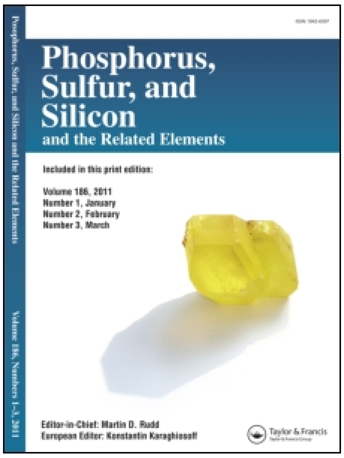

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DIASTEREOSELECTIVE REARRANGEMENTS AND EPIMERIZATION OF ORGANOPHOSPHORUS COMPOUNDS

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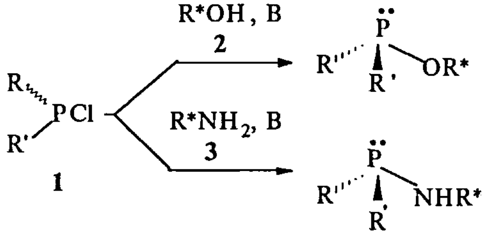
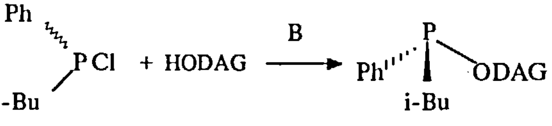
Abstract New examples of asymmetric syntheses of organophosphorus compounds are described.

The presented work concerns the asymmetric synthesis of organophosphorus compounds proceeding under condition of kinetic or thermodynamic control and the application of obtained compounds for the organic synthesis. [1]
We found, that the stereoselectivity of the reaction of dialkyl- and diarylchlorophosphines **1** with chiral secondary alcohols **2** or with chiral primary amines **3** depends strongly on the structure of starting reagents and on the experimental conditions. Next factors increase the stereoselectivity:
a- starting reagents **1-3** are sterically hindered: R(R')P = t-Bu(i-Bu)P, t-Bu(Ph)P, i-Bu(Ph)P, i-Pr(Ph)P; R*=L-menthyl, 1:2;5:6-diisopropylidene-D-hlucofuranose, CH(Me)Ph, CH(R)CO$_2$Me, CH(Me)CH$_2$NEt$_2$; CH(Me)CH$_2$CO$_2$Et; *b*- base B is strong, sterically hindered tertiary amine, such as DABCO or triisopropylamine; *c*- lowering of the temperature; *d*- excess of the chlorophosphine.

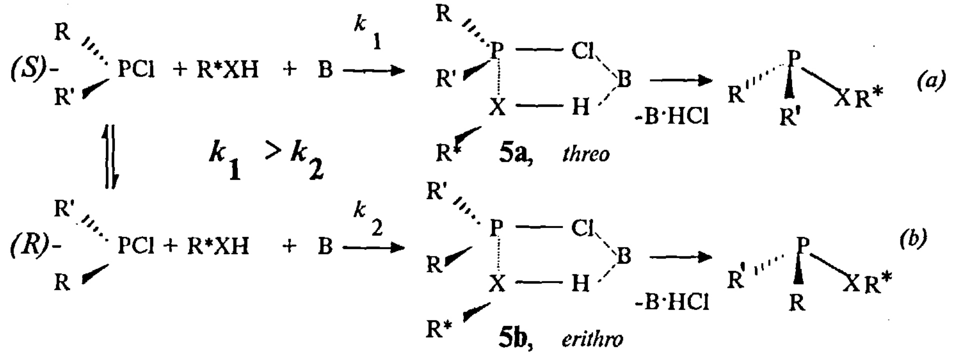


Thus, the diastereomer ratio of **4** in case of the reaction of isobutylphenylchlorophosphine with 1:2;5:6-diisopropylidene-D-hlucofuranose (HODAG) in depending on the nature of the base B is changed in the next sequence: DABCO (11:1), Et$_3$N (9:1), PhNMe$_2$ (1:1), Pyridine (4:6). It is remarkably that in the presence of pyridine the minor diastereomer becomes major. The asymmetric induction is absent when chlorophosphines **1** react with sodium alcoxides. The proposed method is simple, quick and convenient for the preparation of chiral phosphinic acid esters.

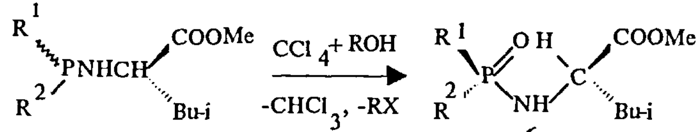


4

The reaction of the nucleophilic substitution at the tervalent phosphorus atom of the chlorophosphines **1** proceeds under conditions of kinetic control, via the formation of intermediate complexes **5** having the structure of *threo-* or *erithro*-diastereomers. Free activation energies of two competing directions *(a)* and *(b)* are different, that determines a difference between the rate constants k_1 and k_2 and the stereoselectivity of the reaction. The complex **5** is probably formed via frontal attack of the tervalent phosphorus atom by the nucleophile [2]



The oxidation of amines of phosphinic acids by the pair of tetrachloromethane-methanol (or water) proceeds with high stereoselectivity. In some cases the stereoselectivity achieves 100%. This reaction is especially of interest for the preparation of stereochemically pure derivatives of N-phosphorylated amino acids **6**, having important practical significance, because existing methods for their synthesis are not stereoselective. [3,4]



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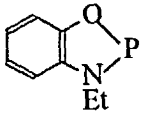
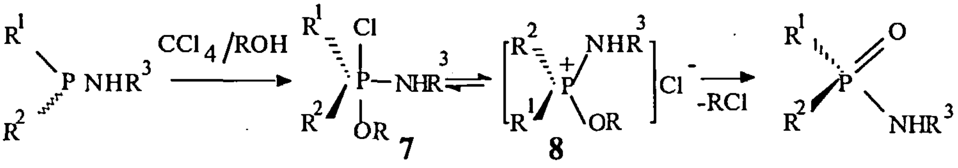
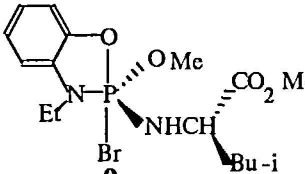
N of Comp.	$R^1(R^2)P$	Yield, %	diastereoisomeric ratio
6a	t-Bu(i-Bu)P	85	~100:0
6b	t-Bu(Ph)P	80	88:12
6c		80	75:25

The NMR spectroscopic studies showed that the reaction proceeds via the formation of alcoxyhalogenophosphorane **7**, which result in the pseudorotation gives the most thermodynamic stable diastereomer and via the alcoxyphosphonium salt **8** converts into the amidophosphinate. Alcoxyhalogenophosphorane have been succeeded to register in case of the compounds bearing the five-membered 1,3,2-oxazophospholane cycle, stabilizing pentacoordinate state of phosphorus atom. The ratio 94:6 (δ_P -56 and -58 ppm) shows high thermodinamical advantage of the one of the diastereomers. Phosphorane **9** converts gradually into the resulting amidophosphate **6c** (half-life time ~5h). Analogously the hydroxybromophosphorane **10** have been obtained by the reaction of amidophosphinate **5** with $CBrCl_3/H_2O$. The chemical shift of the **10**, δ_P -55 ppm, responds to the pentacoordinate phosphorus atom.[4]



7 **8**



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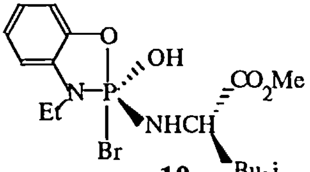
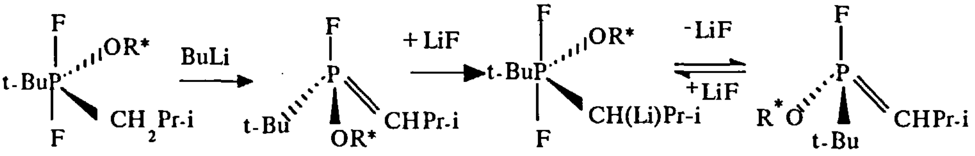


10

The dehydrofluorination of alcoxyfluorophosphoranes **11** bearing chiral ligands, resulting in the mixture of diastereomers of P-fluoroylids **12** in 1:1 ratio. However then in the presence of the lithium fluoride the epimerisation of P-fluoroylids proceeds. As a result the ratio of diastereomers changes strongly in favor of one of them, thermodynamically more advantageous. The epimerization is explained by the formation of the fluorophosphorane intermediates **13**, which adds and eliminates the lithium fluoride to convert gradually into the most thermodynamic stable diastereomer.[5]



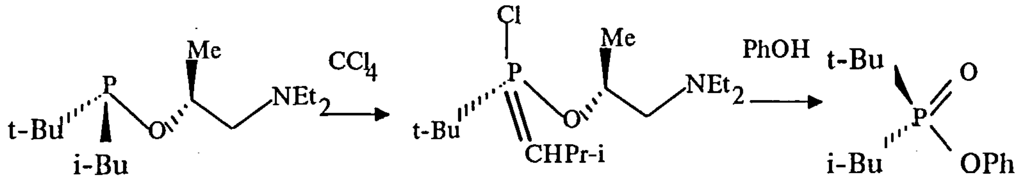
11 **12**, ratio 1:1 **13** **12**,ratio 95:5 - 75:25

R* = DAG (a), (S)- CH(Me)CH$_2$NEt$_2$ (b); Menthyl (c)

The determination of heats of formation for ylid **11b** bearing the (S)-diethylamino-2-propoxyl group by means of CNDO calculation revealed, that the (R ,S) diastereomer is energetically more advantageous, than (S,S)-diastereomer. The difference 3.2 kkal/mol corresponds to the position of equilibrium, which is really observed.

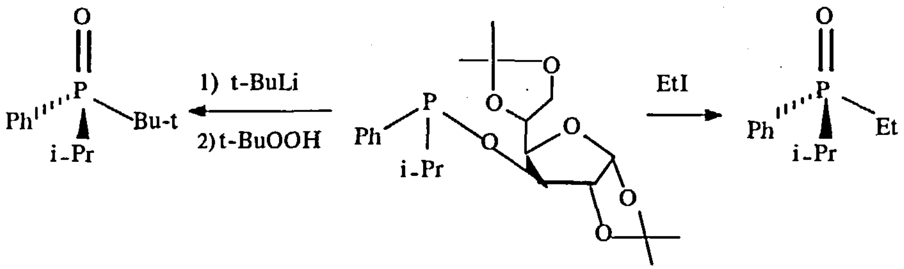
Chiral phosphinic acid esters are starting compounds for the synthesis of the enantiomers of valuable organophosphorus compounds, in particular of P-chloroylids **14**. The reaction of chiral phosphinic acid esters with tetrachloromethane proceeds stereospecifically without the change of the sign of optical rotation. Chiral P-chloroylids **14** easily add compounds bearing mobile hydrogen atom the (phenols, ammonium) to convert into chiral derivatives of phosphinic acids, with abstraction of the chiral alcoxyl group.

The optical active P-chloroylids are perspective chirons for the organic synthesis. [6]



14

The chiral phosphinic esters react with haloid alkyls to form stereospecifically enantiomers of tertiary phosphines oxide. The comparison of the optical rotation with this one of the compounds described in the literature allows to determine the configuration of the phosphorus atom, including the configuration of starting phosphinic acid esters. The phosphinic acid esters smoothly oxidized by peroxides, add the sulfur. Reactions of phosphinic acid esters with organolithium compounds provide chiral tertiary phosphines.



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