stirring ethereal solution of imidoyl chloride **1a** (2.48 g, 10 mmol) and 2-methylbutadiene **2b** (1.02 g, 15 mmol) for 25 hrs at room temperature. Compound **3b** was purified by column chromatography (silica gel, hexane/ethyl acetate 10:1). Yield: 2.2 g (70%), yellow oil.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  = 1.91 (s, 3H, Me), 2.85 (m, 2H, CCH<sub>2</sub>), 3.78 (m, 1H, NCH<sub>A</sub>), 4.06 (m, 1H, NCH<sub>B</sub>), 5.89 (br, 1H, 5-H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  = 22.32 (Me), 41.49 (d,  $^3J_{\text{CP}} = 4$  Hz, 3-C), 46.18 (d,  $^2J_{\text{CP}} = 5$  Hz, 6-C), 81.48 (q,  $^2J_{\text{CF}} = 35$  Hz, 2-C), 118.73 (d,  $^3J_{\text{CP}} = 5$  Hz, 5-C), 122.50 (q,  $^1J_{\text{CF}} = 284$  Hz, CF<sub>3</sub>), 134.66 (4-C).  $^{19}\text{F}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  = -77.42.  $^{31}\text{P}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  = 10.9. Anal. Calcd for C<sub>7</sub>H<sub>8</sub>Cl<sub>3</sub>F<sub>3</sub>NOP: C 26.57, H 2.55, Cl 33.61, N 4.43, P 9.79. Found: C 26.91; H 2.43; Cl 33.11; N 4.68; P 9.85.

**2-Chloro-1-dichlorophosphoryl-4,5-dimethyl-2-(trichloromethyl)-1,2,3,6-tetrahydro-pyridine (3c)** was synthesized analogously to **3a** by refluxing ethereal solution of imidoyl chloride **1b**<sup>14</sup> (2.98 g, 10 mmol) and dimethylbutadiene **2a** (1.2 g, 15 mmol) for 5 hrs. Yield: 2.95 g (78%), white solid, mp 158-160 °C (hexane-benzene, 3:1).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  = 1.92 (s, 3H, Me), 1.94 (s, 3H, Me), 3.21 (m, 2H, CCH<sub>2</sub>), 3.83 (dd,  $^2J_{\text{HH}} \sim 14$  Hz,  $^3J_{\text{HP}} \sim 15$  Hz, 1H, NCH<sub>A</sub>), 4.03 (dd,  $^2J_{\text{HH}} = 14$  Hz,  $^3J_{\text{HP}} \sim 15$  Hz, 1H, NCH<sub>B</sub>).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  = 17.22, 18.24 (4-Me, 5-Me), 45.59 (d,  $^3J_{\text{CP}} = 5$  Hz, 3-C), 53.43 (d,  $^2J_{\text{CP}} = 5$  Hz, 6-C), 93.82, 105.86 (2-C, CCl<sub>3</sub>) 128.36,

128.44 (4-C, 5-C).  $^{31}\text{P}$  NMR ( $\text{CDCl}_3$ ):  $\delta = 13.26$  (t,  $^3J_{\text{PH}} \sim 15$  Hz). Anal. Calcd for  $\text{C}_8\text{H}_{10}\text{Cl}_6\text{NOP}$ : C 25.30; H 2.65; Cl 56.00; N 3.69; P 8.15. Found: C 24.98; H 2.91; Cl 55.87; N 3.57; P 7.87.

**Compounds 3d, 4 and 5** were synthesized analogously to **3a** by refluxing benzene solution of imidoyl chloride **1b** (2.98 g, 10 mmol) and methylbutadiene **2b** (1.02 g, 15 mmol) for 3 hrs. Column chromatography (silica gel, hexane/ethyl acetate 10:1) afforded tetrahydropyridines **3d**, **5** and dihydropyridine **4**.

**2-Chloro-1-dichlorophosphoryl-4-methyl-2-(trichloromethyl)tetrahydropyridine (3d)**. Yield 1.83 g (50%), yellow oil.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta = 2.00$  (s, 3H, Me), 3.26 (m, 2H,  $\text{CCH}_2$ ), 3.74 (m, 1H,  $\text{NCH}_A$ ), 4.25 (m, 1H,  $\text{NCH}_B$ ), 6.11 (m, 1H, 5-H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta = 22.57$  (Me), 44.56 (d,  $^3J_{\text{CP}} = 5$  Hz, 3-C), 48.51 (d,  $^2J_{\text{CP}} = 6$  Hz, 6-C), 92.57, 105.90 (2-C,  $\text{CCl}_3$ ), 121.00 (5-C), 137.68 (4-C).  $^{31}\text{P}$  NMR ( $\text{CDCl}_3$ ):  $\delta = 13.4$  (t,  $^3J_{\text{PH}} = 16$  Hz). Anal. Calcd for  $\text{C}_7\text{H}_8\text{Cl}_6\text{NOP}$ : C 22.98; H, 2.20; Cl 58.15; N, 3.83; P, 8.47. Found: C 22.73; H 2.14; Cl 57.76; N 3.51; P 8.36.

**5-Chloro-6-(dichloromethyl)-1-dichlorophosphoryl-4-methyl-1,2-dihydropyridine (4)**. Yield 0.35 g (12%), white solid, mp 129-131 °C.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta = 1.92$  (s, 3H, Me), 3.85 (m, 1H,  $\text{NCH}_A$ ), 4.18 (m, 1H,  $\text{NCH}_B$ ), 5.18 (br, 1H, 5-H), 6.66 (s, 1H,  $\text{CHCl}_2$ ).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta = 20.48$  (Me), 46.33 (d,  $^2J_{\text{CP}} = 7$  Hz, 2-C), 54.20 ( $\text{CHCl}_2$ ), 120.59 (d,  $^3J_{\text{CP}} = 7$  Hz, 3-C), 126.06 (d,  $^3J_{\text{CP}} = 9$  Hz, 5-C), 130.92 (4-C), 133.63 (d,  $^2J_{\text{CP}} = 1$  Hz, 6-C).  $^{31}\text{P}$  NMR ( $\text{CDCl}_3$ ):  $\delta = 9.2$  (t,  $^3J_{\text{PH}} = 12$  Hz). Anal. Calcd for  $\text{C}_7\text{H}_7\text{Cl}_5\text{NOP}$ : C, 25.53; H, 2.14; Cl 53.82; N 4.25; P 9.40. Found: C 25.37; H 2.09; Cl 53.27; N 4.21; P 9.26

**2-Chloro-4-methyl-2-(trichloromethyl)-1,2,3,6-tetrahydropyridine (5)**. Yield 0.06 g (3%), oil.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta = 2.03$  (s, 3H, Me), 3.34 (s, 2H,  $\text{CCH}_2$ ), 4.04 (d, 1H,  $^2J_{\text{HH}} = 16$  Hz,  $\text{NCH}_A$ ), 4.72 (dd, 1H,  $^2J_{\text{HH}} = 16$  Hz,  $^3J_{\text{HH}} = 6$  Hz,  $\text{NCH}_B$ ), 6.11 (m, 1H, 5-H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta = 22.53$  (Me), 44.76, 51.17 (6-C, 3-C), 90.49, 92.51 (2-C,  $\text{CCl}_3$ ), 121.04 (5-C), 136.45 (4-C). Anal. Calcd for  $\text{C}_7\text{H}_9\text{Cl}_4\text{N}$ : C 33.77; H 3.64; Cl 56.96; N 5.63. Found: C 33.41; H 3.58; Cl 56.61; N 5.51.

**1-Dichlorophosphoryl-3,4-dimethyl-6-(trifluoromethyl)-1,2-dihydropyridine (7a)**. A solution of the tetrahydropyridine **3a** (3.3 g, 10 mmol) in 3 mL of trifluoroacetic acid- $d_1$  was stirred for 25 hrs, the solvent was evaporated in vacuum at 30-35 °C to afford oily compound **7a**, which was purified by column chromatography (silica gel, hexane/ethyl acetate 10:1). Yield: 1.85 g (64%).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta = 1.83$  (s, 3H, Me), 1.87 (s, 3H, Me), 4.09 (d, 2H,  $^3J_{\text{HP}} = 26$  Hz,  $\text{NCH}_2$ ), 6.55 (s, 1H, 5-H).  $^{19}\text{F}$  NMR ( $\text{CDCl}_3$ ):  $\delta = -63.2$ .  $^{31}\text{P}$  NMR ( $\text{CDCl}_3$ ):  $\delta = 14.9$  (t,  $^3J_{\text{PH}} = 26$  Hz). Anal. Calcd for  $\text{C}_8\text{H}_9\text{Cl}_2\text{F}_3\text{NOP}$ : C, 32.68; H, 3.09; Cl, 24.11; N, 4.76; P, 10.53. Found: C, 32.81; H, 3.19; Cl, 23.68; N, 4.61; P, 9.97.

**1-Dichlorophosphoryl-4-methyl-6-(trifluoromethyl)-1,2-dihydropyridine (7b)** was obtained by thermal distillation of the tetrahydropyridine **3b** (3.16 g, 10 mmol) in vacuum (0.05 mmHg). Yield: 1.9 g (67%); bp 118-121 °C/0.05 mmHg.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta = 1.80$  (s, 3H, Me), 4.19 (dd,  $^3J_{\text{HP}} = 26$  Hz,  $^3J_{\text{HH}} = 2.5$  Hz,  $\text{NCH}_2$ ), 5.7 (br, 1H, 3-H), 6.47 (s, 1H, 5-H).  $^{19}\text{F}$  NMR ( $\text{CDCl}_3$ ):  $\delta = -63.3$ .  $^{31}\text{P}$  NMR ( $\text{CDCl}_3$ ):  $\delta = 14.1$  (t,  $^3J_{\text{PH}} = 26$  Hz). Anal. Calcd for  $\text{C}_7\text{H}_7\text{Cl}_2\text{F}_3\text{NOP}$ : C 30.03; H 2.52; Cl 25.32; N 5.00; P 11.06. Found: C 29.83; H 2.49; Cl 25.91; N 4.87; P 10.84.

**General procedures for the synthesis of pyridines (8) and (9)**

The mixture of respective tetrahydropyridine **3** or dihydropyridine **7** (10 mmol), dioxane (15 mL) and 35% aq HCl (15 mL) was refluxed for 3 hrs. After cooling to r.t. the mixture was neutralized with 10% NaOH, extracted with dichloromethane (2x25 mL), dried (MgSO<sub>4</sub>) and the solvent was removed in vacuum at 50-60 °C.

**4,5-Dimethyl-2-(trifluoromethyl)pyridine (8a)**. Yield 63% (from **3a**) or 66% (from **7b**); bp 75-80 °C (14 mm) (lit.<sup>15</sup> bp 85 °C (17 mm) <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ = 2.29 (s, 3H, Me), 2.33 (s, 3H, Me), 7.41 (s, 1H, 3-H), 8.40 (s, 1H, 6-H). <sup>19</sup>F NMR (CDCl<sub>3</sub>): δ = -67.40.

**4-Methyl-2-(trifluoromethyl)pyridine (8b)**. Yield: 81 % (from **3b**); *n*<sub>D</sub><sup>20</sup> 1.4292 (lit.<sup>16</sup> *n*<sub>D</sub><sup>20</sup> 1.429). <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ = 2.44 (s, 3H, Me), 7.27 (d, 1H, <sup>3</sup>*J*<sub>HH</sub> = 5 Hz, 5-H), 7.49 (s, 1H, 3-H), 8.56 (d, 1H, <sup>3</sup>*J*<sub>HH</sub> = 5 Hz, 6-H). <sup>19</sup>F NMR (CDCl<sub>3</sub>): δ = -68.77. *m/z* (APCI) 162.2 (M+1, 100%). Calculated for C<sub>7</sub>H<sub>6</sub>F<sub>3</sub>N, M = 161.13.

Compound **8b** was prepared also by the following procedure: 3.17 g (10 mol) of tetrahydropyridine **3b** was distilled, fraction with bp 170-180 °C was collected, dissolved in dichloromethane (50 mL), washed with 10% NaOH and dried (MgSO<sub>4</sub>). The solvent was removed in vacuum at 50-60 °C to afford 1.1 g (68 %) of pyridine **8b**.

**2-(Dichloromethyl)-4,5-dimethylpyridine (9a)**. Yield: 1.2 g (63%); bp 115-120 °C (14 mm); mp 70-72 °C (hexane-benzene 3:1). <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ = 2.19 (s, 3H, Me), 2.25 (s, 3H, Me), 6.63 (s, 1H, CHCl<sub>2</sub>), 7.45 (s, 1H, 3-H), 8.19 (s, 1H, 6-H). <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ = 16.28 (Me), 19.43 (Me), 71.48 (CHCl<sub>2</sub>), 121.77 (3-C), 133.61 (5-C), 147.71 (4-C), 148.74 (6-C), 155.50 (2-C). Anal. Calcd for C<sub>8</sub>H<sub>9</sub>Cl<sub>2</sub>N: C 50.55; H 4.77; Cl 37.30; N 7.37. Found: C 49.97; H 4.68; Cl 37.26; N 7.41.

**2-(Dichloromethyl)-4-methylpyridine (9b)**. Yield: 1.1 g (68%); bp 160-170 °C (lit.<sup>17</sup> bp 74-75 °C (14 mm); <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ = 2.43 (s, 3H, Me), 6.71 (s, 1H, CHCl<sub>2</sub>), 7.14 (d, 1H, <sup>3</sup>*J*<sub>HH</sub> = 5 Hz, 5-H), 7.58 (s, 1H, 3-H), 8.43 (d, 1H, <sup>3</sup>*J*<sub>HH</sub> = 5 Hz, 6-H). <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ = 21.12 (Me), 71.59 (CHCl<sub>2</sub>), 121.73, 125.38 (3-C, 5-C), 148.50, 149.13 (4-C, 6-C), 157.68 (2-C).

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