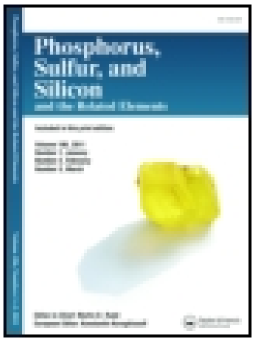

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Isomerization and application of phospholene oxides

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ABSTRACT
In this research, an investigation of the isomerization and the applications of 3-phospholene oxides were elaborated. The isomerization of 3-phospholene oxides to 2-phospholene oxides was investigated under thermal condition. The application of bases and acids was also tested in this reaction. Moreover, the isomerization was also elaborated via the formation of halophosphonium salt intermediates. The 3-phospholene oxides were deoxygenated and transformed to the corresponding palladium complexes.

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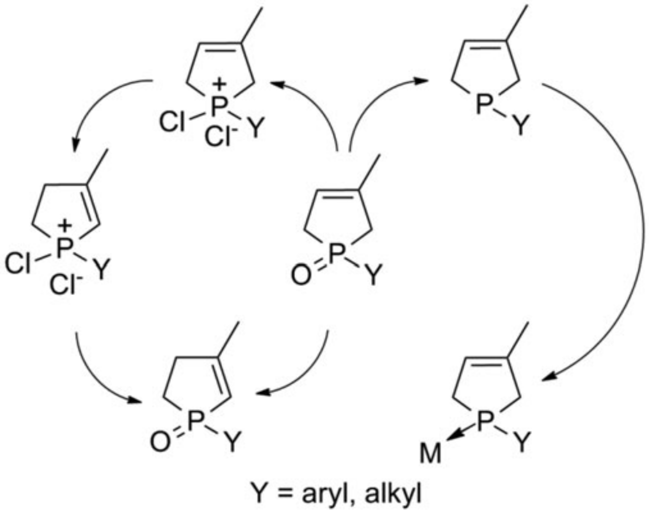
KEYWORDS
3-phospholene oxide; 2-phospholene oxide; halophosphonium salt; isomerization; palladium complex

GRAPHICAL ABSTRACT



Introduction

Phospholene oxides form an important class, as they are valuable starting materials for ligands.[1] The preparation of the 3-phospholene core is well-established,[2–7] but the 2-phospholene derivatives can only be prepared by a few methods,[2, 8] despite the fact that the 2-phospholene oxides (**2**) are considered as the main starting materials for phospha-sugars having antitumor activity.[9–11] In our research group, 2-phospholene oxides (**2**) were formed as side products under thermal or MW conditions during the alkylating esterification of cyclic phosphinic acids or the acidic hydrolysis of phosphinic acid esters.[12–14] The formation of the 2-phospholene derivatives was also observed in the preparation of phospholene borane complex via the chlorophosphonium salts (**3** and **4**).[15] These observations prompted us to investigate in detail the isomerization of the 3-phospholene oxides (**1**) to the corresponding 2-phospholene derivatives (**2**).

Platinum complexes incorporating 3-phospholene ligands have already been synthesized and applied in hydroformylation.[16–18] However, the preparation of the corresponding palladium complexes (**6**) is still an unexplored field.

Results and discussion

Investigation of isomerization of 1-substituted-3-methyl-3-phospholene oxides (1) to 2-phospholene oxides (2)

As the first step of this study, we investigated whether the isomerization occurs at elevated temperature without any reagent. It was concluded, that the isomerization of the 3-phospholene oxides (**1**) did not occur under reflux conditions in toluene, dimethylformamide or dimethyl sulfoxide.

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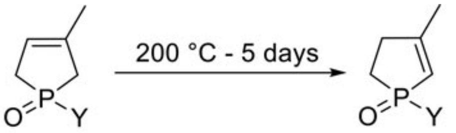
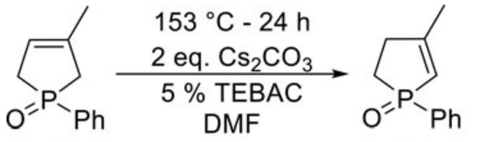


1 **2**

Y	Ph (**a**)	2-Me-C_6H_4 (**b**)	4-Me-C_6H_4 (**c**)	1-Napht (**d**)	Et (**e**)	Pr (**f**)	^{n}Bu (**g**)	^{i}Bu (**h**)	^{i}Pent (**i**)
Yield (%)*	40	69	92	92	40	71	64	32	44
Ratio of **1** (%)	29	27	31	18	42	47	50	39	47
Ratio of **2** (%)	71	73	69	82	58	53	50	61	53

* Yield of the product mixture

Scheme 1. Investigation of isomerization without using solvent and reagent.



1a **2a**

Isomerization : 84 %
Yield : 90 %

Scheme 2. Investigation of isomerization in the presence of base.

However, when the 3-phospholene oxides (**1**) were stirred at 200 °C without any solvent for five days, the isomerization ratio was up to 82% in every case (Scheme 1).

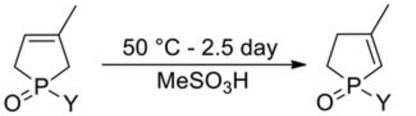
The next step was the investigation of the effects of bases on the reaction. During the optimization reactions, several organic or inorganic bases were tested. It was concluded, that carbonates, such as K_2CO_3 and Cs_2CO_3 are sufficient bases for the isomerization. The highest isomerization ratio (84%) was reached by refluxing the phenyl-3-methyl-3-phospholene oxide (**1a**) in dimethyl-formamide using 2 equivalent of Cs_2CO_3 in the presence of TEBAC (triethyl-benzyl-ammonium chloride). It was also concluded, that the isomerization ratio could not be increased by changing the reaction conditions (Scheme 2).

The isomerization was then investigated in the presence of acids. The 1-phenyl-3-phospholene-oxide (**1a**) was refluxed in different solvents in the presence of several organic or inorganic acids, but no isomerization was observed. Then, the isomerization of 3-phospholene oxides (**1**) was accomplished using methanesulfonic acid as solvent and reagent. The optimal conditions were 50 °C and 2.5 d, and the isomerization was almost complete in every case (Scheme 3).

In our previous study, the isomerization of cyclic chloro-3-phospholenium salts (**3**) to the corresponding chloro-2-phospholenium species (**4**) was identified as a side reaction.[15] Thus, the isomerization of 3-phospholene oxides (**1**) was also investigated via the formation of chloro-phospholenium salts (**3** and **4**). The 1-substituted-3-phospholene oxides (**1**) were converted to chloro-3-phospholenium salts (**3**) using oxalyl chloride. The cyclic chlorophosphonium salts (**3**) were stirred at 50 °C in sealed tube to promote the formation of the thermodinamically more stable chloro-2-phospholenium salts (**4**). The reaction mixture was quenched with water to give the corresponding 2-phospholene oxides (**1**) (Scheme 4).

Palladium complex formation of cyclic phosphines

In our research group, the deoxygenation and the transition metal complex formation of cyclic phosphines have been investigated for decades.[1] The platinum complexes of 3-phospholenes were also prepared previously, and they were applied as catalysts in the hydroformylation of styrene.[16–18] In the literature, the palladium complexes of 3-phospholenes (**6**) were unknown, so our aim was the preparation of these compounds (**6**). The deoxygention of phospholene oxides (**1**) was accomplished according to the method developed by us.[17,18] The 3-phosphelenes (**5**) thus prepared were reacted with bis(benzonitrile)palladium(II) to give the corresponding palladium complexes (**6**) (Scheme 5).

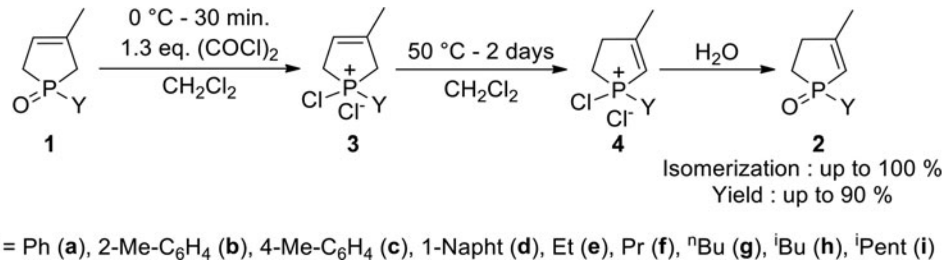


1 **2**

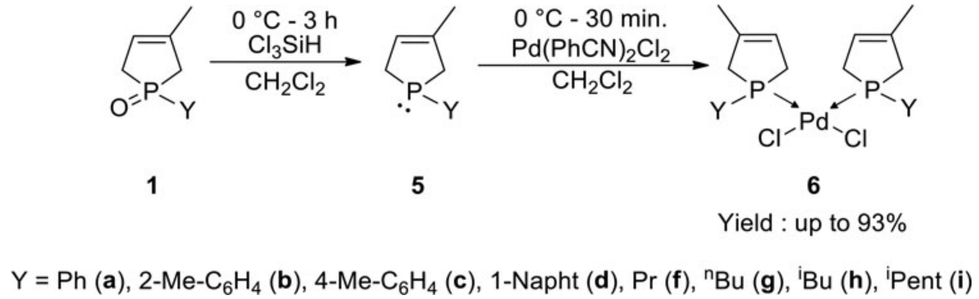
Isomerization : up to 100 %
Yield : up to 96 %

Y = Ph (**a**), 2-Me-C_6H_4 (**b**), 4-Me-C_6H_4 (**c**), 1-Napht (**d**), Et (**e**), Pr (**f**), ^{n}Bu (**g**), ^{i}Bu (**h**), ^{i}Pent (**i**)

Scheme 3. Investigation of isomerization using methanesulfonic acid.



Scheme 4. Investigation of isomerization via the formation of chloro phosphonium salts.



Scheme 5. Preparation of palladium complexes from racemic phospholene oxides.

Conclusions

In summary, the isomerization of 3-phospholene oxides (**1**) to 2-phospholene oxides (**2**) was accomplished. Several methods were evaluated, among which two afforded the 2-phospholene oxides (**2**) in good or excellent yields. Palladium complexes incorporating 3-phospholene (**6**) ligands were also synthesized.

References

[1] Kollár, L.; Keglevich, G. P-heterocycles as Ligands in Homogeneous Catalytic Reactions. *Chem. Rev.* 2010, *110*, 4257–4302.

[2] Quin, L. D.; . Barket, T. P. Structure of Isoprene-Phenylphosphonous Dihalide Cyclo-adducts. *Chem. Commun.* 1967, *18*, 914–915. DOI: 10.1039/C19670000914.

[3] Hunger, K.; Hasserodt, U.; Korte, F. Phospholin-derivate—II. *Tetrahedron* 1964, *20*, 1593–1604. DOI: 10.1016/S0040-4020(01)99156-2.

[4] Pav, O.; Zbornikova, E.; Budensinsky, M.; Rosenberg, I. A New Class of Phosphanucleosides Containing a 3-hydroxy-1-hydroxy-methylphospholane 1-oxide Ring. *Tetrahedron* 2013, *69*, 9120–9129. DOI: 10.1016/j.tet.2013.08.021.

[5] Montchamp, J.-L.; Tian, F.; Frost, J. W. Double Arbuzov Reaction of in Situ Generated Bis(trimethylsiloxy)phosphine with Dielectrophiles: Methodology for the Synthesis of Cyclic Phosphinic Acids. *J. Org. Chem.* 1995, *60*, 6076–6681. DOI: 10.1021/jo00124a018.

[6] Bujard, M.; Gouverneur, V.; Mioskowski, C. A Highly Efficient and Practical Synthesis of Cyclic Phosphinates Using Ring-Closing Metathesis. *J. Org. Chem.* 1999, *64*, 2119–2123.

[7] Briot, A.; Bujard, M.; Gouverneur, V.; Nolan, S. P.; Mioskowski, C. Improvement in Olefin Metathesis Using a New Generation of Ruthenium Catalyst Bearing an Imidazolylidene Ligand: synthesis of Heterocycles. *Org. Lett.* 2000, *2*, 1517–1519.

[8] Quin, L. D.; Gratz, J. P.; Barket, T. P. Structure of Diene-phosphonous Dihalide Addition Products and of Derived Phospholenes and Phospholene Oxides. *J. Org. Chem.* 1968, *33*, 1034–1041.

[9] Fujie, M.; Nakamura, S.; Asai, K.; Niimi, T.; Yamashita, J.; Kiyofuji, K.; Shibata, K.; Suzuki, M.; Aoshima, R.; Urano, T.; et al. A Novel Phospha Sugar Analogue: Synthesis and Evaluation of 2,3-dibromo-3-methyl-1-phenylphospholane 1-oxide as a New Class of Potential Anti-Proliferative Materials for Leukemia Cells. *Heterocycl. Commun.* 2009, 15, 273–278.

[10] Yamashita, M.; Iida, A.; Mizuno, H.; Miyamoto, Y.; Morishita, T.; Sata, N.; Kiguchi, K.; Yabui, A.; Oshikawa, T. Reactions of 2-phospholene 1-oxides with Bromine in Some Media: Facile Preparation of Bromohydrin Derivatives of 2-Phospholenes. *Heteroat. Chem.* 1993, *4*, 553–557. DOI: 10.1002/hc.520040606.

[11] Yamashita, M.; Reddy, V. K.; Rao, L. N.; Haritha, B.; Maeda, M.; Suzuki, K.; Totsuka, H.; Takahashi, M.; Oshikawa, T. An Efficient Approach towards the Stereospecific Synthesis of Epoxides from Phospholene Oxides. *Tetrahedron Lett.* 2003, *44*, 2339–2341. DOI: 10.1016/S0040-4039(03)00255-7.

[12] Bálint, E.; Jablonkai, E.; Bálint, M.; Keglevich, G. Alkylating Esterification of 1-hydroxy-3-phospholene Oxides Under Solventless MW Conditions. *Heteroatom Chem.* 2010, 21, 211–214.

[13] Kiss, N. Z.; Ludányi, K.; Drahos, L.; Keglevich, G. Novel Synthesis of Phosphinates by the Microwave-Assisted Esterification of Phosphinic Acids. *Synt. Commun.* 2009, *39*, 2392–2404. DOI: 10.1080/00397910802654880.

[14] Keglevich, G.; Rádai, Z.; Harsági, N.; Szigetvári, Á.; Kiss, N. Z. A Study on the Acidic Hydrolysis of Cyclic Phosphinates: 1-Alkoxy-3-phospholene 1-oxides, 1-ethoxy-3-methylphospholane 1-oxide, and 1-ethoxy-3-methyl-1,2,3,4,5,6-hexahydrophosphinine 1-Oxide. *Heteroatom Chem.* 2017, *28*, e21394. DOI: 10.1002/hc.21394.

[15] Herbay, R.; Bagi, P.; Mucsi, Z.; Mátravölgyi, B.; Drahos, L.; Fogassy, E.; Keglevich, G. A Novel Preparation of Chlorophospholenium Chlorides and Their Application in the Synthesis of Phospholene Boranes. *Tetrahedron Lett.* 2017, *58*, 458–461. DOI: 10.1016/j.tetlet.2016.12.059.

[16] Keglevich, G.; Kollár, L. Platinum Complexes of Five- and Six-Membered P-Heterocycles as Potential Catalysts. *Lett. Org. Chem.* 2010, *7*, 612–620. DOI: 10.2174/157017810793811713.

[17] Bagi, P.; Kovács, T.; Szilvási, T.; Pongrácz, P.; Kollár, L.; Drahos, L.; Fogassy, E.; Keglevich, G. Platinum(II) complexes Incorporating Racemic and Optically Active 1-alkyl-3-phospholene P-ligands: Synthesis, Stereostructure, NMR Properties and Catalytic Activity. *J. Organomet. Chem.* 2014, *751*, 306–313. DOI: 10.1016/j.jorganchem.2013.03.045.

[18] Bagi, P.; Szilvási, T.; Pongrácz, P.; Kollár, L.; Drahos, L.; Keglevich, G. Platinum(II) Complexes Incorporating Racemic and Optically Active 1-Aryl-3- phospholene P-Ligands as Potential Catalysts in Hydroformylation. *Curr. Org. Chem.* 2014, *18*, 1529–1538. DOI: 10.2174/1385272819666140609224751.