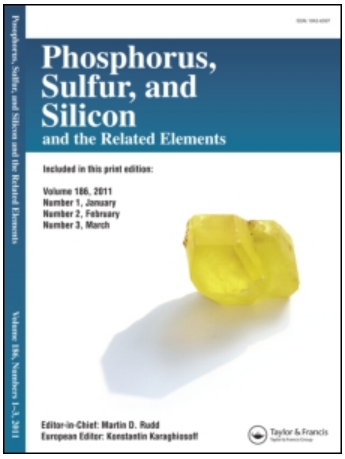
This article was downloaded by:
On: *27 January 2011*
Access details: *Access Details: Free Access*
Publisher *Taylor & Francis*
Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Phosphorus, Sulfur, and Silicon and the Related Elements

Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

Imidoyl Chlorides: New Promising Building Blocks in Synthesis of α-Aminophosphoryl Compounds

P. P. Onys'ko[a]; Yu. V. Rassukana[a]; O. A. Sinitsa[a]
[a] Institute of Organic Chemistry, NAS of Ukraine, Kyiv, Ukraine

To cite this Article Onys'ko, P. P. , Rassukana, Yu. V. and Sinitsa, O. A.(2008) 'Imidoyl Chlorides: New Promising Building Blocks in Synthesis of α-Aminophosphoryl Compounds', Phosphorus, Sulfur, and Silicon and the Related Elements, 183: 2, 399 — 405

To link to this Article: DOI: 10.1080/10426500701735338

URL: http://dx.doi.org/10.1080/10426500701735338

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: http://www.informaworld.com/terms-and-conditions-of-access.pdf

This article may be used for research, teaching and private study purposes. Any substantial or systematic reproduction, re-distribution, re-selling, loan or sub-licensing, systematic supply or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

Phosphorus, Sulfur, and Silicon, 183:399–405, 2008
Copyright © Taylor & Francis Group, LLC
ISSN: 1042-6507 print / 1563-5325 online
DOI: 10.1080/10426500701735338

Taylor & Francis
Taylor & Francis Group

Imidoyl Chlorides: New Promising Building Blocks in Synthesis of α-Aminophosphoryl Compounds

P. P. Onys'ko, Yu. V. Rassukana, and O. A. Sinitsa
Institute of Organic Chemistry, NAS of Ukraine, Kyiv, Ukraine

Synthetic and mechanistic aspects relevant to nucleo philic phosphorylation of imidoyl chlorides, their potentialities in preparing functionalized α-aminophosphoryl compounds were discussed.

Keywords Aminophosphonates; H-transfer; imidoyl chlorides; imines; phosphorylation; rearrangements

Downloaded At: 17:43 27 January 2011

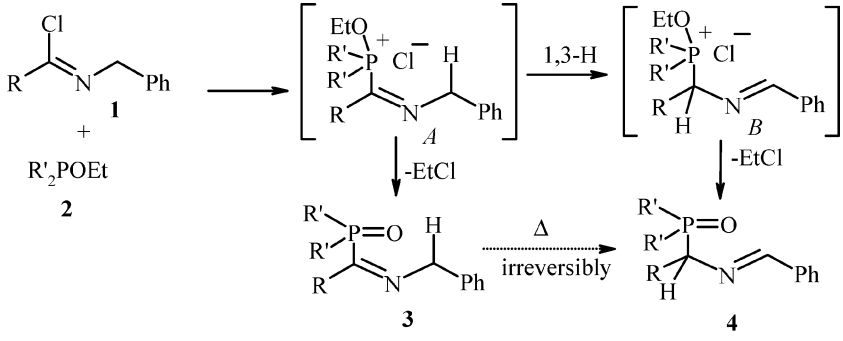
INTRODUCTION

Imidoyl chlorides combine properties of imines and acid chlorides and are widely used in organic synthesis and in mechanistic studies. Phosphorylation of imidoyl chlorides represents a new synthetic tool for preparation of iminoalkylphosphonic derivatives and their transformations into various biorelevant functionalized aminophosphoryl compounds.

RESULTS AND DISCUSSIONS

Phosphorylation of N-benzylimidoyl chlorides **1** is accompanied by prototropy (Scheme 1). The latter is favored by electron-withdrawing substituent R in imidoyl chloride **1** and electron-releasing group in phosphorus reagent **2** but the *nature of these effects* is essentially different. Acceptor groups R in imidoylchlorides **1** favor H-transfer *directly*, by increasing C-H acidity. Donor groups R′ at phosphorus atom in compounds **2** increase relative stability of phosphonium intermediates *A*. With R′ = OEt, the dealkylation ($A \rightarrow$ **3**) proceeds faster than H-shift due to low stability of salt *A*, and the imidoylphosphonate **3** is the major product. With R=Ph, the lifetime of quasi-phosphonium salt is long enough for the H-shift $A \rightarrow B$, and the imine **4** becomes predominant.

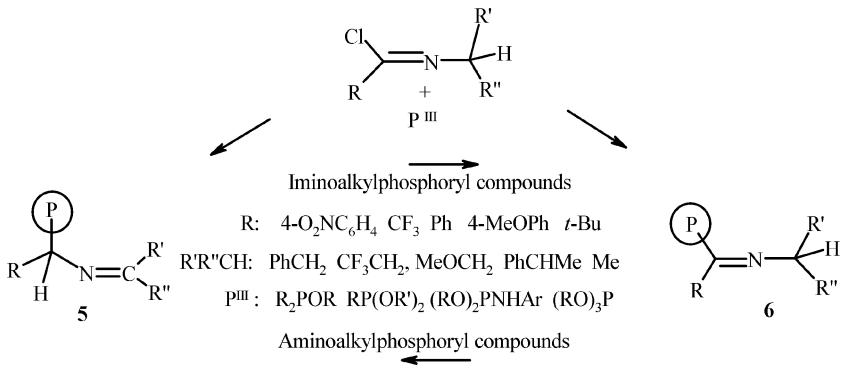
Address correspondence to P. P. Onys'ko, Institute of Organic Chemistry, NAS of Ukraine, 02094 Kyiv, 5 Murmans'ka St., Ukraine. E-mail: onysko@rambler.ru



			$(EtO)_3P$	$(EtO)_2PPh$	$EtOPPh_2$
3/4	R = *t*-Bu	(σ_I–0.02)	95:5	60:40	5:95
	R = Ph	(σ_I 0.10)	~70:30	—	30:70
	R = COOEt	(σ_I 0.30)	~50:50	—	0:100
	R = CF_3	(σ_I 0.42)	~50:50	20:80	0:100

SCHEME 1

The regularities found allow purposeful preparing of imino- or aminoalkylphosphonic compounds (Scheme 2).

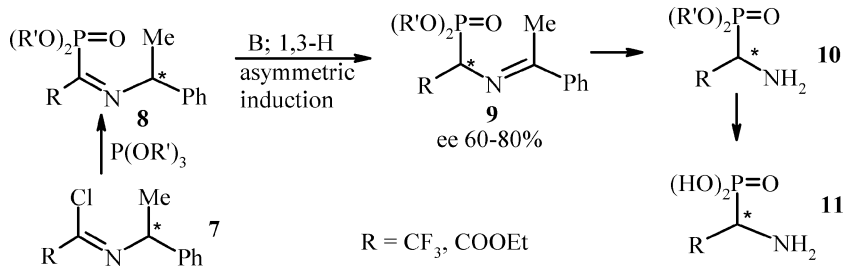


SCHEME 2

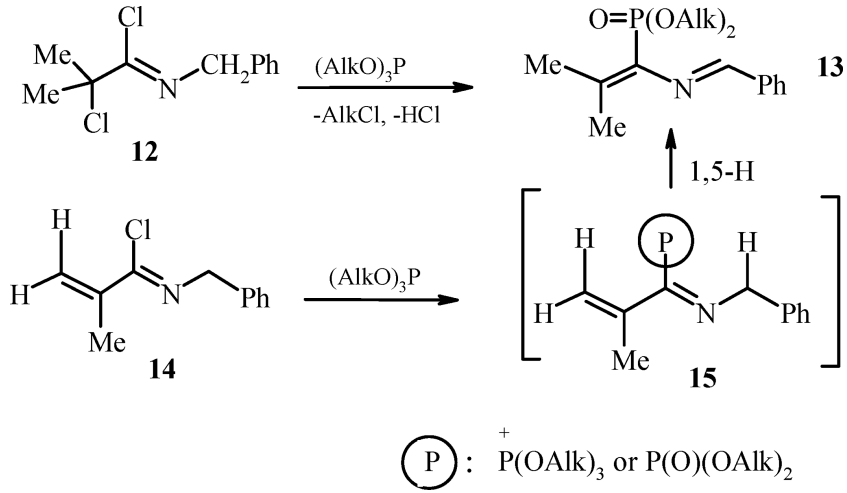
Transformation of imidoylphosphoryl compounds into α-phosphorylated imines, e.g. **3** → **4**, **5** → **6**, being similar to biochemical trans amination reaction, is a fundamental property of N-alkylimidoyl phosphonates and an important preparative way to α-aminophosphonic derivatives. We have found[1] that proton transfer in imines **8** is stereoselective and leads to enantiomerically enriched aminophosphonates **9,10** and aminophosphonic acids **11**. Scheme 3 demonstrates a new

Downloaded At: 17:43 27 January 2011

approach to asymmetric synthesis of α-aminophosphoryl derivatives, based on asymmetric induction during 1,3-proton transfer.



SCHEME 3



SCHEME 4

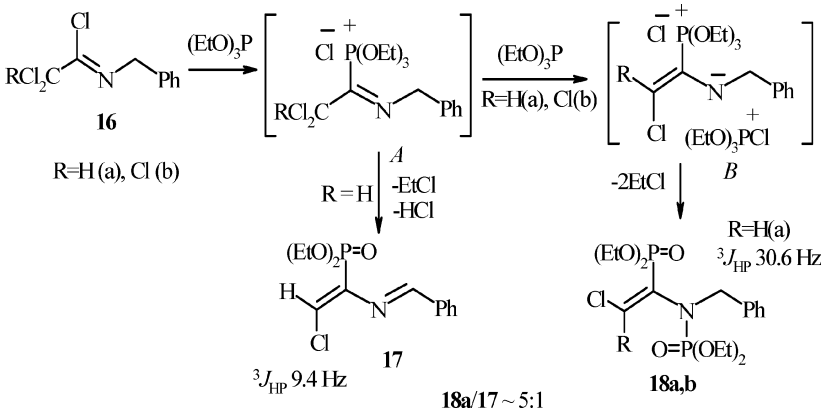
Specific influence of phosphoryl group is an important factor, defining steroselectivity of prototropy. It is worth to note that analogs of imine **8** (R = CF_3), bearing COOAlk group instead of phosphoryl, undergo prototropic transfer with complete racemization,[2] although COOAlk and (RO_2)PO groups have close electronic parameters.

Phosphorylation of haloalkylimidoyl chloride **12** is accompanied by dehydrochlorination and leads to synthetically promising phosphorylated azadienes **13**, that can be prepared also from imidoyl chloride **14** via formal 1,5-H shift in **15** (Scheme 4).

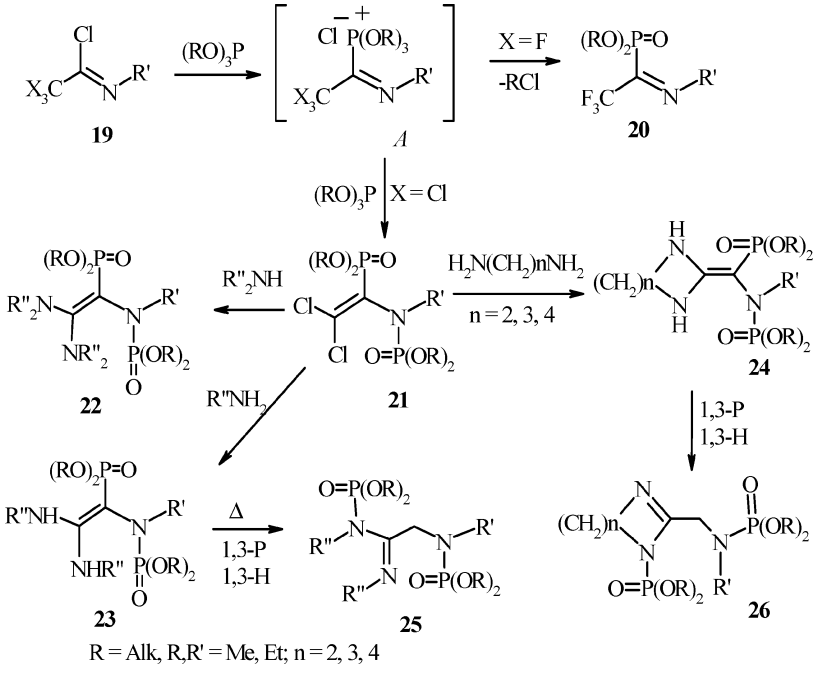
Amassing of chlorine atoms in haloalkyl substituent of imidoyl chlorides **16** leads to domination, irrespective of reagents ratio, of C,N-diphosphorylated products **18** (Scheme 5). It was shown, for the first

Downloaded At: 17:43 27 January 2011

time, that *aza*-Perkow type reaction of imino analogs of α-halocarbonyl compounds with phosphites proceeds stereoselectively.



SCHEME 5



SCHEME 6

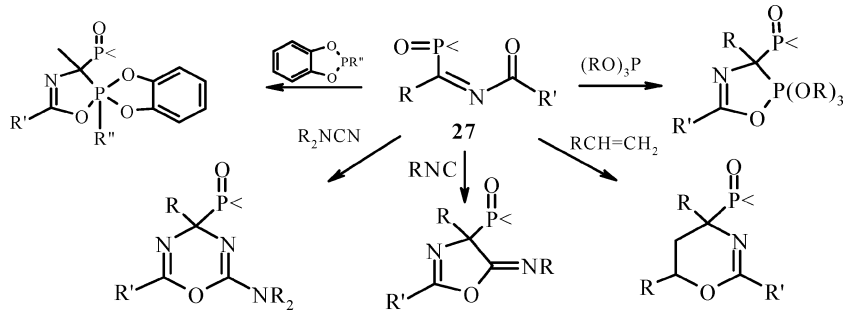
The nature of halogen atom determines the cause of phosphorylation of imidoyl chlorides **19** bearing CF_3 or CCl_3 group (Scheme 6).

Downloaded At: 17:43 27 January 2011

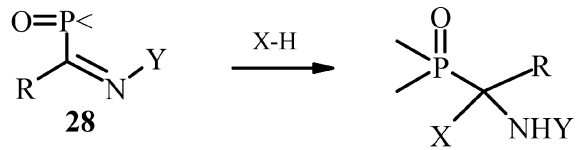
In the first case (X = F) imidoylphosphonates **20** are formed, while chloroderivatives produce C,N-diphosphorylated enamides **21**, able for further functionalization due to high mobility of chlorine atoms. In particular, they react with primary or secondary amines to give ketene aminals **22**, **23**. Interaction with diamines leads to 5-, 6-, and 7-membered heterocyclic compounds **24**. Compounds **22–24** are stable at ambient conditions. At the same time, both acyclic and heterocyclic N-H keteneaminales **23**, **24** on heating undergo unusual C→N transfer of phosphoryl group, accompanied by N → C proton shift. The approach can be used for preparation of functionalized amidines **25**, **26**.

Phosphorylation of imidoyl chlorides bearing EWG group at N atom leads to activated imidoylphosphonates, representing new promising building blocks for preparation of acyclic and heterocyclic aminophosphoryl derivatives. Schemes 7 and 8 below demonstrates some examples of synthetic application of activated C-phosphorylated imines **27**, **28**.

Downloaded At: 17:43 27 January 2011



SCHEME 7

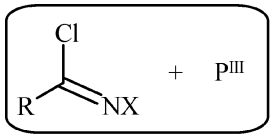


X-H: $R_2P(O)H$, ROH, RSH, RNH_2, enamines, electron rich aromatic and heteroaromatic compounds

SCHEME 8

Reactivity of Imidoylchlorides on Interaction with P^{III} Compounds

In a whole, electron-withdrawing substiuents in imidoylchloride and electron-releasing in P^{III} compound increase reactivity (Scheme 9).



$X = RCO, ArSO_2 > R_2PO > Ar > Alk$
$CF_3CH_2 > MeOCH_2CH_2 > Me$

P^{III}: $Ph_2POEt > PhP(OEt)_2 > (AlkO)_3P > (ArO)_3P$
$(RO)_2PF > (RO)_2PCl$

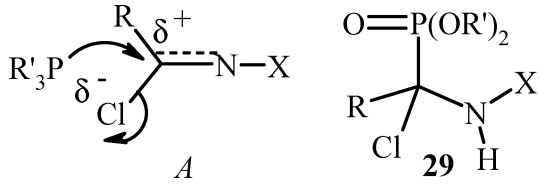
SCHEME 9

At the same time, we have found some peculiarities of substituents effect. Thus, N-benzyl- or N-phenylimidoyl chlorides bearing donor- (*t*-Bu), or acceptor (CF_3) substituent at imine C atom, react with $(EtO)_3P$ with almost the same relative rates.

R	*t*-Bu	Ph	CF_3	R	*t*-Bu	$CHCl_2$	COOEt	CF_3
σ_p	−0.197	−0.01	0.54	σ_p	−0.197	−0.01	0.45	0.54
E_s	−1.54	−2.48	−1.16	E_s	−1.54	−1.54	—	—
k_{rel}	8.5	1	7.6	k_{rel}	15	1	5	15

Downloaded At: 17:43 27 January 2011

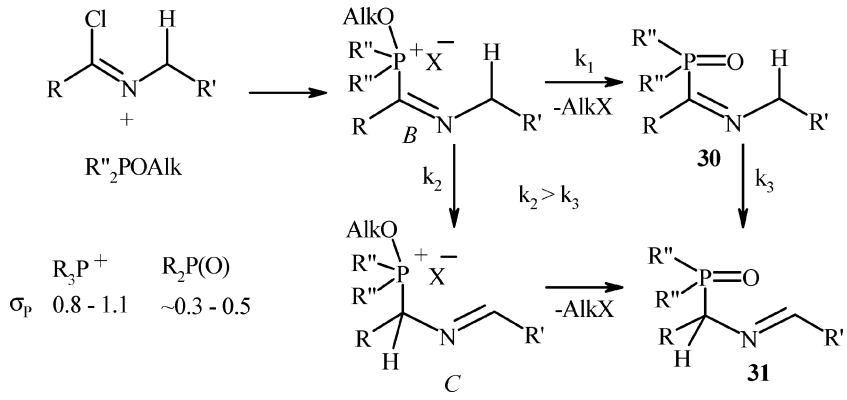
These data indicate on realization of different mechanism of phosphorylation in the series. It is likely that with R = *t*-Bu the dissociation of C—Cl bond in transition state *A* dominates over creation of new P—C bond (Scheme 10). This is favored by steric shielding of imine C atom with *t*-Bu group. With $R = CF_3$, on the contrary, the formation of new P—C bond dominates.



SCHEME 10

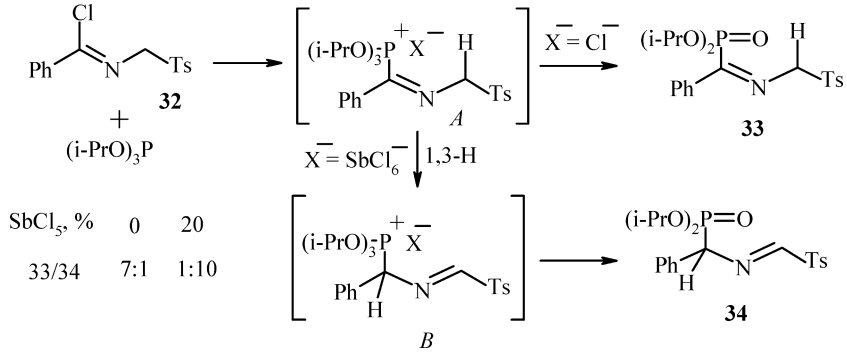
The formation of stable adducts **29**, found for highly electrophilic imidoyl chlorides ($R = CF_3, CCl_3$, $X = ArSO_2, R_2PO$), can be considered as limiting case of the above mechanism.

Elementotropic rearrangements, accompanying phosphorylation of imidoyl chlorides. Dynamic processes are typical for phosphorylated aza-allylic systems whereas effects of phosphorus-containing groups are crucial for their realization. Generation of phosphonium center *B* during phosphorylation of imidoyl chlorides facilitates rearrangements, as electronic parameters of phosphoryl and phosphonium groups essentially differ (Scheme 11).



SCHEME 11

By varying stability of intermediates *B* and rates of competing reactions (k1 and k2 in Scheme 11), it is possible, in principle, to alter the reaction direction. Generation of phosphonium ions is particularly favorable for H-transfer. For example, by changing stability of quasi-phosphonium salt *A* (Scheme 12) one can prepare imidoyl- (**33**) or alkylideneaminophosphoryl compound (**34**).



SCHEME 12

The above approach can be applied for the design and interpretation of prototropic and elementotropic rearrangements in other related systems.

REFERENCES

[1] P. P. Onys'ko, T. V. Kim, E. I Kiseleva, A. D. Sinitsa, and M. Y. Kornilov, *Zh. Obshch. Khim.*, **60,** 1304 (1990).

[2] V. A. Soloshonok and V. P. Kukhar, *Tetrahedron.*, **53,** 8307 (1997).

Downloaded At: 17:43 27 January 2011