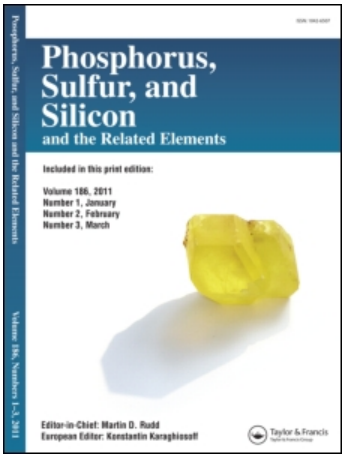

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Phosphorylation of Imino Analogs of α -Halocarbonyl Compounds

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Phosphorylation of Imino Analogs of α-Halocarbonyl Compounds

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Phosphorylation of the α-haloimines leads mainly to C- or N-phosphorylated compounds as the final products, and selectivity being dependent on the type of halogen, substituents at the imine carbon and nitrogen atoms, and on the nature of phosphorus regeant. Variety of transformations is connected with rearrangements accompanied by umpolung of C- and N-center of imine function, possible participation of C═N bond, halogen atoms or N-substituents, in ractions involving the Hal-C—C═N skeleton.

Keywords Halogenoalkylimines; C/N-phosphorylation; imidoyl chlorides; aminophosphonates; phosphorylation; umpolung; rearrangements

INTRODUCTION

Nucleophilic phosphorylation of α-halocarbonyl compounds, proceeding with P—C or P—O bond formation and represented by two named reactions (Arbuzov and Perkow), is well studied and have received wide synthetic use. The interaction of their iminoanalogs-α-haloimines-with P^{III} nucleophiles was not investigated systematically. In distinction from two-valent oxygen in carbonyl compounds, three-valent nitrogen in haloimines provides additional center of attachment of substituent R and therefore increase the variety of reaction pathways and synthetic potentialities.

Haloalkylimidoyl Chlorides

The labile chlorine atom can be easily substituted by various functional groups, in particular, by phosphorus-containing moiety. The phosphorylation of imidoyl chlorides can occur at the C or at the N atom. We have

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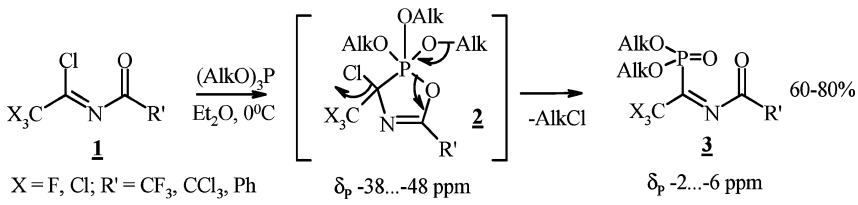
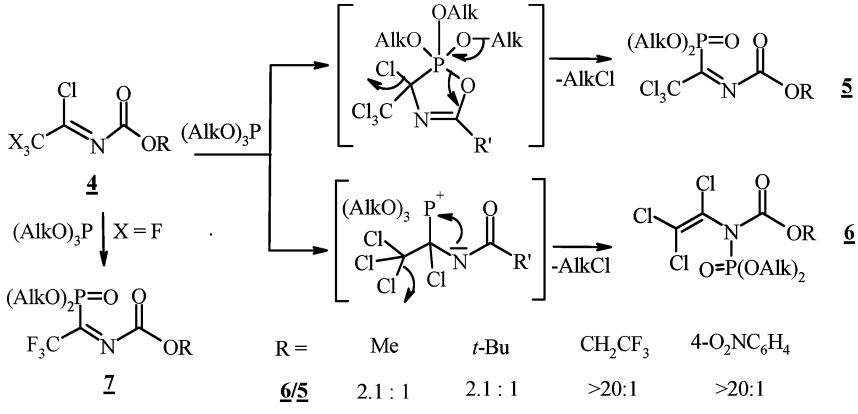


SCHEME 1

found that N-acyl imidoyl chlorides **1** react with trialkyl phosphites to afford new type of C-phosphorylated heterodienes **3**. Most likely, the reaction starts with the nucleophilic attack by the phosphorus on the most electrophilic center, the imine carbon atom, followed by dealkylation in the intermediate phosphonium salt or phosphorane **2**, detected by ^{31}P NMR (Scheme 1).

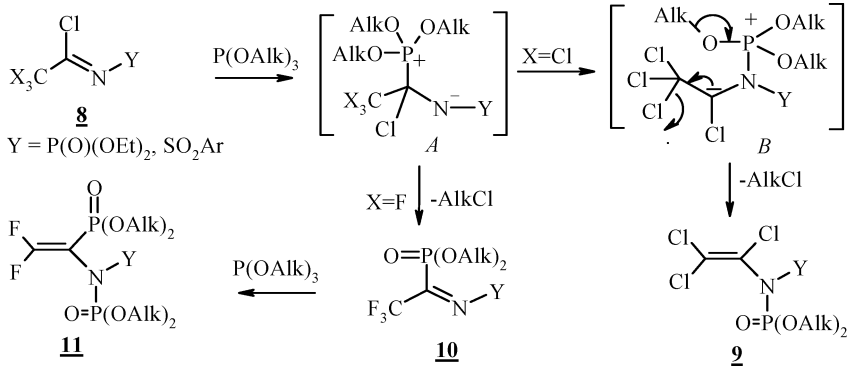
Compounds **4** with less electron-withdrawing alkoxycarbonyl group at the N atom are less selective in the reaction with phosphites and give a mixture of C- (**5**, **7**) and N-phosphorylated products **6** (Scheme 2). The selectivity of the process depends on the substituent R and the type of halogen atom.[1]

N-Sulfonyl- and N-phosphorylimidoyl chlorides **8**. The absence of conjugate bond system and also the nature of halogen atom and phosphorus reagent to a large extent predetermine the peculiarity of phosphorylation. With X = Cl only N-phosphorylation occurs, whereas imidoyl chlorine atom remains untouched. In case of X=F initial C-phosphorylation is accompanied by the fast N-phosphorylation of more reactive phosphonate **10** (Scheme 3).



R =	Me	*t*-Bu	CH_2CF_3	4-$O_2NC_6H_4$
6/5	2.1 : 1	2.1 : 1	>20:1	>20:1

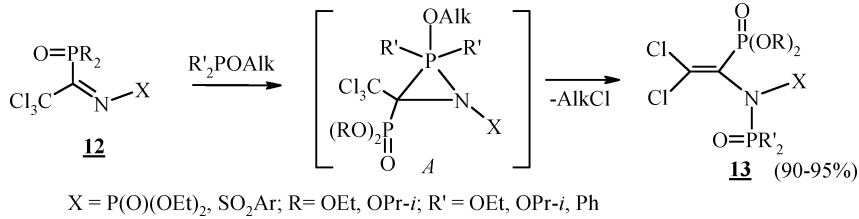
SCHEME 2



SCHEME 3

Thus, varying substiuents in substrate and P^{III} reagent allows controlling chemoselectivity.

Trihaloacetimidoylphosphonates 10, 12 react with involvement of trihalomethyl group to form N-phosphorylation products **11**, **13** (Schemes 3, 4). Unusually easy involvement of fluorine atom (**10** → **11)** is apparently caused by generation of carbanion in α-position to CF_3 group.

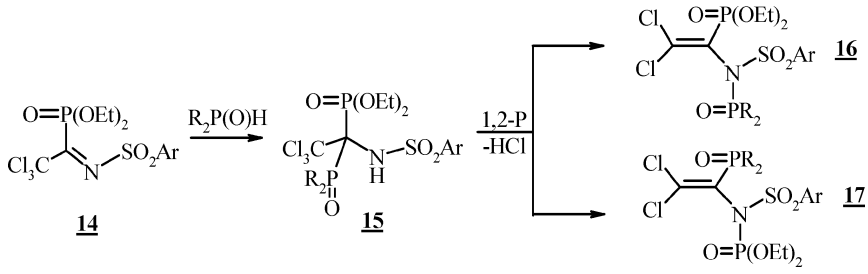


X = P(O)(OEt)$_2$, SO_2Ar; R= OEt, OPr-*i*; R' = OEt, OPr-*i*, Ph

SCHEME 4

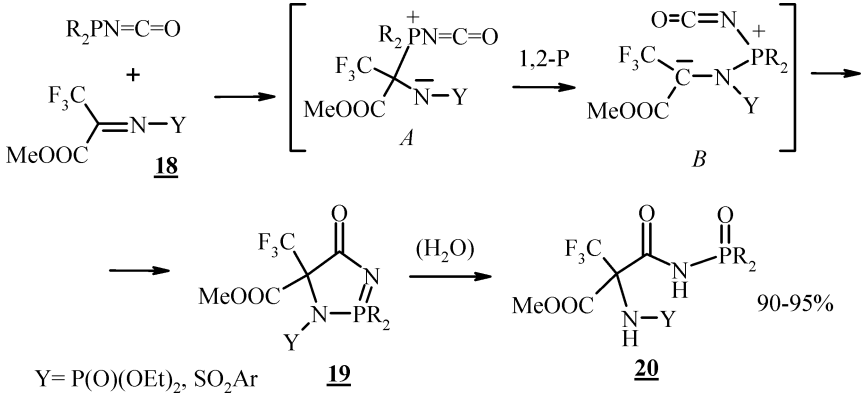
Hydrophosphoryl compounds (HPC) add to C=N bond of imines **14** to give unstable *C*, *C*-diphosphorylated adducts **15** undergoing competitive 1,2-C→N phosphorotropic rearrangement and dehydrochlorination with the formation of aza-Perkow type reaction products (Scheme 5). This is the first reliably identified case of aza-Perkow transformation for HPC and their initial nucleophilic attack on the C atom of the azomethine bond in the aza-substrates [2]. With nonequivalent phosphorus groups, both of them can migrate and their migration ability depends on the substituents at the phosphorus atom: $Ph_2P(O) \gg (PhO)_2P(O) > (EtO)_2P(O)$.

N-Sulfonyl- and N-phosphoryliminocarboxylates 18 on reaction with phosphorus isocyanates undergo unprecedented C-acylation



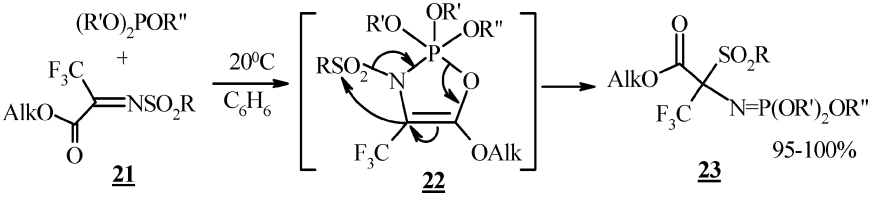
SCHEME 5

of electrophilic imine C atom caused by umpolung of C- and N reactive centers of the C=N bond, to produce C- acylated trifluoroalanines **20** (Scheme 6).



SCHEME 6

In the reaction of N-sulfonylimines **21** with phosphites, a radically new reaction pathway for imines is realized. It involves N–C transfer of the RSO_2 group and leads to biorelevant sulfonyl-substituted trifluoroalanine derivatives **23** (Scheme 7).



SCHEME 7

In summary, a variety of pathways were revealed in the reactions of α-haloimines with phosphorus nucleophiles. The stabilization of intermediates allows stepwise monitoring of phosphorylation. In a majority of cases the interaction starts with P—C bond formation, whereas N-phosphorylation products are the result of secondary processes. The possibility to control chemoselectivity offers substantial preparative possibilities in targeted syntheses of practically important derivatives with aminophosphonic fragment.

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