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To the 85th Anniversary of birthday of late Yu.G. Gololobov

(2-Carbamoylethyl)bis(pentafluorophenyl)phosphine Oxides: Synthesis and Structure

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Abstract—The interaction of a series of acrylic and cinnamic acid amides with bis(pentafluorophenyl)-phosphinic acid proceeds vigorously at room temperature without any catalyst in the presence of the organic solvents providing for a high fraction of the >P–OH tautomer of the phosphinic acid. The reactions have afforded (2-carbamoylethyl)bis(pentafluorophenyl)phosphine oxides in a high yield.

Keywords: bis(pentafluorophenyl)phosphinic acid, amides, unsaturated carboxylic acids, Pudovik reaction, (2-carbamoylethyl)phosphine oxides, P,P-bis(pentafluorophenyl) derivatives, NMR, X-ray diffraction analysis

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Addition of diorganylphosphoryl compounds to the activated C=C bond (Pudovik reaction) has been recognized as a general approach to the synthesis of substituted phosphine oxides [1]. In particular, this method has been widely used to prepare the β-phosphorylated ketones and esters of the β-phosphorylated carboxylic acids [2]; these products are of significant interest in view of the application as extracting agents for *f*-elements [3], fire-retardant additives of polymer materials [4], and as precursors of various diorganylphosphorylated heterocyclic systems [5].

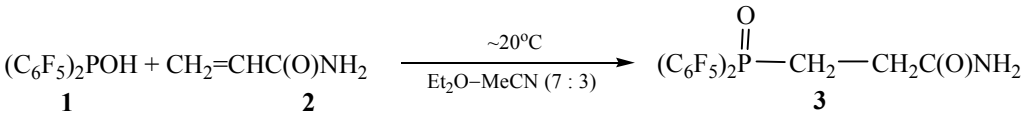
Noteworthily, Pudovik reaction is efficient in the presence of different types of catalysts [6] or at heating (in particular, at microwave-assistance) [7],[1] even in the cases of the highly reactive α,β-enones and esters of α,β-unsaturated carboxylic acids containing terminal double bonds.

The interaction of diorganylphosphinic acids with amides of α,β-unsaturated carboxylic acids is far more complicated. It has been recently demonstrated that the catalyzed addition of the corresponding hydrophosphoryl compounds to the *N*,*N*-disubstituted amides of these carboxylic acids is possible [8, 9]; however, unsubstituted acrylamide does not react with diphenylphosphinic acid even in the presence of highly efficient catalysts [6].

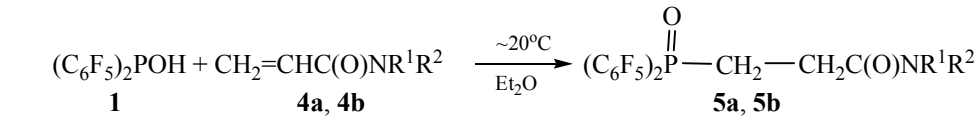
It should be noted that the majority of the known diorganylphosphinic acids exist as the >P(O)H forms of the >P(O)H ↔ >P–OH tautomeric equilibrium [10], whereas the >P–OH tautomer should be more reactive towards electrophiles [11]. Only a few examples of diorganylphosphinic acids with the >P–OH tautomer existing (or even dominating) in the solutions (NMR data) have been found so far, practically all of them being the perfluorinated derivatives of alkyl, aryl, or hetaryl types [12, 13]. Owing to a combination of high stability (including that against oxidation, hydrolysis, and disproportionation) and synthetic availability, bis(pentafluorophenyl)phosphinic acid **1** [12] has been recognized as the most promising precursor of the

[1] Such high-temperature processes should be applied to the synthetic procedure with extreme care, due to the well known capability of the diorganylphosphinic acids (especially the corresponding *P*,*P*-diaryl derivatives) to thermal disproportionation.

Scheme 1.



Scheme 2.



R^1 = H, R^2 = $CMe_2CH_2C(O)Me$ (**4a**, **5a**); R^1 = R^2 = Me (**4b**, **5b**).

functionalized *P*,*P*-bis(pentafluorophenyl)-substituted phosphine oxides.

Apparently, the choice of a solvent to be used in the discussed reaction is crucial; in particular, the solvent should favor a high content of the reactive >P–OH form of the acid **1** in the solution, the solution should be stable, and the solvent should be efficiently and easily removed from the reaction mixture.

A number of organic solvents have been tested for the content of the >P–OH tautomer of the acid **1**; the highest fraction of the desired form has been detected in the cases of *N*-methylpyrrolidone (90%) [13], DMSO (76%) [12], and diethyl ether (60%) [12]. Even though the ether has not shown the superior fraction of the reactive form of the acid **1**, it has been recognized as the best solvent for Pudovik reaction involving amides of α,β-unsaturated carboxylic acids in view of the other above-mentioned requirements.

If the starting amide was poorly soluble in pure Et_2O, acetonitrile (a better solvent for the amide) was introduced in the reaction mixture; it afforded the comparably high stability of the acid **1** in the solution.

We started the investigation of synthetic possibilities of the Pudovik reaction between hydrophosphoryl compound **1** and amides of α,β-unsaturated carboxylic acids using the simplest amide (acrylamide **2**) as an example.

We observed the sufficiently high rate of the reaction between those compounds even at room temperature in the absence of any catalysts when a 7 : 3 mixture of anhydrous diethyl ether and acetonitrile was used as a solvent;[2] the reaction afforded (2-carbamoylethyl)bis(pentafluorophenyl)phosphine oxide **3** in 83% yield (Scheme 1).

The product structure was confirmed by the data of IR and NMR (^1H, ^1H–{^{31}P}, ^{13}C, ^{19}F, and ^{31}P) spectroscopy. Correct assignment of the close signals of methylene groups in ^1H NMR spectrum of amide **3** was assisted by 2D NMR (^1H–^{13}C HMQC) data (Fig. 1).

The ^1H and ^{13}C signals of the methylene group adjacent to the phosphorus atom were shifted downfield.

The proton signals assigned to the NH_2 group of amide **3** appeared as fairly distant singlets in the ^1H and ^1H–{^{31}P} NMR spectra, $\Delta\delta_H$ being of about 0.5(!) ppm. This spectral feature showed magnetic nonequivalence of the corresponding protons, apparently due to the hindered rotation around the C–N bond in the terminal $C(O)NH_2$ group.

The sufficiently high solubility of *N*-alkyl- and *N*,*N*-dialkylacrylamides **4a** and **4b** in diethyl ether allowed for carrying out their reactions with compound **1** without using the co-solvent; as a result, the reaction occurred faster than in the case of the unsubstituted amide **2**, and the yield of the target *N*-alkyl- and *N*,*N*-dialkyl (2-carbamoylethyl)bis(pentafluorophenyl)phosphine oxides **5a** and **5b** was up to about 90% (Scheme 2).

Structure of amides **5a** and **5b** was confirmed by the data of IR and NMR (^1H, ^1H–{^{31}P}, ^{13}C, ^{19}F, and ^{31}P) spectroscopy.

Structure of the *N*-alkyl derivative **5a** was further confirmed by means of X-ray diffraction (XRD) analysis (Fig. 2). According to the obtained data, compound **5a** was crystallized in the centrosymmetrical *C*2/*c* group as the crystal solvate containing 0.5 molecule of CH_2Cl_2. The bond lengths in

[2] Content of the >P–OH form of acid **1** in that mixture of solvents was about 20% (^{31}P NMR data).

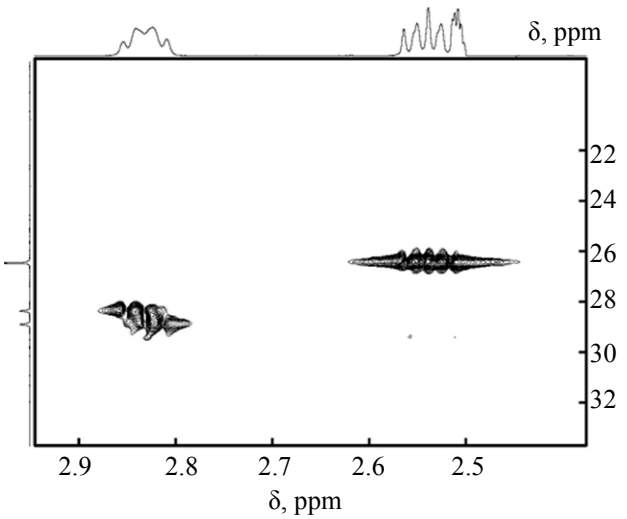


Fig. 1. Part of the $^{1}H–^{13}C$ HMQC spectrum (the CH_2 groups region) of (2-carbamoylethyl)bis(pentafluorophenyl)-phosphine oxide **3**.

compound **5a** were close to the expected ones; in particular, the P=O bond length was 1.484(2) Å. Analysis of the crystal packing revealed that the NH group was involved in the formation of a weak N–H···OP hydrogen bond (H···O 2.09 Å and N···O 2.931(2) Å; NHO 159°) uniting the compound molecules in the centrosymmetrical dimers (Fig. 3).

IR and ^{13}C NMR spectra of compound **5a** revealed the presence of two types of the carbonyl group: the amide and the ketone ones. In the case of the *N*,*N*-dimethylamide **5b**, the *N*-alkyl substituents were magnetically nonequivalent, and their signals appeared as distinct singlets in the ^{1}H and ^{13}C NMR spectra, the effect being the most prominent in the latter case ($\Delta\delta_C \approx 1.4$ ppm).

An important feature of ^{13}C NMR spectra of the synthesized *P*,*P*-bis-(pentafluorophenyl)(2-carbamoyl-ethyl)phosphine oxides **3** and **5** was the value of the spin-spin coupling constant $^{3}J_{CP}$ of the carbon nucleus of the terminal –C(O)N< group, 13.7–15.4 Hz. Lately the XRD data have earlier confirmed that such $^{3}J_{CP}$ value of the carbon nucleus of the C=O group in the spectra of β-[bis(pentafluorophenyl)phosphorylated alkanones $(C_6F_5)_2P(O)CR_2CH_2C(O)Me$ (R = H, Me) clearly indicates the transoid location of the phosphoryl and the carbonyl groups [14]. We assumed that a similar relationship between the $^{3}J_{C(O)P}$ value and the molecule geometry could exist in the case of amides of β-phosphorylated carboxylic acids. Indeed, the XDR data showed (Fig. 2) that the P=O and $C^{15}=O^{2}$ groups in the crystal of compound **5a** were *trans*-located (the $O^{1}P^{1}C^{15}O^{2}$ pseudo-torsion angle was 161.4°). Hence, the analysis of the $^{3}J_{C(O)P}$ values can serve as a simple and general method to determine the corresponding geometry parameters of the organo-phosphorus molecules containing the >P(O)C–C–C(O)– group.

We observed as well the addition of the hydro-phosphoryl compound **1** under mild conditions in the absence of any catalysts in the case to the less reactive derivatives of cinnamic acid. In particular, the reaction of compound **1** with cinnamic acid piperidide **6** at room temperature in a 14 : 1 mixture of anhydrous

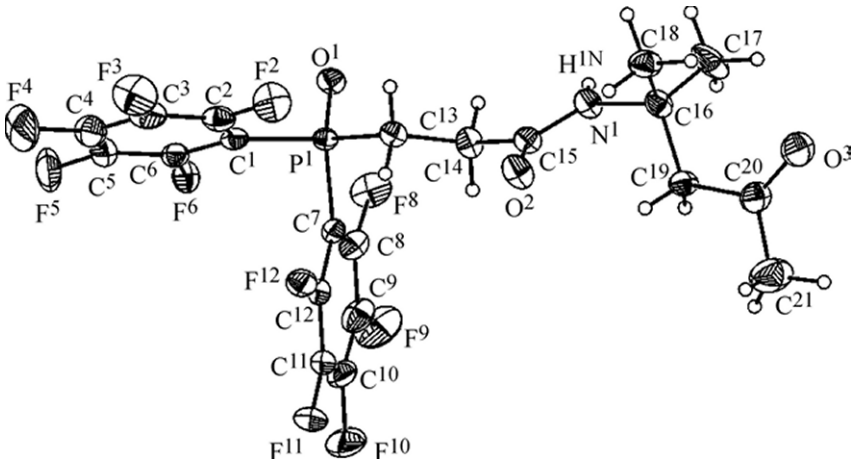


Fig. 2. General view of the molecule of [2-(3-oxo-1,1-dimethylbutylcarbamoyl)ethyl]bis(pentafluorophenyl)phosphine oxide **5a** with the atoms represented as ellipsoids of thermal vibrations (p = 50%).

diethyl ether and acetonitrile[3] afforded bis(pentafluorophenyl)[2-(piperidinocarbonyl)-1-phenylethyl]phosphine oxide **7** in a 82% yield (Scheme 3).

The noticeably lower rate of this reaction as compared with the similar reactions involving acrylamides was evidently due to the steric hindrance at the addition of the hydrophosphoryl compound due to the non-terminal position of the C=C bond in the electrophile molecule.

The structure of the bis(pentafluorophenyl)phosphorylated amide **7** was confirmed by the data of IR and NMR spectroscopy. The presence of both –C(O)N< fragment and the asymmetric carbon atom in the molecule resulted in the nonequivalence of many among the indicative nuclei, seriously complicating the analysis of the ^{1}H, ^{13}C, and ^{19}F NMR spectra. This was likely the most striking in the case of the $^{13}C–\{^{1}H\}$ NMR spectra containing the doubled signals of all four types (*o*-, *m*-, *p*-, and *ipso*-) of carbon nuclei in the *P*-pentafluorophenyl groups and the carbon atoms of α- and β-methylene fragments of the piperidine cycle.

The reaction of the hydrophosphoryl compound **1** with amides of α,β-unsaturated carboxylic acids containing a pharmacophore group (for instance, an alkaloid fragment) was of particular interest; the interaction could result in the formation of new F,P,N-containing potentially biologically active compounds.

N^{12}-Acryloylcytisine **8** was used as an example of such amide. It was prepared following the specially designed procedure:[4] acylation of the natural cytisine with acryloyl chloride in the presence of 2,6-lutidine and catalytic amount of 4-dimethylaminopyridine in anhydrous CH_2Cl_2 followed by the target product isolation by means of chromatography (Scheme 4).

It was demonstrated that the interaction of compounds **1** and **8** in a 4 : 5 mixture of anhydrous diethyl ether and acetonitrile[5] was fairly vigorous at room temperature, despite the relatively low concentration of the >P–OH form of the hydrophosphoryl compound. The reaction yield was practically quantitative, affording N^{12}-{2-[bis(pentafluorophenyl)phosphoryl]propionyl}cytisine **9**, the first alkaloid-containing amide of phosphorylcarboxylic acid ever reported, to the best of our knowledge (Scheme 5).

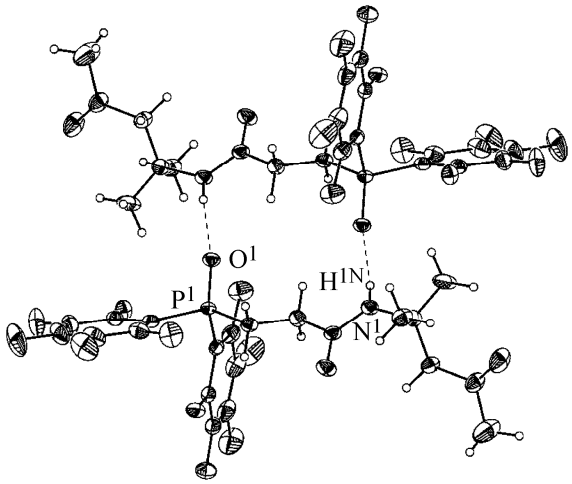
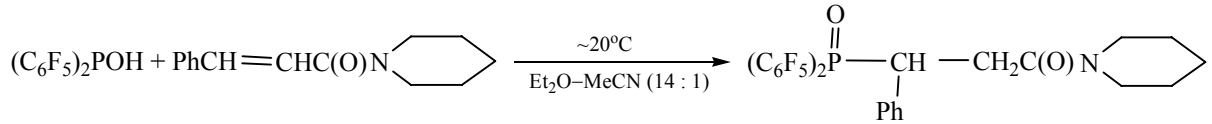


Fig. 3. Centrosymmetrical hydrogen-bonded dimers in the crystal of compound **5a**.

Noteworthily, the ^{31}P NMR spectra of compounds **3**, **5**, and **7** registered at 293 K contained singlet signals, whereas that of the cytisine derivative **9** recorded under the same conditions contained a pair of close singlets, the upfield one being somewhat stronger (Fig. 4, cf. Experimental). The signal duplication in the case of compound **9** was apparently a sign of coexistence of its two conformers. This was supported by observation of the only singlet signal in the ^{31}P NMR spectrum of that compound at elevated temperature (360 K) (Fig. 5).

In summary, we demonstrated that the Pudovik reaction between amides of acrylic or cinnamic acid and bis(pentafluorophenyl)phosphinic acid vigorously

Scheme 3.



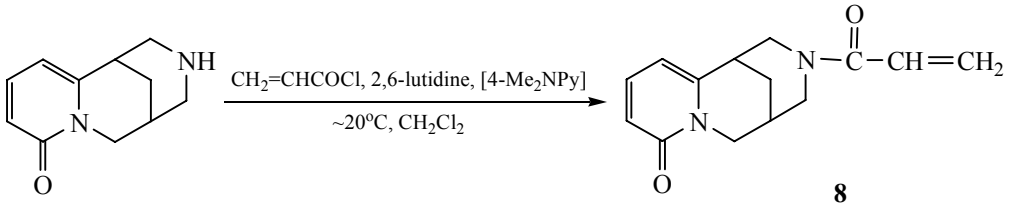
1 **6** **7**

[3] Content of the >P–OH form of acid **1** in the mixture of solvents was about 68% (^{31}P NMR data).

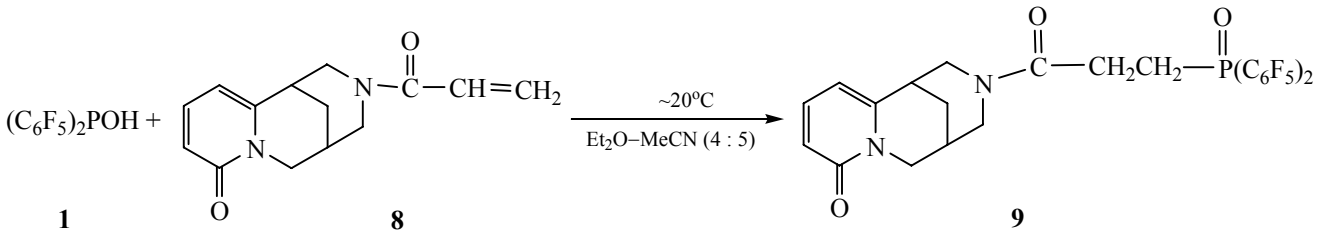
[4] Synthesis and isolation of the compound in pure form was reported in [15]; however, the preparation method and the elemental analysis data were not published.

[5] Content of the >P–OH form of acid **1** in the mixture of solvents was about 17% (^{31}P NMR data).

Scheme 4.



Scheme 5.



occurred at room temperature in the absence of any catalysts if the reaction medium favored the sufficiently high content of the >P–OH tautomer of the hydrophosphoryl compound. The studied process was recognized as a simple and efficient approach towards the preparation of new (2-carbamoylethyl)bis(pentafluorophenyl)phosphine oxides.

EXPERIMENTAL

^{1}H, ^{1}H–{^{31}P}, ^{13}C, ^{19}F, and ^{31}P NMR spectra of 0.1 mol/L solutions in DMSO-d_6 or $CDCl_3$ were recorded using a Bruker AV-400 instrument [400.13 (^{1}H and ^{1}H–{^{31}P}), 100.61 (^{13}C), 376.49 (^{19}F), and 161.98 MHz (^{31}P)]. The following references were applied: residual non-deuterated solvent (^{1}H and ^{1}H–{^{31}P}; internal), $CFCl_3$ (^{19}F; external), and 85% H_3PO_4 (^{31}P; external). IR spectra of pellets with KBr were registered using a Bruker Tensor 37 spectrometer (400–4000 cm^{-1}). The reaction course was monitored by means of ^{31}P NMR spectroscopy. Elemental analysis was carried out at the Laboratory of Microanalysis, Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences.

X-ray diffraction analysis was performed using a Bruker APEX II CCD diffractometer [λ(MoK_α) = 0.71072 Å, ω-scanning, 2θ < 60°]. The crystals of compound **5a** suitable for X-ray analysis were prepared via isothermal evaporation of the solution in a 3 : 1 dichloromethane–benzene mixture at room temperature. The crystals of **5a**·0.5CH_2Cl_2 were monoclinic, $C_{21.50}H_{17}ClF_{10}NO_3P$, M = 593.78, μ = 3.14 cm^{-1}, d_{calc} = 1.567 g/cm^3, space group $C2/c$, a = 20.7201(6), b = 19.6151(6), c = 14.6070(5) Å, β = 122.0240(10)°, V = 5033.3(3) Å^3. The intensity of 33289 reflections (7357 independent ones) were measured (R_{int} = 0.0278) and used for the structure refinement. The structure was solved by the direct method and refined by the least-squares method over F^2_{hkl} in the full-matrix anisotropic approximation. Analysis of the Fourier reconstruction of the electronic density showed that the substituent at N^1 was disordered between two equally populated positions. The hydrogen atom at N^1 was localized from the differential Fourier reconstructions and refined in the isotropic approximation; the positions of the other hydrogen atoms were calculated from geometry considerations. Final values of the uncertainty factors are as follows: wR_2 = 0.1324 and GOF = 0.981 for all the independent reflections [R_1 = 0.0453 was calculated from F for the 5794 reflections with $I > 2\sigma(I)$]. All the computations were carried out using SHELXTL PLUS software package. Atomic coordinates and complete structural data were deposited at the Cambridge Crystallographic Data Centre (CCDC 1413347).

Bis(pentafluorophenyl)phosphinic acid **1** [14] and cinnamic acid piperidide **6** [16] were prepared as described elsewhere. 2,6-Lutidine (Acros) was dried over NaOH and distilled prior to use; *N*,*N*-dimethylacrylamide **4b** (Aldrich) and acryloyl chloride (Aldrich) were distilled prior to use; acrylamide **2** (Acros), *N*-(3-oxo-1,1-dimethylbutyl)acrylamide **4a** (Aldrich), and 4-(dimethylamino)pyridine (Acros) were used as received. The basic Al_2O_3 (Brockmann I, 50–200 μm) (Acros) was used.

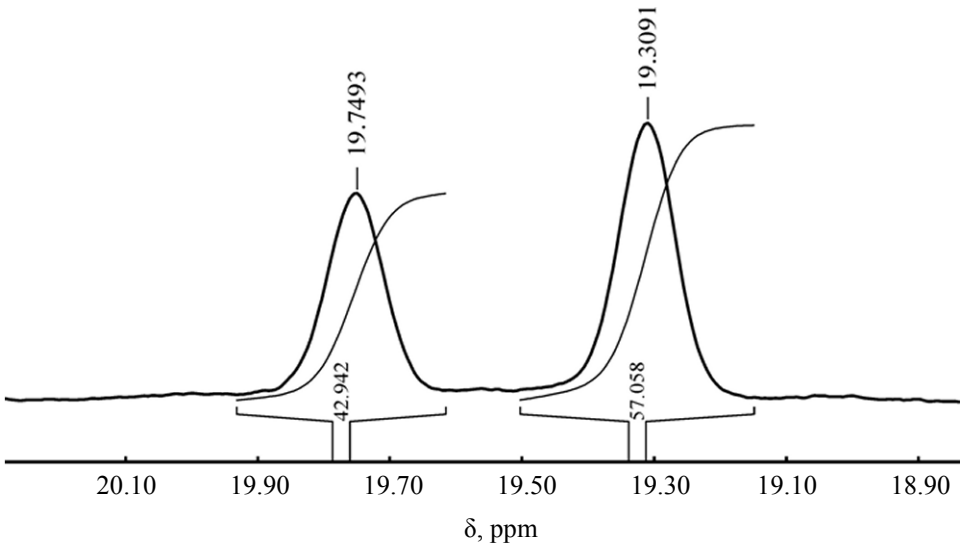


Fig. 4. ^{31}P NMR spectrum of 0.1 mol/L solution of bis(pentafluorophenyl)phosphorylated derivative of cytisine **9** in DMSO-d_6 recorded at 293 K.

(2-Carbamoylethyl)bis(pentafluorophenyl)phosphine oxide (3). A solution of 1.146 g (3 mmol) of compound **1** in 7 mL of anhydrous Et_2O was added dropwise to a solution of 0.234 g (3.3 mmol) of compound **2** in 3 mL of anhydrous acetonitrile. The reaction mixture was kept during 24 h at room temperature; the formed precipitate was separated, washed (2 × 4 mL) with a 3 : 1 Et_2O–MeCN mixture, and dried in air. Yield 1.125 g (82.8%), mp 213–215°C. IR spectrum (KBr), ν, cm^{-1}: 1224 (P=O), 1682, 1690 sh (C=O). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 2.52–2.59 m [2H, $CH_2C(O)$], 2.78–2.88 m (2H, CH_2P), 6.97 s (1H, NH), 7.46 s (1H, NH). ^{1}H–{^{31}P} NMR spectrum (DMSO-d_6), δ, ppm: 2.52–2.58 m [2H, $CH_2C(O)$], 2.84 t (2H, CH_2P, $^3J_{HH}$ 7.0 Hz), 6.95 s (1H, NH), 7.45 s (1H, NH). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm (J, Hz): 26.4 d ($\underline{C}H_2CH_2P$, $^2J_{CP}$ 3.7), 28.6 d (CH_2P, $^1J_{CP}$ 80.7), 107.4 d.t.m (*ipso*-C_6F_5, $^1J_{CP}$ 89.5, $^2J_{CF}$ 19.8), 137.7 d.m (*m*-C_6F_5, $^1J_{CF}$ 251.6), 144.2 d.m (*p*-C_6F_5, $^1J_{CF}$ 257.5), 147.1 d.m (*o*-C_6F_5, $^1J_{CF}$ 251.6), 172.0 d (C=O, $^3J_{CP}$ 15.4). ^{19}F NMR spectrum (DMSO-d_6), δ_F, ppm (J, Hz): –131.8 d (4F, *o*-C_6F_5, $^3J_{FF}$ 20.7), –146.3 t.m (2F, *p*-C_6F_5, $^3J_{FF}$ 21.8), –159.9 t.m (4F, *m*-C_6F_5, $^3J_{FF}$ 21.2). ^{31}P NMR spectrum (DMSO-d_6): δ_P 19.8 ppm. Found, %: C 39.76; H 1.33; F 41.65; N 3.04; P 6.94. $C_{15}H_6F_{10}NO_2P$. Calculated, %: C 39.76; H 1.33; F 41.92; N 3.09; P 6.83.

[2-(3-Oxo-1,1-dimethylbutylcarbamoyl)ethyl]bis(pentafluorophenyl)phosphine oxide (5a). A solution of 1.146 g (3 mmol) of compound **1** in 7 mL of anhydrous Et_2O was added dropwise to a solution of 0.558 g (3.3 mmol) of compound **4a** in 5 mL of anhydrous diethyl ether. The mixture was maintained for 2 h at room temperature and evaporated to dryness. The so obtained foamed residue was triturated with 10 mL of hexane; the formed precipitate was filtered off, washed with 6 mL of a 1 : 1 hexane–diethyl ether mixture and with 6 mL of hexane, and dried in air. Yield 1.514 g (91.6%), mp 97–98°C. IR spectrum (KBr), ν, cm^{-1}: 1224 (P=O), 1672, 1651 (NH$\underline{C=O}$), 1710 (Me$\underline{C=O}$). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm

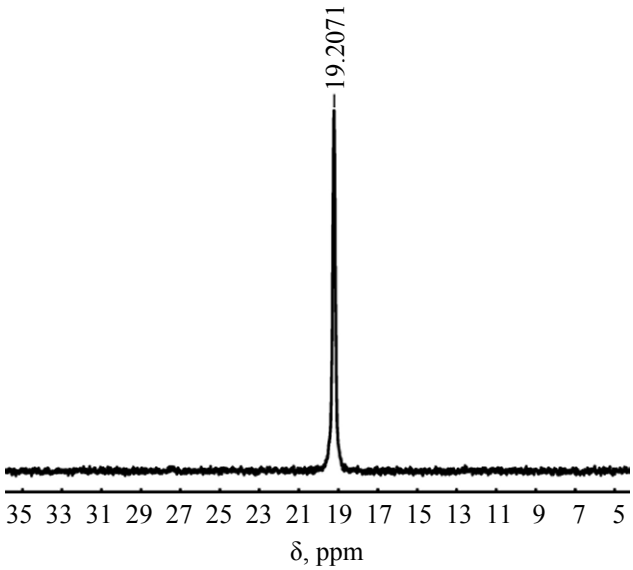


Fig. 5. ^{31}P NMR spectrum of 0.1 mol/L solution of bis(pentafluorophenyl)phosphorylated derivative of cytisine **9** in DMSO-d_6 recorded at 360 K.

(*J*, Hz): 1.34 s (6H, Me_2C), 2.11 s [3H, $CH_3C(O)$], 2.67 d. t (2H, $C\underline{H}_2CH_2P$, $^3J_{HH}$ 7.4, $^3J_{HP}$ 14.9), 2,89 s [2H, $C\underline{H}_2C(O)Me$], 2.92 d. t (2H, CH_2P, $^3J_{HH}$ 7.5, $^2J_{HP}$ 9.1), 6.47 s (1H, NH). $^1H–\{^{31}P\}$ NMR spectrum ($CDCl_3$), δ, ppm: 1.34 s (6H, Me_2C), 2.12 s [3H, $CH_3C(O)$], 2.68 t[6] (2H, $C\underline{H}_2CH_2P$), 2.90 s [2H, $C\underline{H}_2C(O)Me$], 2.93 t[6] (2H, CH_2P), 6.46 s (1H, NH). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm (*J*, Hz): 27.2 s ($\underline{Me}_2C$), 27.8 d ($\underline{C}H_2CH_2P$, $^2J_{CP}$ 3.7), 28.7 d.m (CH_2P, $^1J_{CP}$ 80.0), 31.7 s [$\underline{C}H_3C(O)$], 50.7 s ($Me_2\underline{C}$), 52.4 s [$\underline{C}H_2C(O)Me$], 107.2 d.t.m (*ipso*-C_6F_5, $^1J_{CP}$ 94.6, $^2J_{CF}$ 17.6), 137.8 d.m (*m*-C_6F_5, $^1J_{CF}$ 256.0), 144.6 d.m (*p*-C_6F_5, $^1J_{CF}$ 264.8), 147.2 d.m (*o*-C_6F_5, $^1J_{CF}$ 254.6), 169.1 d [C(O)NH, $^3J_{CP}$ 14.7], 207.7 s [$\underline{C}$(O)Me]. ^{19}F NMR spectrum ($CDCl_3$), δ_F, ppm (*J*, Hz): –131.4 d (4F, *o*-C_6F_5, $^3J_{FF}$ 19.5), –143.8 t.m (2F, *p*-C_6F_5, $^3J_{FF}$ 20.7), –158.0 t.m (4F, *m*-C_6F_5, $^3J_{FF}$ 20.0). ^{31}P NMR spectrum ($CDCl_3$): δ_P 20.7 ppm. Found, %: C 45.71; H 2.79; F 34.20; N 2.53; P 5.75. $C_{21}H_{16}F_{10}NO_3P$. Calculated, %: C 45.75; H 2.93; F 34.46; N 2.54; P 5.62.

[2-(Dimethylcarbamoyl)ethyl]bis(pentafluorophenyl)phosphine oxide (5b). A solution of 0.764 g (2 mmol) of compound **1** in 8 mL of anhydrous Et_2O was added dropwise to 0.209 g (2.10 mmol) of compound **4b**. The mixture was kept during 1 h at room temperature and evaporated to dryness. The residue was dissolved in 4 mL of chloroform, and the solution was filtered through 0.38 g of the basic alumina. The alumina was washed with chloroform (2 × 2 mL). The filtrates were combined and evaporated to dryness; the residue was triturated with a mixture of 2.1 mL of hexane and 0.7 mL of diethyl ether. The formed powder precipitate was filtered off, washed with a mixture of 2.1 mL of hexane and 0.7 mL of diethyl ether, and dried in air. Yield 0.873 g (90.8%), mp 107–108°C. IR spectrum (KBr), ν, cm^{-1}: 1228 (P=O), 1641 (C=O). ^1H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 2.87 d. t (2H, $C\underline{H}_2CH_2P$, $^3J_{HH}$ 7.3, $^3J_{HP}$ 14.5), 2.92 s (3H, CH_3), 3.00 d. t (2H, CH_2P, $^3J_{HH}$ 7.5, $^2J_{HP}$ 9.1), 3.04 s (3H, CH_3). $^1H–\{^{31}P\}$ NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 2.87 t (2H, $C\underline{H}_2CH_2P$, $^3J_{HH}$ 7.3), 2.92 s (3H, CH_3), 3.00 t (2H, CH_2P, $^3J_{HH}$ 7.1), 3.04 s (3H, CH_3). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm (*J*, Hz): 24.9 d ($\underline{C}H_2CH_2P$, $^2J_{CP}$ 2.3), 29.0 d. quintets (CH_2P, $^1J_{CP}$ 80.9, $^4J_{CF}$ 3.1), 35.7 s (CH_3), 37.1 s (CH_3), 107.7 d.t.m (*ipso*-C_6F_5, $^1J_{CP}$ 90.0, $^2J_{CF}$ 18.3), 137.8 d.m (*m*-C_6F_5, $^1J_{CF}$ 256.3), 144.5 d.m (*p*-C_6F_5, $^1J_{CF}$ 261.7), 147.2 d.m (*o*-C_6F_5, $^1J_{CF}$ 254.1), 169.5 d (C=O, $^3J_{CP}$ 13.7). ^{19}F NMR spectrum ($CDCl_3$), δ_F, ppm (*J*, Hz): –131.6 d (4F, *o*-C_6F_5, $^3J_{FF}$ 18.7), –144.2 t.m (2F, *p*-C_6F_5, $^3J_{FF}$ 20.1), –158.2 t.m (4F, *m*-C_6F_5, $^3J_{FF}$ 20.2). ^{31}P NMR spectrum ($CDCl_3$): δ_P 20.6 ppm. Found, %: C 42.48; H 2.04; F 39.21; N 2.90; P 6.58. $C_{17}H_{10}F_{10}NO_2P$. Calculated, %: C 42.43; H 2.09; F 39.48; N 2.91; P 6.44.

Bis(pentafluorophenyl)[2-(piperidinocarbonyl)-1-phenylethyl]phosphine oxide (7). A solution of 0.382 g (1 mmol) of compound **1** in 4 mL of anhydrous Et_2O was added dropwise to a solution of 0.226 g (1.05 mmol) of compound **6** in a mixture of 10 mL of anhydrous diethyl ether and 1 mL of anhydrous acetonitrile. The mixture was kept during 72 h at room temperature and filtered through 3 g of the basic alumina; the alumina was washed with 15 mL of CH_2Cl_2. The combined filtrates were evaporated to dryness. Yield 0.487 g (81.6%), mp 154–155°C (hexane–CCl_4, 8 : 1). IR spectrum (KBr), ν, cm^{-1}: 1231, 1222 sh (P=O), 1655, 1636 (C=O). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.30–1.67 m (6H, $^{3–5}CH_2$-piperidine), 3.09–3.21 m (1H, $C\underline{H}_AH_BCHP$), 3.32–3.55 m (5H, $^{2,6}CH_2$-piperidine + $CH_A\underline{H}_BCHP$), 4.61–4.69 m (1H, CHP), 7.16–7.27 m (3H, *m*- + *p*-C_6H_5), 7.45 d (2H, *o*-C_6H_5, $^3J_{HH}$ 6.9 Hz). $^1H–\{^{31}P\}$ NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.30–1.67 m (6H, $^{3–5}CH_2$-piperidine), 3.15 d (1H, $C\underline{H}_AH_BCHP$, $^2J_HA_HB$ 15.6), 3.32–3.55 m (5H, $^{2,6}CH_2$-piperidine + $CH_A\underline{H}_BCHP$), 4.65 d (1H, CHP, $^3J_{HH}B$ 8.5), 7.16–7.27 m (3H, *m*,*p*-C_6H_5), 7.47 d (2H, *o*-C_6H_5, $^3J_{HH}$ 6.6). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm (*J*, Hz): 24.4 s (^{4}C-piperidine), 25.4 s [$^{3(5)}$C-piperidine], 26.3 s [$^{5(3)}$C-piperidine], 33.9 s [$\underline{C}H_2C(O)$], 43.2 s [$^{2(6)}$C-piperidine], 46.0 d (CH, $^1J_{CP}$ 76.3), 46.6 s [$^{6(2)}$C-piperidine], 106.6 d.t.m (*ipso*-C_6F_5, $^1J_{CP}$ 93.9, $^2J_{CF}$ 18.7), 108.6 d.t.m (*ipso*-C_6F_5, $^1J_{CP}$ 84.9, $^2J_{CF}$ 20.3), 128.4 d (*p*-C_6H_5, $^5J_{CP}$ 3.7), 128.9 d (*m*-C_6H_5, $^4J_{CP}$ 2.2), 129.2 d (*o*-C_6H_5, $^3J_{CP}$ 8.1), 135.2 d (*ipso*-C_6H_5, $^2J_{CP}$ 5.9), 137.3 d.m (*m*-C_6F_5, $^1J_{CF}$ 256.0), 137.9 d.m (*m*-C_6F_5, $^1J_{CF}$ 256.0), 143.9 d.m (*p*-C_6F_5, $^1J_{CF}$ 263.3), 144.4 d.m (*p*-C_6F_5, $^1J_{CF}$ 261.9), 146.5 d.m (*o*-C_6F_5, $^1J_{CF}$ 258.2), 147.0 d.m (*o*-C_6F_5, $^1J_{CF}$ 254.5), 166.7 d (C=O, $^3J_{CP}$ 16.9). ^{19}F NMR spectrum ($CDCl_3$), δ_F, ppm: –129.9 d.m (2F, *o*-C_6F_5, $^3J_{FF}$ 18.7), –132.0 d.m (2F, *o*-C_6F_5, $^3J_{FF}$ 20.2), –144.2 t.m (1F, *p*-C_6F_5, $^3J_{FF}$ 20.9), –144.6 t.m (1F, *p*-C_6F_5, $^3J_{FF}$ 20.1), –157.8 t.m (2F, *m*-C_6F_5, $^3J_{FF}$ 20.2), –159.0 t.m (2F, *m*-C_6F_5, $^3J_{FF}$ 19.4). ^{31}P NMR spectrum ($CDCl_3$): δ_P 24.5 ppm. Found, %: C 52.33; H 3.01; F 31.69; N 2.33; P 5.15.

[6] The spin-spin interaction constant $^3J_{HH}$ could not be determined due to the poor resolution of the signal.

$C_{26}H_{18}F_{10}NO_2P$. Calculated, %: C 52.27; H 3.04; F 31.80; N 2.34; P 5.18.

***N*[12]-Acryloylcytisine (8).** A solution of 1.332 g (7 mmol) of natural cytisine, 0.862 (8.05 mmol) of 2,6-lutidine, and 43 mg (0.35 mmol) of 4-dimethylaminopyridine in 5 mL of anhydrous CH_2Cl_2 was added dropwise under argon atmosphere to a solution of 0.697 g (7.7 mmol) of acryloyl chloride in 10 mL of anhydrous CH_2Cl_2. The mixture was kept during 24 h at room temperature and filtered through 10 g of neutral alumina; the alumina was washed with 30 mL of CH_2Cl_2. The combined filtrates were evaporated; the residue was dried under reduced pressure (20 mmHg) during 1 h at 25°C, recrystallized from a 10 : 3 hexane–chloroform mixture, washed with hexane (2 × 3 mL), and dried in a vacuum (~1 mmHg) during 10 h at 100°C. Yield 0.807 g (47.2%), mp 131.5–132.5°C (mp 130°C [15]). Found, %: C 68.83; H 6.62; N 11.41. $C_{14}H_{16}N_2O_2$. Calculated, %: C 68.83; H 6.60; N 11.47.

***N*[12]-{2-[Bis(pentafluorophenyl)phosphoryl]propionyl}cytisine (9).** A solution of 0.382 g (1 mmol) of compound **1** in 4 mL of anhydrous Et_2O was added dropwise to a solution of 0.244 g (1 mmol) of compound **8** in 5 mL of anhydrous acetonitrile. The mixture was kept during 20 h at room temperature and evaporated to dryness. The residue was triturated with 5 mL of diethyl ether; the formed crystalline precipitate was filtered off, washed with diethyl ether (2 × 3 mL), and dried in air. Yield 0.612 g (97.8%), mp 220.5–222°C (decomp.). ^{19}F NMR spectrum ($CDCl_3$, 293 K), δ_F, ppm: –132.5 to –133.1 m (4F, *o*-C_6F_5), –145.8 to –146.6 m (2F, *p*-C_6F_5), –159.5 to –160.1 m (4F, *m*-C_6F_5). ^{31}P NMR spectrum (DMSO-d_6, 293 K), δ_P, ppm: 19.3, 19.7. ^{31}P NMR spectrum (DMSO-d_6, 360 K): δ_P 19.2 ppm. Found, %: C 49.67; H 2.90; F 30.17; N 4.52; P 5.07. $C_{26}H_{17}F_{10}N_2O_3P$. Calculated, %: C 49.85; H 2.73; F 30.33; N 4.47; P 4.94.

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