O,O-Diphenyl *N*-sulfonylbenzimidoylphosphonates, a novel type of C-phosphorylated imines*

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A preparative method for the synthesis of first representatives of *O*,*O*-diphenyl *N*-sulfonylbenzimidoylphosphonates was proposed. The method involves oxidation of the corresponding α-(sulfonylamino)benzylphosphonates. The σ-constants of the *N*-sulfonylbenzimidoylphosphonate group were estimated by ^{19}F NMR spectroscopy. The imidoylphosphonates obtained easily formed stable adducts at the C=N bond with P- and O-nucleophiles.

Key words: imidoylphosphonates, α-amino phosphonates, sulfonamides, oxidation, σ-constants.

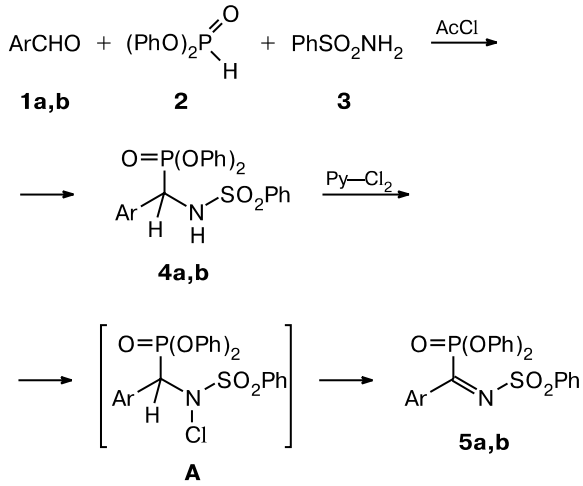
Esters of imino phosphonic acids (imidoylphosphonates) are important precursors in the synthesis of functionalized amino phosphonic acids combining a number of practically valuable properties.[1] For synthetic purposes, imines with electron-withdrawing substituents at the N atom are particularly attractive because of their enhanced reactivities. *N*-Sulfonylimines of carbonyl compounds have found wide use in synthetic practice.[2] However, examples of such imines with a phosphoryl group at the azomethine C atom are few,[3] while *N*-sulfonylbenzimidoylphosphonates have not been documented so far. In the series of imidoylphosphonates, only alkyl and silyl esters are known.[1] Aryl imidoylphosphonates have not been obtained hitherto because of the absence of appropriate synthetic procedures. In particular, reactions of imidoyl chlorides with phosphites cannot be applied for this purpose since the Arbuzov reaction is not characteristic of aryl esters of P^{III} acids. An unusual synthesis of diphenyl benzimidoylphosphonates has been described involving reactions of the Schiff bases with diphenyl phosphorochloridate and triethylamine.[4] We failed to reproduce this reaction with *N*-benzylideneaniline as an example: the starting reagents remained virtually unchanged under the specified[4] conditions and the cited results were probably erroneous.

Alkyl imidoylphosphonates are alkylating agents and their functionalization can be accompanied by *N*-alkylation as side reactions. Such processes are not characteristic of aryl esters. In the present work, we developed a method for the synthesis of *O*,*O*-diphenyl *N*-sulfonylbenzimidoylphosphonates and studied some of the properties of this novel type of *N*-sulfonylimines.

Results and Discussion

Our approach to the synthesis of *O*,*O*-diphenyl *N*-(phenylsulfonyl)fluorobenzimidoylphosphonates is shown in Scheme 1.

Scheme 1



Ar = 4-FC_6H_4 (**a**); 3-FC_6H_4 (**b**)

Initially, a three-component condensation of benzaldehydes **1**, diphenyl phosphite **2**, and benzenesulfonamide **3** in acetyl chloride as a condensation agent gives

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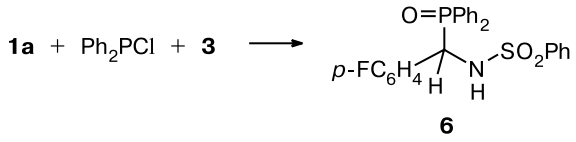
α-(phenylsulfonylamino)benzylphosphonates **4**, which are further oxidized with a Py—Cl_2 system into benzimidoylphosphonates **5** in high yields. The conversion **4**→**5** is the key step of the synthesis and probably[3,5] involves chlorination of the N atom of sulfonamide **4** followed by elimination of HCl from intermediate *N*-chloro sulfonamide **A** (see Scheme 1).

[α-(Phenylsulfonylamino)-4-fluorobenzyl]diphenylphosphine oxide (**6**) obtained according to Scheme 2 yielded no phosphorylated imine in the reaction with Py—Cl_2 under similar conditions, which agrees with our previous data.[3]

Scheme 2



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Compounds **5** are the first representatives of imidoylphosphonates with aryloxy groups linked to the P atom. They are crystalline substances that are stable in dry atmosphere but are easily hydrolyzed in air.

The spectroscopic data for sulfonylimines **5** are in full agreement with their structures. The ^{1}H NMR spectra contain no signals for the CH—NH fragment. The IR spectra show an intense band of the C=N stretching vibrations (1640—1650 cm^{-1}). The band of the P=O bond (1280 cm^{-1}) is shifted by 20 to 30 cm^{-1} to the higher frequencies compared to the starting phosphonates **4** (1250—1260 cm^{-1}), which is consistent with the effect of the withdrawing imidoyl substituent. The positions of signals for phosphorus nuclei in the ^{31}P NMR spectra (δ −5.9 to −5.2), which are typical of imidoylphosphonates,[1] are most convenient for structural identification. The presence of the P—C=N fragment was confirmed by the ^{13}C NMR spectra showing a signal for the sp^2-C atom of the imino group with a high direct coupling constant with the phosphorus nuclei (δ_C ~175, $^1J_{C,P}$ = 204 Hz).

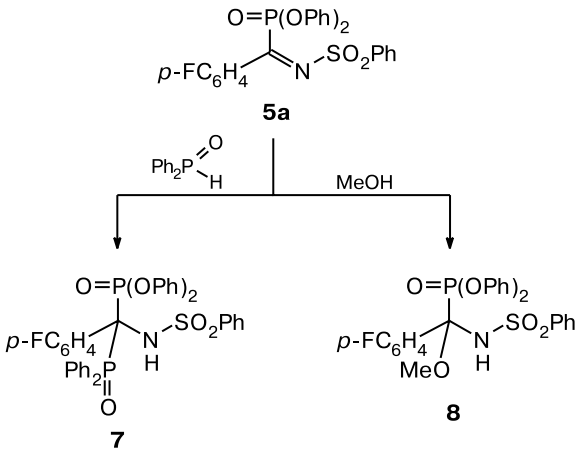
Magnetic shielding of the fluorine nuclei in substituted fluorobenzenes depends on the electronic parameters of substituents in the benzene ring and is widely used for their quantitative determination.[6,7] Measuring the chemical shifts of the F nuclei in the ^{19}F NMR spectra of imidoylphosphonates **5** ($CDCl_3$, fluorobenzene as the internal standard) and using the Taft relations[8]

$$\sigma_I = (\delta_m + 0.6)/7.1 \qquad \sigma_R = (\delta_p^F - \delta_m^F)/29.5,$$

we estimated for the first time the inductive and resonance σ-constants of the *N*-sulfonylbenzimidoylphosphonate group ($PhSO_2N{=}C[P(O)(OPh)_2]$—): σ_I = 0.43, σ_R = 0.20, and $\sigma_p = \sigma_I + \sigma_R$ = 0.63. Hence, the *N*-sulfonylbenzimidoylphosphonate group is a strong electron acceptor exceeding substantially the imidoylphosphonate group with the *N*-benzyl substituent in the withdrawing strength: for $PhCH_2N{=}C[P(O)(OEt)_2]$—, σ_I = 0.34 and σ_R = 0.02 (see Ref. 9). Replacement of the *N*-benzyl substituent by the sulfonyl one affects the resonance σ-constant ($\Delta\sigma_R$ = 0.18) to a larger extent than the inductive σ-constant ($\Delta\sigma_I$ = 0.09), which suggests higher polarizability of the C=N bond in sulfonylimines.

High electron-withdrawing ability of the sulfonylimidoyl group predetermines an increased reactivity of the C=N bond in imines **5**. For instance, imidoylphosphonate **5a** readily reacts with P- and O-centered nucleophiles at 20 °C even in the absence of bases to give stable (under normal conditions) compounds **7** and **8** containing the α-(phenylsulfonylamino)benzylphosphonate fragment (Scheme 3).

Scheme 3



Benzimidoylphosphonates containing the *N*-alkyl or *N*-benzyl group react with neither P- nor O-nucleophiles in the absence of bases.

An interesting spectral feature of compound **7** with two nonequivalent geminal P-containing groups at the carbon atom is the manifestation of a long-range spin-spin coupling between the phosphorus and fluorine nuclei, the coupling constant for the $Ph_2P(O)$ group ($^6J_{P,F}$ = 5 Hz) being substantially higher than that for the $(PhO)_2P(O)$ substituent ($^6J_{P,F}$ = 1 Hz). For monophosphorylated derivatives **4a** and **6**, the relationship between the coupling constants is opposite: $^6J_{P,F}$ = 4.5 and 3 Hz, respectively.

Thus, imidoylphosphonates of the type **5** are promising precursors in the synthesis of polyfunctional derivatives of α-amino phosphonic acids.

Experimental

^{1}H, ^{19}F, and ^{31}P NMR spectra were recorded on a Varian VXR-300 NMR spectrometer (299.95, 282.20, and 121.42 MHz,

respectively). Chemical shifts are referenced to Me_4Si (^1H) and $CFCl_3$ and PhF (^{19}F) as the internal standards and to 85% H_3PO_4 as the external standard (^{31}P). IR spectra were recorded on a UR-20 instrument in KBr pellets or as solutions in CCl_4. Solvents were thoroughly purified and dried according to standard methods. Aldehydes **1**, sulfonamide **3**, chloro(diphenyl)phosphine (Merck), diphenyl phosphite **2**, and diphenylphosphine oxide (Sigma-Aldrich) were used.

Synthesis of phosphonates 4 (general procedure). Sulfonamide **3** (2.67 g, 17 mmol) was added to a stirred solution of diphenyl phosphite **2** (3.98 g, 17 mmol) in AcCl (50 mL). The mixture was stirred for 2 h and then aldehyde **1** (2.11 g, 17 mmol) was added. The reaction mixture was left for 16 h. The solvent was removed and the residue was washed with ether and dried in air.

***O,O*-Diphenyl α-(phenylsulfonylamino)-4-fluorobenzylphosphonate (4a).** The yield was 49%, m.p. 181—182 °C. Found (%): C, 60.47; H, 4.14; P, 6.11. $C_{26}H_{21}FNO_5PS$. Calculated (%): C, 60.36; H, 4.25; P, 6.23. IR (KBr), ν/cm^{-1}: 1180, 1350 (S=O); 1250 (P=O); 3280 (NH). ^1H NMR ($CDCl_3$), δ: 5.23 (dd, 1 H, CH, $^2J_{H,P}$ = 25 Hz, $^3J_{H,H}$ = 9.6 Hz); 6.68—6.82 (m, 5 H, Ar, NH); 7.13—7.22 (m, 10 H, Ar); 7.29—7.33 (m, 3 H, Ar); 7.52 (d, 2 H, Ar, $^3J_{H,H}$ = 8 Hz). ^{19}F NMR ($CDCl_3$), δ: −113.39 ($CFCl_3$). ^{31}P NMR ($CDCl_3$), δ: 12.1 ($^2J_{P,H}$ = 25 Hz); ^{31}P—{H} NMR, δ: 12.1 (d, $^6J_{P,F}$ = 4.4 Hz).

***O,O*-Diphenyl α-(phenylsulfonylamino)-3-fluorobenzylphosphonate (4b).** The yield was 56%, m.p. 200 °C. Found (%): C, 60.23; H, 4.28; P, 6.37. $C_{26}H_{21}FNO_5PS$. Calculated (%): C, 60.36; H, 4.25; P, 6.23. IR (KBr), ν/cm^{-1}: 1180, 1350 (S=O); 1260 (P=O); 3250 (NH). ^1H NMR ($CDCl_3$), δ: 5.25 (dd, 1 H, CH, $^2J_{H,P}$ = 26 Hz, $^3J_{H,H}$ = 9.9 Hz); 6.74 (d, 2 H, Ar, $^3J_{H,H}$ = 8 Hz); 6.83 (dd, 1 H, NH, $^3J_{H,H}$ = 9.9 Hz, $^3J_{H,P}$ = 10 Hz); 6.92—7.35 (m, 15 H, Ar); 7.47 (d, 2 H, Ar, $^3J_{H,H}$ = 8 Hz). ^{19}F NMR ($CDCl_3$), δ: −115.49 ($CFCl_3$). ^{31}P NMR ($CDCl_3$), δ: 11.6 (d, $^2J_{P,H}$= 26 Hz).

Synthesis of imidoylphosphonates 5 (general procedure). Pyridine (1.27 g, 16 mmol) was added dropwise to a stirred solution of chlorine (6.24 g, 8.8 mmol) in CCl_4 (25 mL) with ice cooling. The reaction mixture was warmed to room temperature and phosphonate **4** (3.98 g, 8 mmol) was added portionwise with stirring. After 8 h, the precipitate that formed was filtered off, the solvent was removed, and the residue was washed with light petroleum.

***O,O*-Diphenyl *N*-(phenylsulfonyl)-4-fluorobenzimidoylphosphonate (5a).** The yield was 68%, m.p. 93 °C. Found (%): C, 60.84; H, 3.95; P, 6.34. $C_{25}H_{19}FNO_5PS$. Calculated (%): C, 60.60; H, 3.87; P, 6.25. IR (CCl_4), ν/cm^{-1}: 1180, 1350 (S=O); 1280 (P=O); 1640 (C=N). ^1H NMR ($CDCl_3$), δ: 7.02 (d, 4 H, $^3J_{H,H}$= 8 Hz); 7.11—7.23 (m, 8 H); 7.50 (t, 2 H, $^3J_{H,H}$ = 8 Hz); 7.61 (t, 1 H, $^3J_{H,H}$ = 8 Hz); 7.83 (d, 2 H, $^3J_{H,H}$ = 8 Hz); 7.94 (dd, 2 H, $^3J_{H,H}$ = 8 Hz, $^3J_{H,F}$ = 5.7 Hz). ^{13}C NMR ($CDCl_3$), δ: 115.8 (d, C(3), ArF, $^2J_{CF}$ = 22 Hz); 120.3 (d, C(2), PhO, $^3J_{C,P}$ = 3.8 Hz); 125.7 (s, C(4), PhO); 127.7 (s, C(2), $PhSO_2$); 129.0 (s, C(3) $PhSO_2$); 129.7 (s, C(3), PhO); 129.3 (dd, CC=N, $^2J_{C,P}$ = 25 Hz, $^4J_{C,F}$ = 2.5 Hz); 131.8 (dd, C(2), ArF, $^3J_{CP}$ = 9.2 Hz, $^3J_{C,F}$ = 4.9 Hz); 133.59 (s, C(4), $PhSO_2$); 139.6 (s, CSO_2); 150.0 (d, C—O, $^2J_{C,P}$ = 10 Hz); 165.1 (d, C—F, $^1J_{C,F}$ = 255 Hz); 174.7 (d, C=N, $^1J_{C,P}$ = 204 Hz). ^{19}F NMR ($CDCl_3$), δ: −105.09 ($CFCl_3$); 7.42 (PhF). ^{31}P NMR ($CDCl_3$), δ: −5.2.

***O,O*-Diphenyl *N*-(phenylsulfonyl)-3-fluorobenzimidoylphosphonate (5b).** The yield was 72%, m.p. 90 °C. Found (%): C, 60.41; H, 3.91; P, 6.18. $C_{25}H_{19}FNO_5PS$. Calculated (%): C, 60.60; H, 3.87; P, 6.25. IR (CCl_4), ν/cm^{-1}: 1180, 1350 (S=O); 1280 (P=O); 1650 (C=N). ^1H NMR ($CDCl_3$), δ: 7.03 (d, 4 H, $^3J_{H,H}$ = 8 Hz); 7.12—7.24 (m, 8 H); 7.44—7.55 (m, 4 H); 7.62 (t, 1 H, $^3J_{H,H}$ = 8 Hz); 7.83 (m, 2 H). ^{13}C NMR ($CDCl_3$), δ: 115.7 (dd, C(2), ArF, $^2J_{C,F}$ = 24 Hz, $^3J_{C,P}$ = 4.3 Hz); 119.3 (d, C(4), ArF, $^2J_{C,F}$ = 21.6 Hz); 120.2 (d, C(2), PhO, $^3J_{C,P}$ = 4.5 Hz); 124.4 (dd, C(6), ArF, $^3J_{C,P}$ = 4.4 Hz, $^4J_{C,F}$ = 2.4 Hz); 125.7 (s, C(4), PhO); 127.8 (s, C(4), $PhSO_2$); 129.0 (s, C(3), $PhSO_2$); 129.7 (s, C(3), PhO); 130.2 (d, C(5), ArF, $^3J_{C,F}$ = 7 Hz); 134.8 (dd, CC=N, $^2J_{C,P}$ = 28 Hz, $^3J_{C,F}$ = 8 Hz); 139.3 (s, CSO_2); 149.9 (d, C—O, $^2J_{C,P}$ = 9 Hz); 161.9 (d, C—F, $^1J_{C,F}$ = 249 Hz); 174.6 (d, C=N, $^1J_{C,P}$ = 204 Hz). ^{19}F NMR ($CDCl_3$), δ: −111.16 ($CFCl_3$); 2.48 (PhF). ^{31}P NMR ($CDCl_3$), δ: −5.9.

***N*-[(Diphenylphosphinoyl)(4-fluorophenyl)methyl]benzenesulfonamide (6).** Aldehyde **1a** (0.68 g, 5.5 mmol) and chloro(diphenyl)phosphine (1 g, 4.5 mmol) were added to a solution of benzenesulfonamide (0.71 g, 4.5 mmol) in glacial AcOH (10 mL) and the reaction mixture was refluxed for 3 h. The solvent was removed and the residue was washed with ethanol and crystallized from EtOH—$CHCl_3$ (1 : 3). The yield of compound **6** was 1.4 g (66%), m.p. 254 °C. Found (%): C, 64.62; H, 4.42; S, 6.63. $C_{25}H_{21}FNO_3PS$. Calculated (%): C, 64.51; H, 4.55; S, 6.89. IR (KBr), ν/cm^{-1}: 1170, 1340 (S=O); 1198 (P=O). ^1H NMR ($CDCl_3$), δ: 5.23 (dd, CH, 1 H, $^2J_{H,P}$= 9.9 Hz, $^3J_{H,H}$= 9.5 Hz); 6.5 (m, 2 H); 6.9 (m, 2 H); 7.1 (m, 2 H); 7.40—8.10 (m, 14 H). ^{19}F NMR ($CDCl_3$), δ: −114.56 ($CFCl_3$). ^{31}P—{H} NMR ($CDCl_3$), δ: 32.6 (d, $^6J_{P,F}$ = 3 Hz).

***O,O*-Diphenyl α-diphenylphosphinoyl-α-(phenylsulfonylamino)-4-fluorobenzylphosphonate (7).** Diphenylphosphine oxide (0.035 g, 0.17 mmol) was added to a solution of imidoylphosphonate **5a** (0.086 g, 0.17 mmol) in benzene (5 mL). After 1 h, the solvent was removed and the residue was washed with light petroleum. The yield of compound **7** was 0.11 g (91%), m.p. 146—148 °C. Found (%): C, 63.87; H, 4.28; P, 9.03. $C_{37}H_{30}FNO_6P_2S$. Calculated (%): C, 63.70; H, 4.33; P, 8.88. IR (KBr), ν/cm^{-1}: 1180, 1350 (S=O); 1210, 1280 (P=O); 3180 (NH). ^1H NMR ($CDCl_3$), δ: 4.86 (br., 1 H, NH); 6.18 (m, 2 H); 6.47 (t, 1 H, $^3J_{H,H}$ = 8 Hz); 6.73 (d, 2 H, $^3J_{H,H}$ = 8 Hz); 6.95—7.54 (m, 22 H); 7.89 (dd, 1 H, $^3J_{H,H}$ = 8 Hz, $^3J_{H,F}$ = 5.7 Hz); 8.02 (dd, 1 H, $^3J_{H,H}$ = 8 Hz, $^3J_{H,F}$ = 5.7 Hz). ^{19}F NMR ($CDCl_3$), δ: −113.96 ($CFCl_3$). ^{31}P—{H} NMR ($CDCl_3$), δ: 8.75 (dd, 1 P, POPh, $^2J_{P,P}$ = 12 Hz, $^6J_{P,F}$ = 1 Hz); 37.94 (dd, 1 P, PPh, $^2J_{P,P}$ = 12 Hz, $^6J_{P,F}$ = 5 Hz).

***O,O*-Diphenyl α-methoxy-α-(phenylsulfonylamino)-4-fluorobenzylphosphonate (8).** A solution of imidoylphosphonate **5a** (0.15 g) in anhydrous methanol (10 mL) was left at room temperature for 12 h. The solvent was removed and the residue was crystallized from diethyl ether—light petroleum (1 : 2). The yield of compound **8** was 0.16 g (90%), m.p. 146—148 °C. Found (%): C, 58.89; H, 4.42; P, 6.11. $C_{26}H_{23}FNO_6PS$. Calculated (%): C, 59.20; H, 4.39; P, 5.87. IR (KBr), ν/cm^{-1}: 1180, 1350 (S=O); 1280 (P=O); 3200 (NH). ^1H NMR ($CDCl_3$), δ: 3.58 (s, 3 H, OMe); 6.60 (d, 1 H, NH, $^3J_{H,P}$ = 8.7 Hz); 6.86 (m, 4 H, Ar); 7.41 (t, 2 H, Ar, $^3J_{H,H}$ = 8 Hz); 7.54—7.62 (m, 6 H, Ar). ^{19}F NMR ($CDCl_3$), δ: −113.75 ($CFCl_3$). ^{31}P NMR ($CDCl_3$), δ: −8.50.

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