Budapesti Műszaki és Gazdaságtudományi Egyetem

Synthesis and structure elucidation of tetra- and hexahydrophosphinine oxides P-functionalized at position three

Ph.D. thesis

by Sipos Melinda

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Publications on the subject of the thesis

[1] Keglevich, Gy., **Sipos**, **M**., Imre, T., Ludányi, K., Szieberth, D., Tőke, L., *Tetrahedron Letters* **2002**, *43*, 8515.

[2] Keglevich, Gy., **Sipos**, **M.**, Szieberth, D., Nyulászi, L., Imre, T., Ludányi, K., Tőke, L., *Tetrahedron* **2004**, *60*, 6619.

[3] Keglevich, Gy., **Sipos**, **M**., Szieberth, D., Petőcz, Gy., Kollár, L., *Journal of Organometallic Chemistry* **2004**, *689*, 3158.

[4] Keglevich, Gy., **Sipos**, **M.**, Körtvélyesi, T., Imre, T., Tőke, L., *Tetrahedron Letters* **2005**, *46*, 1655.

[5] Körtvélyesi, T., **Sipos**, **M**., Keglevich, Gy., *Heteroatom Chem.* **2005**, *16*, 520.

[6] Keglevich, Gy., **Sipos**, **M**., Ujj, V., Körvélyesi, T., *Lett. In Org. Chem.* **2005**, *2*, 398.

[7] Keglevich, Gy., **Sipos**, **M**., Takács, D., Greiner, I., *Heteroatom Chem*. **2007**, *18*, 227.

[8] Czugler, M., Fábián, L., Körtvélyesi, T., **Sipos, M**., Keglevich, Gy., **2007**, in press.

[9] **Sipos**, **M**., Körtvélyesi, T., Ujj, V., Ludányi, K., Vékey, K., Keglevich, Gy., *Heteroatom Chem*. **2007**, accepted for publication.

[10] Keglevich, Gy., Kerényi, A., **Sipos**, **M**., Ujj, V., Dudás, E., Hohmann, E., Makó, A., Csontos, I., Novák, T., Bakó, P., Greiner, I., *Periodica Polytechnica* **2007**, in press.

[11] Keglevich, Gy., Kerényi, A., **Sipos**, **M**., Balassa, A., Mayer, B., Körtvélyesi, T., *Phosphorus Sulfur and Silicon* **2007**, accepted for publication.

Other publications

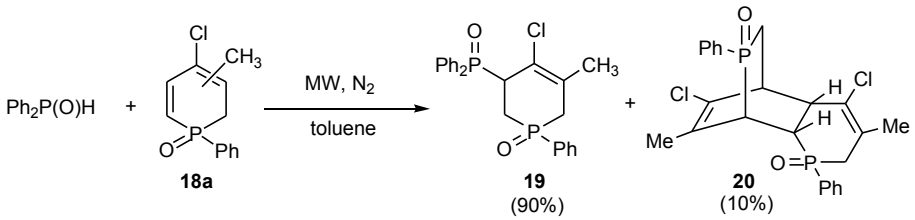
- Keglevich, Gy., Forintos, H., **Sipos**, **M.**, Dobó, A., Ludányi, K., Vékey, K., Tungler, A., Tőke, L., *Heteroatom Chem.* **2001**, *6*, 528.
- Keglevich, Gy., **Sipos**, **M**., Lengyel, D., Forintos, H., Körtvélyesi, T., Imre, T., Tőke, L., *Synthetic Communications* **2004**, *34*, 4159.
- Keglevich, Gy., Dudás, E., **Sipos**, **M.**, Lengyel, D., Ludányi, K., *Synthesis* **2006**, *8*, 1365.

Our aim was to introduce a phosphorus functional group into six-membered P-heterocycles at position three and the modification of the so obtained heterocycles. The most suitable way to introduce a P-funtional group was the phospha-*Michael* addition reaction.

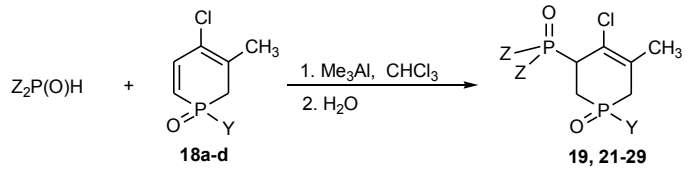
We examined the phospha-*Michael* addition with simple compounds to uncover the most suitable conditions for the addition of different >P(O)H species onto electron deficient double bond. The addition of diethylphosphite to methylvinylketone was chosen to be the model reaction. We found that in the presence of sodium alcoholate or under phase transfer condition or in the presence of DBU 3-oxo-butylphosphonate as major product formed, although the later cases other minor products were also formed. In the presence of trimethyl aluminum α–hydroxy-phosphonate was formed as the major product. Upon microwave irradiation only the more reactive reagent, the diphenylphosphine oxide was able to do the addition onto methylvinylketone.

The phospha-*Michael* addition of cyclic P-compounds such as the H-phosphinic acid or the H-phosphonic acid onto methylvinylketone or cyclohex-2-enone could be performed in the presence of DBU or under microwave irradiation.

We found that the addition of diphenylposphine oxide onto the electron defficient double bond of the 1,2-dihydrophosphinine oxide (**18a**) can not be performed under the same conditions sucessfully applied in case of the additions onto methylvinylketone. The reaction could be performed, as only under microwave irradiation in case of the synthesis of compound **19**.



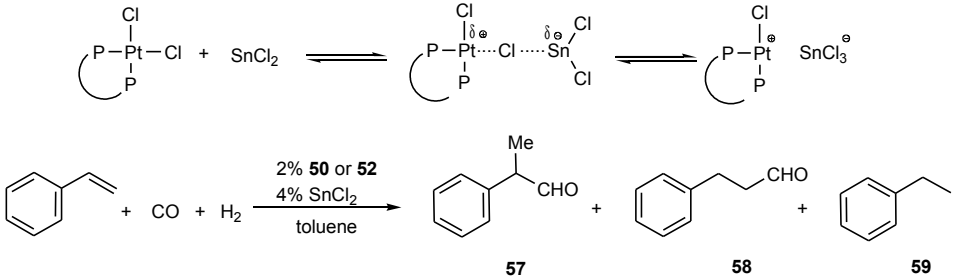
We sucessfully performed the addition of dialkylphosphite, diphenylphosphine oxide, ethyl-phenyl-*H*-phosphinate, as well as dibenzo-oxaphosphorine oxide (**8**) onto the double bond of 1-substituted dihydrophosphinine-oxides (**18a-d**) in the presence of trimethyl aluminum. Interestingly, all additions proceeded in a diastereoselective manner.



Y= Ph, *p*MePh, Et, EtO

Z= Ph, MeO, EtO, BzO

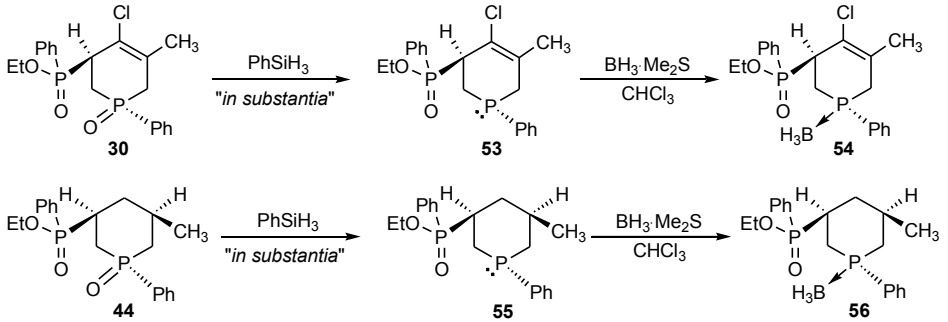
The synthesized **50** and **52** *cis*-chelat complexes were tested as catalysts in the hydroformilation reaction of styrene. To accelerate the hydroformilation reaction **50** and **52** complexes were *in situ* transformed into their trichloro-stannate derivatives.



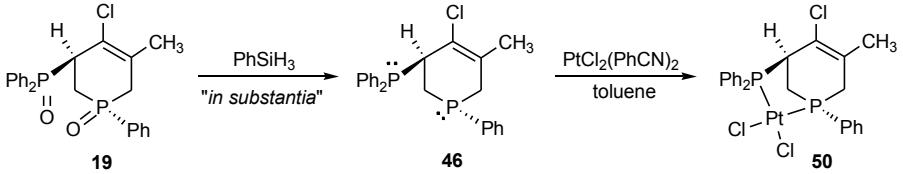
In the presence of our catalysts (**50** and **52**) the hydroformilation reaction proceeded, in both cases, with high regioselectivity. In the presence of the unsaturated-ringed catalyst **50** the selectivity for the branched product was higher (85%) then in the presence of **52** saturated analogue (70%). Interestingly, the regioselectivity for the branched aldehyde was unexpectedly high, although platinum complexes usually show selectivity for the linear product.

We published 11 publications on the subject of my thesis in peer-viewed international journals [1-11].

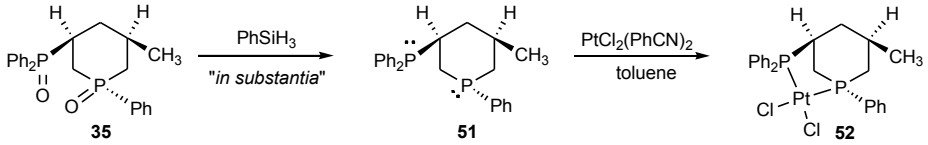
The products (**53** and **55**) of the deoxigenation of the isomeric mixtures of 3-ethyl-phenylphosphinato tetra- és hexahydrophosphinin oxides (**30** és **44**) with phenylsilane were stabilized as borane complexes (**54** and **56**). Compounds **54** and **56** proved to be monoborane complexes.

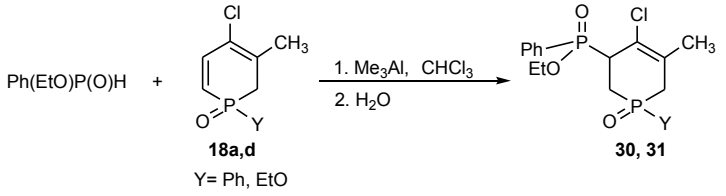


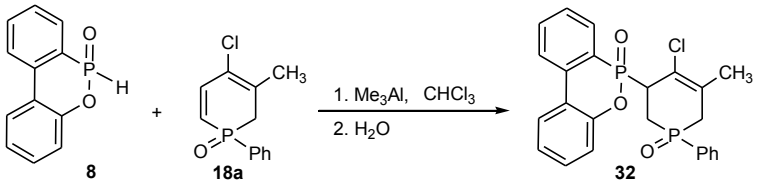
The reaction of diphosphine (**46**) with dichlorodibenzonitrilo platinum(II) led to the *cis*-chelate complex (**50**).



The reduction of diphenylphosphinoxido-hexahydrophosphinin oxide (**35**) led to the corresponding diphosphine (**51**). The complexation of **51** with dichlorodibenzonitrilo platinum(II) resulted in, as before, the *cis*-chelate complex (**52**).

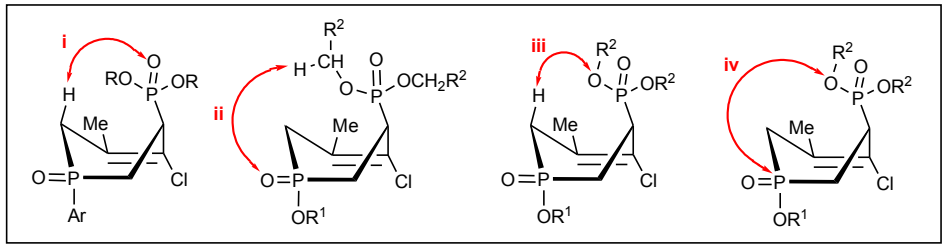




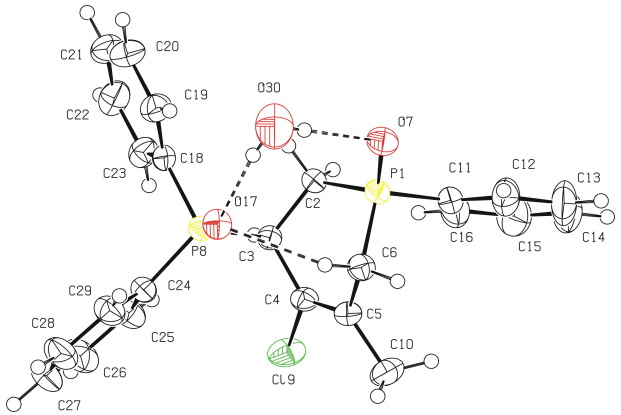


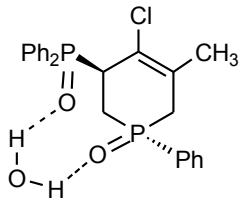
Quantum chemical calculations showed that the tetrahydrophosphinine oxides substituted at position 3 (**19**, **21-29**) exist in a *twist-boat* conformation.

Calculations also suggested a couple of intramolecular interactions had not been reported before. These interactions can be classified into four main groups. These H-bridge interactions are (i) between the oxygen of the exocyclic P=O group and one of the hydrogen of one of the methylene group of the heterocyclic ring in case of the P-Aryl substituted compounds (**19**, **21** and **22**), (ii) between the oxygen of the endocyclic P=O group and one of the hydrogen of one of the methylene group of an exocyclic alkoxy group in case of the P-alkoxy substituted compounds (**27** and **28**), (iii) between the oxygen of the exocyclic P-alkoxy group and one of the hydrogen of one of the methylene group of the heterocyclic ring, and in case of the **27** and **28**, a further interaction can be found between the phosphorus atom of the endocyclic P^1=O and the oxygen of the exocyclic POR group (iv).



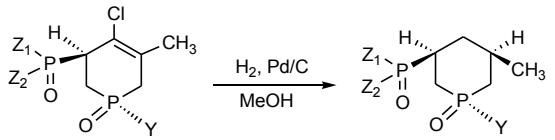
The single crystal X-ray analysis of 3-diphenylphosphinoxido-1-phenyl-tetrahydrophosphonin oxide (**19**) showed that (i) compound **19** crystallized as a monohydrate, (ii) the conformation of the molecule *twist-boat/cis*$_1$, the oxygen of the P^1=O and the exocyclic P(O)Ph$_2$ group are in *cis* position, in the same side of the ring, and (iii) the intramolecular interation between the oxygen of the exocyclic P=O and the hydrogen of the C$_6$ methylene group.

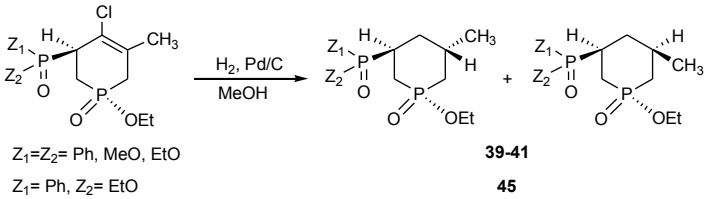




The catalytic hydrogenation of the 3-substituted 1,2,3,6-tetrahydrophosphinine oxides on palladium led to 1,2,3,4,5,6-hexahydrophosphinine oxides (**35-41**, **44** and **45**). In case of the tetrahydrophosphinine oxides having phenyl substituents on the endocyclic

phosphorus, the reduction proceeded in a diastereoselective manner, resulted in the formation of a single isomer of the products (except in case of the compound **44,** but it is the consequence of the starting material).





Quantum chemical calculations suggested that 3-P-functionalized hexahydrofosphinine oxides substituted with alkoxy groups at both phosphorus atoms exist in a *chair* conformation.

The deoxygenation of diphenylphosphinoxido-tetrahydrophosphinine oxide (**19**) with trichlorosilane or phenylsilane led to diphosphine (**46**), which was stabilized with borane (**47**), and therefore, could be stored for a longer period. From the borane complex the diphosphine (**46**) can be recovered by diethylamine.