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A new reaction of phosphorylated *N*-sulfonylimines with hydrophosphoryl agents involving C → N transfer of phosphoryl groups

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Abstract—Hydrophosphoryl nucleophilic agents add to the C=N bond of *N*-sulfonyltrichloroacetimidoylphosphonates to give unstable C,C-diphosphorylated adducts, which undergo competitive 1,2-C → N phosphorotropic rearrangement and dehydrochlorination with the formation of aza-Perkow reaction products, C,N-diphosphorylated dichlorovinylsulfonamides. This is the first reliably identified case of an aza-Perkow transformation for acid phosphites and their initial nucleophilic attack at the C atom of the azomethine bond in the aza-substrates.

Increasing interest in compounds containing P–C–N (α-aminophosphonic acid derivatives) and P–C(N)–P groups (aminomethylenebisphosphonic acid derivatives) is connected primarily with the wide range of their biological activity.[1,2] In particular, α-aminophosphonic acids can mimic the action of natural amino acids in living organisms and act as inhibitors of enzymes.[1] In this respect the study of chemical transformations of such compounds, especially those associated with phosphorotropic migrations, is of considerable importance because the transfer of phosphoryl groups is characteristic of many biochemical processes.

Recently we developed a convenient synthesis of *N*-arylsulfonyltrichloroacetimidoylphosphonates **1**, highly electrophilic imines of a new type, which are very promising intermediates in the synthesis of functionalized aminophosphonates.[3] Now we report a novel C → N migration of phosphoryl groups that occurs during the reaction of the imidoylphosphonates **1** with hydrophosphoryl compounds (HPCs).

It was found that in these reactions the HPC first adds across the C=N bond of the substrate. However the sulfonylaminoalkylidenebisphosphoryl compounds **2** thus formed, and detected spectroscopically in the reaction mixture, turned out to be very unstable. Under the reaction conditions used (benzene, rt), the phosphoryl groups undergo an irreversible 1,2-C → N transfer accompanied by dehydrochlorination and formation of C,N-diphosphorylated dichlorovinylsulfonamides **3** and **4** (Scheme 1).

Thus, the final result of the reaction of imidoylphosphonates **1** with the HPC is the formation of aza-Perkow reaction products after the spontaneous 1,2-C → N migration of the phosphorus groups, that is, after phosphonate–amidophosphate (**2a**,**b** → **3a**,**b**; **2c** → **3c** + **4c**) or phosphine oxide–phosphinoylamide (**2d** → **3d**) rearrangements.

Such rearrangements were postulated earlier for adducts with electron-rich nitrogen atoms, upon heating in the presence of bases, but the initial formation of a C-phosphorylated intermediate, a key to the mechanism, was not established.[4]

Unexpectedly, the phosphoryl C → N transfer we observed proceeds in compounds containing a strong electron-withdrawing sulfonyl group at the nitrogen atom, and under mild conditions and without base catalysis. Additional evidence for the phosphorotropic rearrangement is the competing migration of both phosphoryl groups in **2c**, the $(EtO)_2P(O)$, which was already present in the substrate **1**, and the incoming $(PhO)_2P(O)$ moiety, to give a 1:3 mixture of **4c** and **3c**.

Keywords: *N*-Sulfonylimines; Imidoylphosphonates; Sulfonamides; Diphosphonates; Rearrangement; Aza-Perkow reaction.
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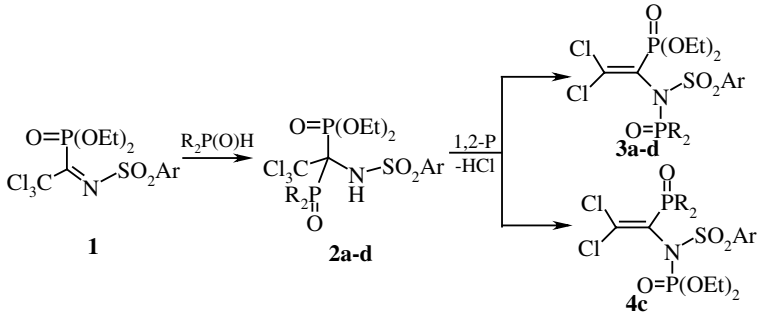


Scheme 1. (**a**) R = EtO, Ar = Ph; (**b**) R = EtO, Ar = 4-MeC_6H_4; (**c**) R = PhO, Ar = Ph; (**d**) R = Ar = Ph.

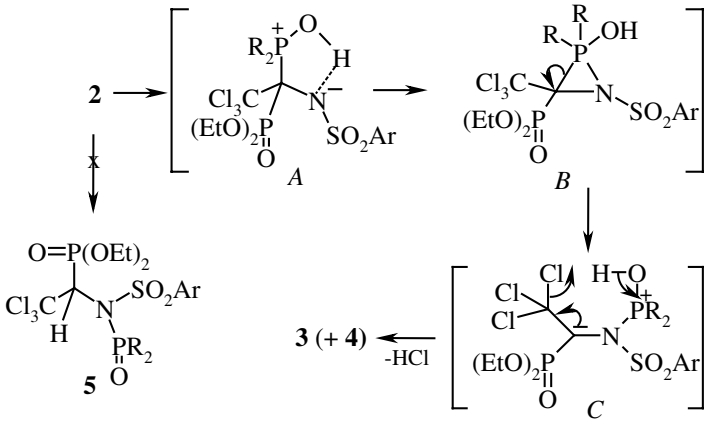
In intermediate **2d**, which has a diethoxyphosphoryl and a diphenylphosphinoyl group at the same carbon atom, only the $Ph_2P(O)$ migrates and the process is so fast that the intermediate formation of **2d** is impossible to detect even spectroscopically. It is evident that in the case of **2d** the rate-limiting step is the addition of the HPC to the C=N bond. In **2a**,**b** both phosphoryl groups are identical in migratory aptitude.

Important from the mechanistic point of view is the fact that the reaction does not involve the intermediate formation of trichloroethylsulfonamides **5** as evidenced by ^{31}P NMR monitoring. Compounds of this type are fairly stable under normal conditions and undergo dehydrochlorination only in the presence of bases or upon heating,[5] while the dehydrochlorination of similar compounds but with a C-phosphonium group, proceeds easily.[6]

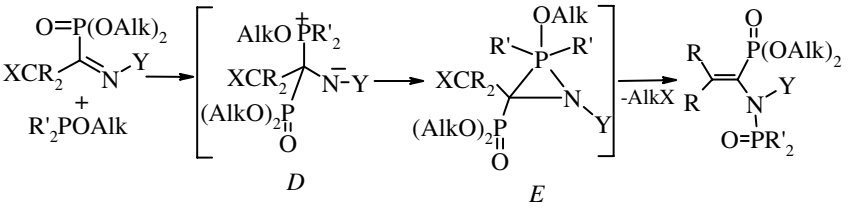
The experimental data presented above are consistent with the multistep course of the rearrangement shown in Scheme 2.

The absence of compounds **5** on the reaction coordinate suggests that the dehydrochlorination occurs in the phosphorane B and/or in the carbanion C. A driving force of the phosphorotropic shift is evidently the high NH-acidity of compounds **2** that assists generation of the phosphonium center in the intermediate A probably through H-bonding. The subsequent umpolung of the C- and N-reaction centers (A → C) promotes the formation of the N-phosphorylation products. The steric strain caused by the bulky substituents at the amine carbon atom in **2** is also conducive to the rearrangement. Specifically, in contrast to bisphosphonates **2**, their trifluoromethyl analogs are fairly stable and not prone to the phosphorotropic rearrangement at room temperature.[7] As the electronic characteristics of CCl_3 and CF_3 groups are similar (σ_p 0.46 and 0.54, respectively),[8] such a difference in behavior can be accounted for mainly by steric factors although the different nucleofugicity of fluoride and chloride anions may also have an effect on the process. The observed distinction in the relative migratory aptitude of the phosphorus substituents [$Ph_2P(O) \gg (PhO)_2P(O) > (EtO)_2P(O)$] is in agreement with a higher proton-acceptor power of the $Ph_2P(O)$ group,[9] that increases its capability to form H-bonds, and also with a more efficient stabilization of the phosphonium center, in the intermediate A, by the phenyl groups.[10] The relief of the steric strain resulting from the 1,2-shift may also contribute to the relative migration ability of the groups in question.

The transformation **1** → **3** is the first example of an aza-Perkow reaction for HPCs, previously this was known only for neutral esters of P^{III} acids (Scheme 3). Its initial step (**1** → **2**) is the uncatalyzed version of the Pudovik reaction. Thus Scheme 1 combines two fundamental reactions of phosphorus chemistry, the Pudovik reaction and the aza-Perkow reaction. Despite the formal



Scheme 2.



Scheme 3. R = X = Cl, Y = CH_2Ph,[11] C(O)Ph,[12] CHO,[13] $C(O)CCl_3$,[14] COOMe,[15] SO_2Ar;[7] R = X = F, Y = $P(O)(OEt)_2$,[16] SO_2Ar;[7] R = H, X = Cl, Y = CH_2Ph.[17]

Table 1. Characteristics of compounds **2**–**4** and reaction conditions

Intermediate	δ_P, ppm ($^2J_{PP}$, Hz)	Product	Reaction time (C_6H_6, rt)	Yield, %	δ_P ($^3J_{PP}$, Hz)	
					CP	NP
2a	13.6	**3a**	7 days[a]	80	9.1	−4.4
2b	13.5	**3b**	7 days	84	9.5	−3.9
2c	4.7; 13.1 (12.0)	**3c**	7 days	—[b]	8.0 (2.0)	−13.1 (2.0)
		4c		—[b]	1.5	−4.6
2d	—	**3d**	1 h	93	9.1	33.3

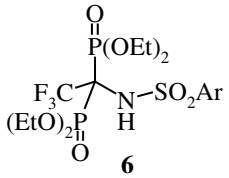
[a] Or 4 h at 80 °C.
[b] **3c**:**4c** = 3:1.

similarity of the end products in Schemes 1 and 3, there are substantial differences between the reactions of imidoylphosphonates **1** with HPCs and with neutral esters of P^{III} acids. In the first case, both of the phosphorus groups in the C,C-diphosphorylated adduct **2** compete for abstraction of the NH proton and both can migrate via the intermediates A and B (Scheme 2). In contrast, in the reaction with R'_2POAlk, the phosphonium center in D is formed exclusively by the incoming phosphite-born phosphorus atom and, hence, only this moiety migrates. Moreover, the phosphonium center in Scheme 3 is created by the attack of the nucleophilic P atom on the imine carbon whereas in Scheme 2 this occurs via the N → O shift of the proton.

It should be emphasized that the stepwise mechanism for the aza-Perkow reaction for phosphites outlined in Scheme 3 was previously only a postulate.[3,7,16] The spectroscopic identification of the diphosphorylated compounds **2** in Scheme 1 is the first unequivocal experimental corroboration of the involvement of a C-phosphorylation step in the aza-Perkow reaction.

The reaction of imidoylphosphonates **1** with HPC is a convenient preparative approach to C,N-diphosphorylated dichlorovinylsulfonamides.

The participants in the reaction of imidoylphosphonates **1** with HPCs give clearly distinguishable ^{31}P NMR signals (Table 1) that allow easy monitoring of the process and identification of the products. The close similarity of the spectral characteristics of adducts **2a**,**c** and their known analogs **6** (δ_P 11.1–11.8 ppm)[7] and **7** (δ_P 12.8 and 3.8 ppm, $^2J_{PP}$ 10 Hz)[18] supports the structure assignments of the former. A rather strong spin coupling of the nonequivalent geminal phosphorus nuclei in **2c** ($^2J_{PP}$ 12 Hz) and its weakening in the isomer **3c** ($^3J_{PP}$ 2 Hz) is an additional argument in favor of the structures proposed.



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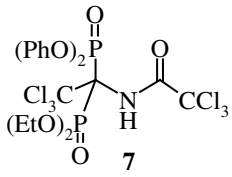

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Typical procedure for preparation of sulfonamides **3**: To a benzene solution of imidoylphosphonate **1** (Ar=Ph) was added an equimolar amount of diphenylphosphine oxide. After stirring the mixtures for 1 h at room temperature, the solvent was evaporated and the waxy residue was washed with petroleum ether and dried in vacuum to give **3d** in 93% yield. ^1H NMR ($CDCl_3$, 300 Hz): δ = 1.24 (t, $^3J_{HH}$ = 6.7 Hz, 3H, CH_3), 1.39 (t, $^3J_{HH}$ = 6.7 Hz, 3H, CH_3), 4.01–4.34 (m, 4H, CH_2O), 7.38–7.81 (m, 12H, Ph), 7.98–8.12 (m, 2H, Ph), 8.30–8.37 (m, 1H, Ph) ppm. ^{31}P NMR ($CDCl_3$, 121.4 MHz): δ = 9.1 (1P, PC), 33.3 (1P, PN) ppm. Calcd for $C_{24}H_{25}Cl_2NO_6P_2S$: C 48.99, H 4.28, Cl 12.05, N 2.38, P 10.53, S 5.45. Found: C 49.10, H 4.31, Cl 12.15, N 2.36, P 10.49, S 5.43.

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