N-ALKOXY-*N*-CHLOROUREAS IN THE SYNTHESIS OF THE PHOSPHORUS CONTAINING *N*-ALKOXYUREAS

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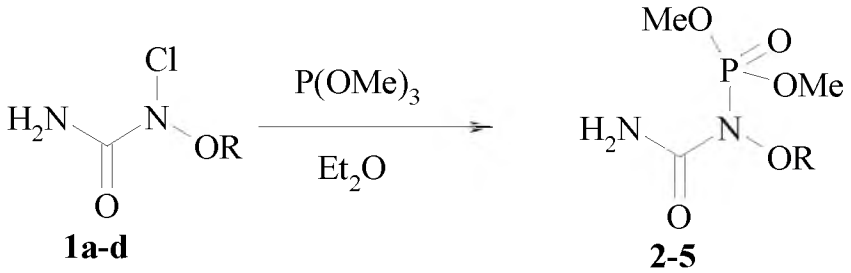
The different kinds of the substituted ureas use as pharmaceutical materials. The chemical properties of *N*-alkoxy-*N*-chloroureas allow to create the new reaction strategies that give access to such new biological relevant scaffolds. But the nucleophilic substitution of the chlorine atom in *N*-alkoxy-*N*-chloroureasby*P*-nucleophiles remained unstudied.

As a rule the common *N*-phosphorylureas are obtained as the result of the amines interaction with dialkylisocianatidophospate, e.g. [1,2]. But the interaction of *N*-alkoxy-*N*-chloroureas with trimethylphosphiteor triphenylphosphine had never been reported before. The *N*-alkoxy-*N*-chloroureas interaction with *P*-nucleophiles had not been reported as well. The synthesis of the *N*-phosphorylureas from other *N*-chloroureas is either unknown.

We have studied the interaction *N*-alkoxy-*N*-chloroureas **1a-d** with trimethyl phosphite in ether. The*N*-alkoxy-*N*-chloroureas **1a-d** react with trimethy lphosphite selectively forming the *N*-alkoxy-*N*-phosphoryl ureas **2–5** [3].



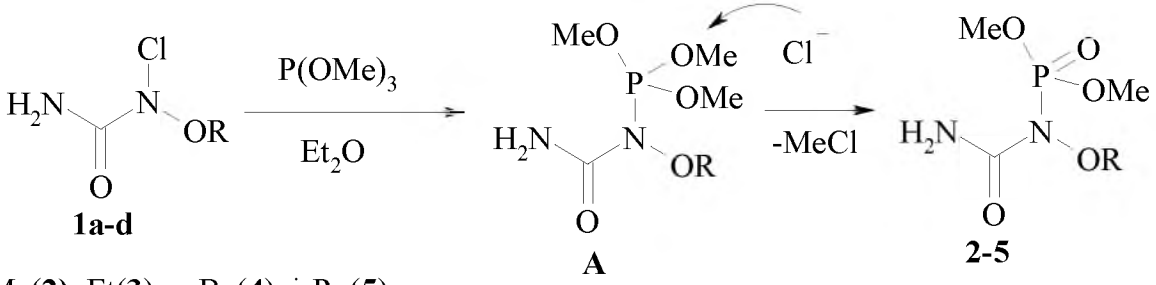
1a-d **2-5**

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

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, structure of compounds **2,4** has been confirmed by the XRD study [3]. In compounds **2,4** both nitrogen atoms have the planar configuration. The carbamoyl group and the N–O bond lie within the plane. Thus, it has been found that N-alkoxy-N-(dimethoxyphosphoryl)ureas have a number of structural features different from those of anomeric ureas.

The obtained N-alkoxy-N-(dimethoxyphosphoryl)ureas **2–5** are the products of the nucleophilic substitution at the nitrogen atom. This reaction is new synthetic route to the N-phosphorylureas.

It may be proposed this is another possible mechanism of N-alkoxy-N-phosphorylureas **2–5** formation.

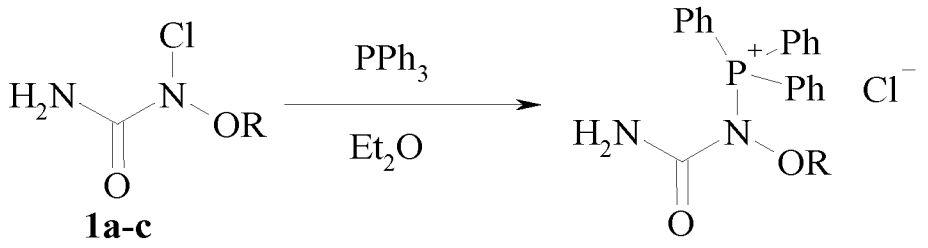


1a-d **A** **2-5**

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 **2a-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). It yields N-alkoxy-N-(dimetoxyphosphoryl)ureas **2–5**.

We had found that N-alkoxy-N-chloroureas1a–c interact with triphenylphosphine selectively yielding the compounds **6–8**.



1a-c

R=Me(**6**), Et(**7**), n-Bu(**8**)

6-8

The structure of *N*-alkoxy-*N*-(triphenylposphonium)ureas chlorides **6–8** has been haracterized by the ^{1}H, $^{13}C$and ^{13}P NMR spectra. These compounds easily decompose by the action of the oisture f air and in the protonic solvents.

Thus, the possibility of the N–P bond formation by *N*-alkoxy-*N*-chloroureas interaction with *P*-nucleophiles become clear.

Compounds **2–8** are the unknown kinds of *N*-alkoxyureas and may be regarded as the potential biologically active scaffolds.

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3. Shtamburg V.G., Klots E.A., Shtamburg V.V., Anishchenko A.A., Shishkina S.V., MazepaA.V. Nucleophilic substitution at nitrogen atom. *N*-Alkoxy-*N*-(dimethoxyphosphoryl)ureas, synthesis and structure.// J. Mol. Struct. – 2023. – Vol. 1277,N 5. – 134865.