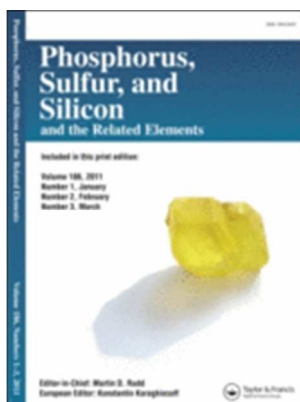




THE SYNTHESIS AND POTENTIAL USE OF CYCLIC PHOSPHINIC ACID DERIVATIVES

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Keywords:	Phosphinic acid derivatives, P-heterocycles, microwave, ring expansion, imides

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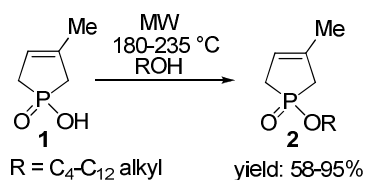
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Abstract Direct derivatizations, such as esterification and amidation of 1-hydroxy-3-methyl-3-phospholene oxide and subsequent transformations including ring enlargement of the phosphinates, and phosphorylation of the phosphinic amides so obtained are described.

Keywords Phosphinic acid derivatives; *P*-heterocycles; microwave; ring expansion; imides.

The five- and six-membered *P*-heterocycles represent a prominent class of heterocyclic compounds with different *P*-functionalities, such as the phosphine oxide, phosphinic ester, or the phosphinic amide function. It was previously thought that phosphinic acids do not undergo direct esterification and amidation. For this reason, cyclic phosphinates and phosphinic amides were generally synthesized by other methods.¹⁻³ We have found that phosphinic acids can be esterified directly by simple alcohols under MW conditions (Scheme 1).⁴⁻⁶



Scheme 1

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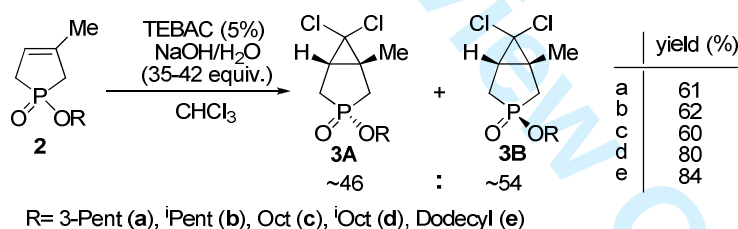
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The direct esterification of phosphinic acids was also accomplished using thiols,⁷ and the derivatization was extended to amidations.⁸ The synthesis of thiophosphinates and phosphinic amides was not too efficient due to the unfavourable energetics of these derivatizations, as suggested by quantum chemical calculations.⁹ The 1-alkoxy- and 1-amino-3-phosholene oxides prepared by MW-assisted direct derivatization or in other way were utilized in the synthesis of other *P*-heterocycles.

Previously, only the dichlorocarbene addition to 3-methyl-3-phosholene 1-oxide (**2**) with simple alkoxy substituents was studied that led to the corresponding phosphabicyclo[3.1.0]hexane 1-oxides (**3**) in variable yields.^{10,11} Since mostly longer carbon chain esters were made available by the MW-assisted direct esterification, these model compounds (**2**) were utilized in the dichlorocarbene addition reactions. The C₅, C₈ and C₁₂ *P*-alkoxy groups enhanced the reactivity of the double-bond in reaction with the electrophilic dichlorocarbene.¹² Compound **3** was formed as a *ca.* 1:1 mixture of two isomers (Scheme 2).

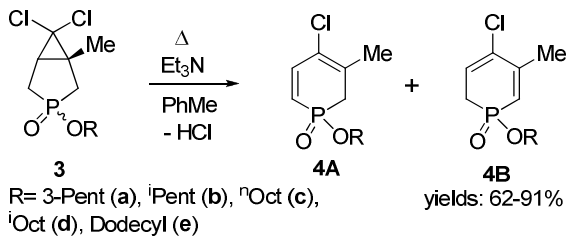


Scheme 2

The relative energetics of the two diastereomers (**3A** and **3B**) were evaluated by B3LYP/6-31G(d,p) calculations. It was found, that diastereomer **B** containing the dichlorocyclopropane ring and the oxygen of the P=O moiety on the same side is more stable than the other isomer. This was in agreement with our earlier findings.¹³

In the next step, the 2-phosphabicyclo[3.1.0]hexane oxides (**3**) were subjected to thermal ring expansion to give 1,2-dihydrophosphinine oxides **4** as a 3:1 mixture of two isomers (**A** and **B**)

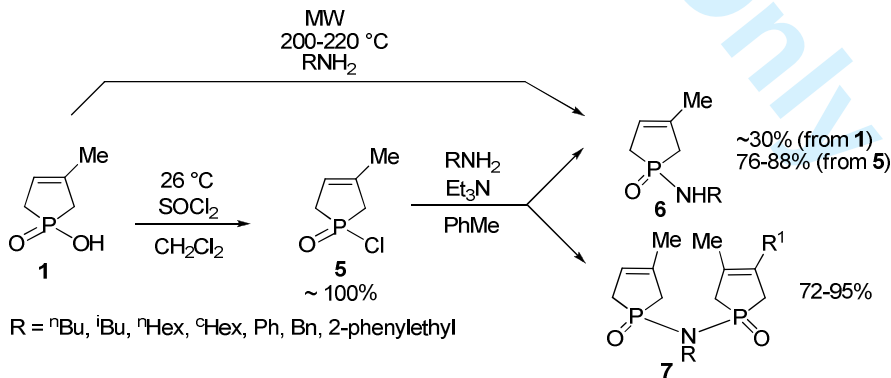
(Scheme 3). B3LYP/6-31G(d,p) calculations showed that in all cases, isomer **A** is more stable than isomer **B**.¹²



Scheme 3

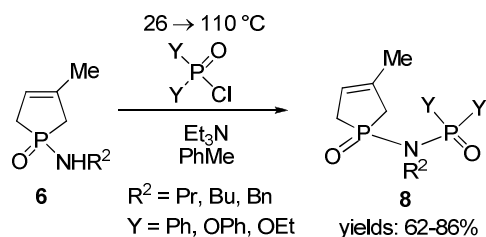
1,2-Dihydrophosphinine oxides are versatile intermediates that can be utilized in the synthesis of other phosphinine derivatives.^{14,15}

1-Alkylamino-3-phospholene oxide (**6**) can be obtained by the MW-assisted direct amidation of 1-hydroxy-3-phospholene 1-oxide (**1**), however, due to the low efficiency, a better choice for the preparation of these compounds is the reaction of the corresponding phosphinic chloride (**5**) with amines. It was found that the reaction with primary amines afforded a mixture of the corresponding 1-amino-3-phospholene 1-oxide (**6**) and its *N*-phosphinoyl derivative (**7**) (Scheme 4). Depending on the molar ratio of the reactants and on the order of mixing, the product composition could be influenced and either the *mono*-, or the *bis*-product could be obtained almost exclusively.¹⁶



Scheme 4

1-Alkylamino-3-phospholene oxides (**6**) could be transformed into different bis(phosphinoyl)amines/phosphinoyl-phosphorylamines (**8**) via phosphorylation reactions (Scheme 5).



Scheme 5

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