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N-CHLORO-N-ALKOXY GEMINAL SYSTEMS IN THE SYNTHESIS OF THE DERIVATIVES OF PHOSPHORIC ACID

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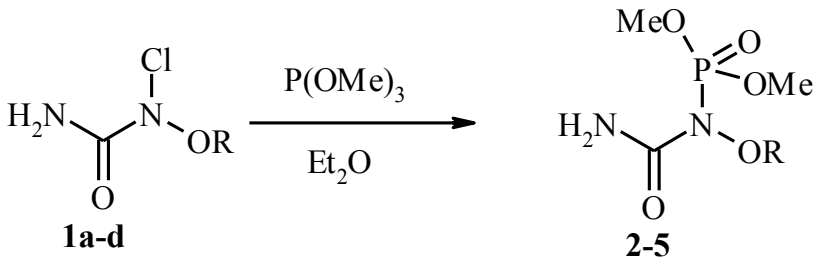
The different organic derivatives of phosphoric acid have biological activity. The different kinds of the substituted ureas use as pharmaceutical materials. The possibility of the nucleophilic substitution of the chlorine atom in *N*-alkoxy-*N*-chloroureas [1,2] and in *N*-alkoxy-*N*-chlorobenzamides [3,4] allow to create the new reaction strategies that give access to such new biological relevant scaffolds. But the interaction of *N*-alkoxy-*N*-chloroureas and *N*-alkoxy-*N*-chlorobenzamides with phosphites remained unstudied.

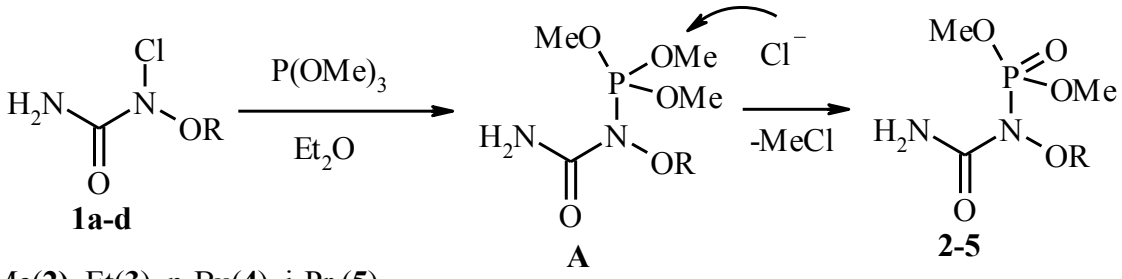
We have studied the interaction of different kinds of *N*-alkoxy-*N*-chloroamides with trimethyl phosphite. The *N*-alkoxy-*N*-chloroureas **1a-d** react with trimethyl phosphite in ether selectively forming the *N*-alkoxy-*N*-(dimethoxyphosphoryl)ureas

2–**5** [5].



R=Me(**1a**,**2)**, Et(**1b**,**3**), n-Bu(**1c**,**4**), i-Pr(**1d**,**5**)

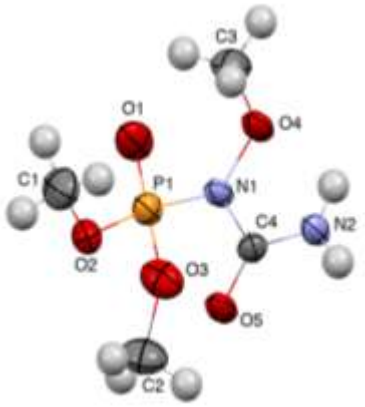
Evidently, the obtained *N*-alkoxy-*N*-(dimethoxyphosphoryl)ureas **2**–**5** are the products of the nucleophilic substitution at the nitrogen. It may be proposed this is another possible mechanism of *N*-alkoxy-*N*-phosphorylureas **2**–**5** formation.



R=Me(**2)**, Et(**3**), n-Bu(**4**), i-Pr (**5**)

At the first stage the labile *N*-alkoxy-*N*-(trimethoxyphosphonium)urea chlorides **A** formed by the nucleophilic substitution at the nitrogen in the *N*-alkoxy-*N*-chloroureas **1a**-**c**. At the second stage the *O*-demethylation of the intermediate **A** by the chloride anion takes place (this is the kind of Arbuzov reaction).

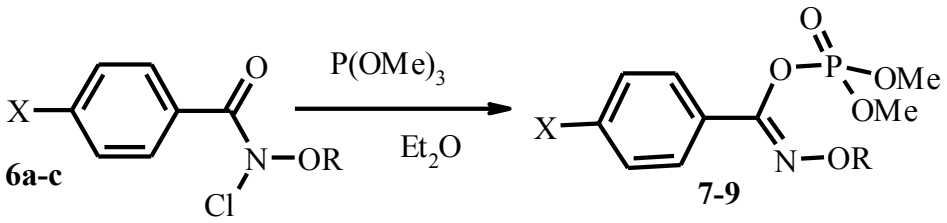
The structure of *N*-alkoxy-*N*-phosphorylureas **2**–**5** has been proved by the ^{1}H, ^{13}C, ^{13}P NMR spectra and mass spectra. Also, the structure of compounds **2,4** has been confirmed by the XRD study [5]. In compounds **2, 4** both nitrogen atoms have planar configuration. The carbamoyl group and the N–O bond lie within the plane.



Molecular structure of *N*-methoxy-*N*-(dimethoxyphosphoryl)urea **2**.

Thus, the possibility of the N–P bond formation by *N*-alkoxy-*N*-chloroureas interaction with *P*-nucleophiles had became clear. Thus ureas **2**–**5** may be regarded as the potential biologically active scaffolds.

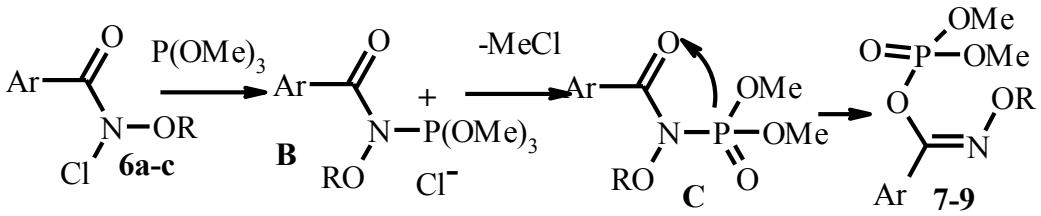
N-Alkoxy-*N*-chlorobenzamides **6a-c** react with trimethyl phosphite in ether leading to the selective formation of compounds **7**–**9**.



X=NO_2, R=Me **(6a,7)**

X=H, R=Me(**6b**,**8**),Et(**6c**,**9**)

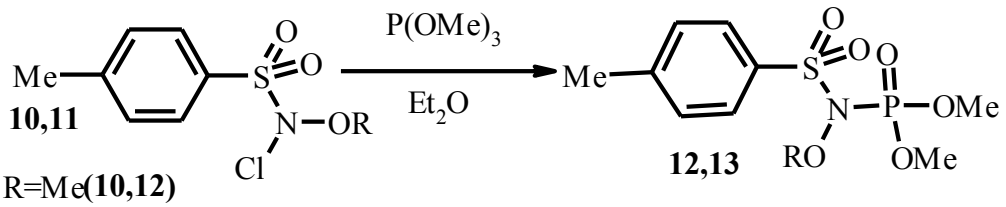
This is supposed to be another possible mechanism of compounds **7**–**9** formation. At the first stage the labile intermediates **B** formed. At the second stage the *O*-demethylation of the intermediates **B** by the chloride anion takes place (this is the kind of Arbuzov reaction). It yields the unstable intermediates **C**. Then the N–O-migration of dimethoxyphosphoryl group occurs yielding compounds **7**–**9**. The driving force behind this migration could be the creation of a robust P–O bond.



The structure of compounds **7**–**9** has been proved by the ^{1}H, ^{13}C, ^{13}P NMR spectra and mass spectra. Also, the structure of compound **7** has been confirmed by XRD study. The structure of compound **7**.

This reaction is a new synthetic pathway to Z-*N*-alkoxy-1-(dimethoxyphosphoryloxy)benzimidates.

N-Alkoxy-*N*-chloroarenesulfonamides **10**,**11** interact with trimethyl phosphite yielding compounds **12**,**13.**



R=Me(**10,12**)
R=Et(**11,13**)

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