chemistry proceedings

Proceedings Paper

3R-Substituted and Norbornane-Annelated 1*H*-Phospholanoxides: Synthesis and Structure †

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† Presented at the 25th International Electronic Conference on Synthetic Organic Chemistry, 15–30 November 2021; Available online: https://ecsoc-25.sciforum.net/.

Abstract: A method for the synthesis of 3R-substituted and norbornane-annelated 1*H*-phospholan oxides has been developed. The method is based on the in situ substitution of the Al atom by the P atom in five-membered cyclic alumolanes using phosphorus trichloride. Substituted alumolanes were prepared by the reaction of cycloalumination of aliphatic and aromatic α-olefins and norbornene derivatives with triethylaluminum in the presence of *bis*(cyclopentadienyl)zirconium(IV) dichloride catalyst.

Keywords: phospholanes; heterocyclic compounds; organoaluminum compounds; zirconocene dichloride; cycloalumination; metal complex catalysis

Citation: Makhamatkhanova, A.L.; Nurislamova, R.R.; D'yakonov, V.A.; Dzhemilev, U.M. 3R-Substituted and Norbornane-Annelated 1*H*-Phospholanoxides: Synthesis and Structure. *Chem. Proc.* **2021**, *3*, x. https://doi.org/10.3390/xxxxx

Academic Editor(s): Julio A. Seijas

Published: 15 November 2021

1. Introduction

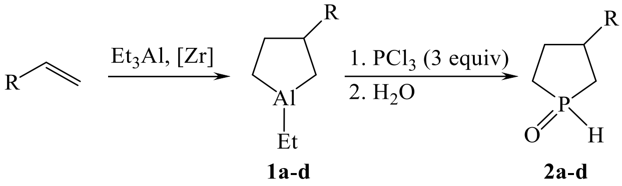
The development of new methods for the synthesis of practically demanded five-membered cyclic organophosphorus compounds is an important area of the chemistry of organoelement compounds [1]. The topic is relevant and arouses constant interest among researchers due to the practical importance of derivatives of phospholanes, phospholenes and phosphols, which are widely used in asymmetric catalysis [2], in organic and organoelement chemistry as effective reagents, synthons for fine organic synthesis, precursors of biologically active compounds.

One of the new and promising directions for the synthesis of cyclic organophosphorus compounds are methods based on the direct conversion of metallacarbocycles into the corresponding phospholenes and phosphols. This is a direct transformation of zirconacyclopentenes [3,4], zirconacyclopentadienes [5–9], titanacyclopentadienes [10].

Recently, we have developed a universal method for the synthesis of phospholanes and phospholenes of various structures, promising for practical application, based on the use of the reaction of catalytic cycloalumination of unsaturated compounds (alkenes, alkynes, α,ω-diolefins, norbornenes) through the stage of formation of alumolanes (aluminacyclopentanes and aluminacyclopentenes) based on the substitution of aluminum atom in alumolanes with phosphorus atoms using alkyl(aryl) phosphorodichlorides (III) [11–13]. However, the replacement of the aluminum atom in substituted alumolanes with a phosphorus atom using $PHal_3$ has hardly been studied. Therefore, in the development of ongoing research on the development of effective methods for the synthesis of cyclic organophosphorus compounds and in order to develop the synthesis of new practically important cyclic organophosphorus compounds, we studied the reaction of alumolanes with phosphorus trichloride.

2. Results and Discussion

Initially, we found that 3-butyl-1-ethylaluminacyclopentane **1a**, obtained in situ by cycloalumination of 1-hexene with Et_3Al in the presence of 5 mol% of Cp_2ZrCl_2, reacts with phosphorus trichloride to form after hydrolysis 3-butyl-1*H*-phospholan oxide **2a** as a mixture of *syn*- and *anti*-isomers in a 1:1 ratio (Scheme 1). The yield of the reaction products strongly depends on the reaction conditions (Table 1).



R = *n*-C_4H_9 (**a**), *n*-C_6H_{13} (**b**), *n*-C_8H_{17} (**c**), Bn (**d**).

Scheme 1. The synthesis of the 3-alkyl(aryl)-1*H*-phospholane oxides **2a-d**.

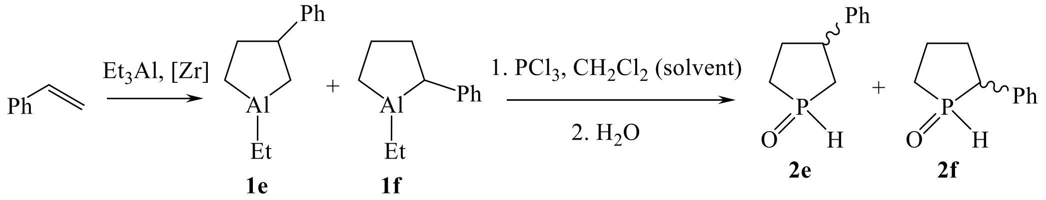
Table 1. Optimization of the reaction to prepare **2a**.

Run	The Ratio of [1-Hexene]:[PCl_3]	Solvent	Solvent Volume, mL	Yield of 2a, %
1	1:1	CH_2Cl_2	15	56 [1]
2	1:1	CH_2Cl_2	15	74
3	1:2	CH_2Cl_2	15	80
4	1:3	CH_2Cl_2	15	85
5	1:3	CH_2Cl_2	15	63 [1]
6	1:3	CH_2Cl_2	30	-
7	1:3	CH_2Cl_2	7	93
8	1:3	toluene	15	-

[1] PCl_3 was added in several portions.

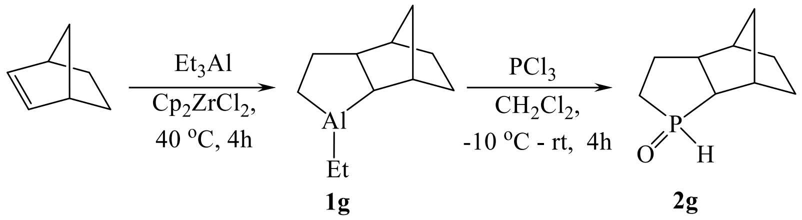
Under the optimal conditions developed we synthesized 3-hexyl-1*H*-phospholan oxide **2b**, 3-octyl-1*H*-phospholan oxide **2c**, and 3-benzyl-1*H*-phospholan oxide **2d** in 83–94% yields (Scheme 1). The isolated products **2b-d** are the mixtures of *syn*/*anti* isomers in a 1:1 ratio.

The reaction of styrene with Et_3Al in the presence of Cp_2ZrCl_2 leads to the formation a mixture of 3-phenyl-1-ethylaluminacyclopentane **1e** and 2-phenyl-1-ethylaluminacyclopentane **1f** (Scheme 2) in a 1:2 ratio, respectively, which in situ react with PCl_3 to give a mixture of 3-phenyl-1*H*-phospholan oxide **2e** and 2-phenyl-1*H*-phospholan oxide **2f**. In this case the ratio of the formed *syn*/*anti* isomers of **2e** and **2f** is 1:1.



Scheme 2. The synthesis of a mixture of 3-substituted **2e** and 2-substituted **2f** 1*H*-phospholane oxides.

The cycloalumination of norbornene followed by the treatment of alumolane formed with PCl_3 gave (3a*R*,4*R*,7*S*,7a*S*)-octahydro-4,7-methanophosphindole 1-oxide **2g** as a mixture of *syn*- and *anti*-isomers in a 2: 1 ratio with a total yield of 87% (Scheme 3).



Scheme 3. The synthesis of (3a*R*,4*R*,7*S*,7a*S*)-octahydro-4,7-methanophosphindole 1-oxide **2g**.

The structure of the synthesized cyclic organophosphorus compounds was proved by mass spectrometry and ^{1}H, ^{13}C, ^{31}P NMR spectroscopy as well as homo- and heteronuclear 2D correlation experiments (COSY ^{1}H-^{1}H, HSQC, HMBC).

3. Conclusions

An original one-pot method for the synthesis of 3R-substituted and norbornane-annelated 1*H*-phospholan oxides by the reaction of substituted alumolanes with phosphorus trichloride is proposed. The obtained cyclic 1*H*-phosphine oxides are of practical interest as key monomers for the synthesis of new catalysts for homogeneous catalysis.

4. Experimental Part

^{1}H, ^{13}C, and ^{31}P NMR spectra were acquired on a Bruker Avance-400 instrument (400, 100, and 162 MHz, respectively) in $CDCl_3$. The two-dimensional homonuclear (COSY) and heteronuclear (^{1}H–^{13}C HSQC, ^{1}H–^{13}C HMBC) NMR spectra were acquired according to the standard procedures from Bruker. Mass spectra (GC-MS) were recorded on a Shimadzu GC-2010 instrument equipped with a GCMSQP2010 Ultra mass selective detector and a Supelco 5 ms capillary column (60 m × 0.25 mm × 0.25 μm); the carrier gas was helium; injector temperature 260 °C, interface temperature 260 °C, ion source temperature 200 °C. Chromatographic analysis was performed on a Shimadzu GC-9A gas chromatograph, using a 2000 × 2 mm column, the stationary phase consisted of silicone SE-30 (5%) on Chromaton N-AW-HMDS carrier (0.125–0.160 mm), the carrier gas was helium (30 mL/min), temperature program from 50 to 300 °C at the rate of 8 °C/min. The reactions with organometallic compounds were accomplished under dry argon flow. The solvents were dried and distilled immediately prior to the use. Commercially available Cp_2ZrCl_2, phosphines (Acros), and 92% $AlEt_3$ (from Redkinsk Experimental Factory) were used.

3-Substituted 1*H*-phospholane oxides 2a–g. General procedure. A round-bottomed flask was charged at 0 °C with Cp_2ZrCl_2 (0.073 g, 0.25 mmol), alkene or norbornene (5 mmol), and Et_3Al (0.75 mL, 5 mmol) in a dry argon atmosphere. The temperature was brought to 40 °C and the mixture was stirred for 4 h. Then the reaction mixture was cooled to –(5–10)°C and CH_2Cl_2 (7 mL) with phosphorus trichloride (15 mmol, 3 equiv) were added. The mixture was stirred at room temperature for 4–6 h until the solution discoloration. The mixture was then hydrolyzed with water, the reaction products were extracted with CH_2Cl_2 and the organic phase was dried with $MgSO_4$. The solvent was evaporated and the residue was vacuum distilled to afford 1*H*-phospholane oxides **2a–g** as colorless oils.

Author Contributions: Conceptualization, U.M.D. and V.A.D.; methodology, A.L.M.; software, R.R.N.; validation, R.R.N. and A.L.M.; formal analysis, R.R.N.; investigation, A.L.M.; resources, A.L.M.; data curation, A.L.M.; writing—original draft preparation, A.L.M.; writing—review and editing, A.L.M.; visualization, A.L.M.; supervision, A.L.M.; project administration, A.L.M.; funding acquisition, V.A.D. All authors have read and agreed to the published version of the manuscript.

Funding: The work was done within approved plans for research projects at the IPC RAS State Registration No. AAAA-A19-119022290008-6 and AAAA-A19-119022290004-8 (2019-2021).

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Acknowledgments: The authors thank the Shared Facility Center «Agidel», Institute of Petrochemistry and Catalysis, Russian Academy of Sciences, for the registration of NMR and mass spectra.

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