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Synthesis of 3-Substituted 1*H*-Phospholanoxides by the Interaction of Alumolanes with PBr_3/H_2O

Alevtina L. Makhamatkhanova * and Tatyana V. Tyumkina

Institute of Petrochemistry and Catalysis, Ufa Federal Research Center of the Russian Academy of Sciences, 141 Prospekt Oktyabrya, Ufa 450075, Russia; email1@email.com

* Correspondence: alena_ink@mail.ru; Tel.: +07-917-4937-149

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Abstract: We have recently developed a method for the synthesis of 3R-substituted and norbornane-annelated 1*H*-phospholanoxides based on the reaction of substitution of aluminum atoms in alumolane with phosphorus atoms using phosphorus trichloride. In development of the ongoing research, a method for the synthesis of 3R-substituted 1*H*-phospholanoxides using phosphorus tribromide with good yields has been proposed.

Keywords: phospholane oxides; phosphorus tribromide; heterocyclic compounds; organoaluminum compounds; cycloalumination

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1. Introduction

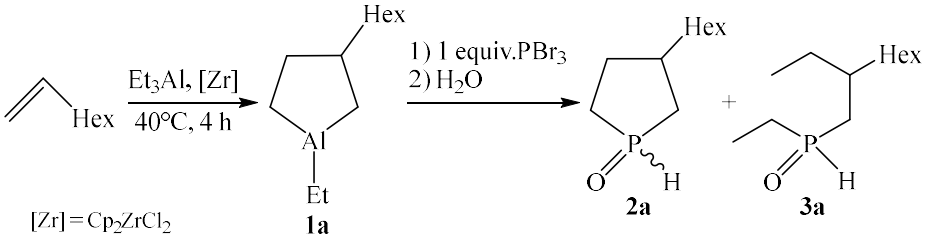
One of the new and promising directions for the synthesis of five-membered cyclic organophosphorus compounds (OPCs) is the direct in situ conversion of aluminolanes (aluminacyclopentanes and aluminacyclopentenes) formed as a result of the catalytic cycloaluminization reaction of unsaturated compounds (alkenes, alkynes, α,ω-diolefins, norbornenes) into the corresponding phospholenes and phosphols using alkyl(aryl)phosphorus dihalides [1–3].

We have recently developed a method for the synthesis of 1*H*-phospholanoxides of various structures based on the substitution reaction of aluminum atoms in 3R-substituted and norbornane-annelated aluminolane with phosphorus atoms using phosphorus trichloride [4,5].

In continuation of our research, we found that the use of PBr_3 as a phosphorus reagent also makes it possible to obtain the target 1*H*-phospholanoxides.

2. Results and Discussion

To establish the possibility of using PBr_3 as a phosphorus reagent in the reaction of substitution of an aluminum atom in alumolane with a phosphorus atom, 3-butyl-1-ethylaluminacyclopentane **1a** was chosen as a model compound. It was found that the reaction of 3-butyl-1-ethylaluminacyclopentane **1a**, obtained in situ by cycloalumination of hexene-1 with Et_3Al in the presence of 5 mol% Cp_2ZrCl_2, with an equimolar amount of PBr_3 after hydrolysis of H_2O leads to the formation of two products -3-butyl-1*H*-phospholane oxide **2a** (46%) and the aluminacyclopropane ring opening product **3a** (21%) in a ratio of ~2:1 (Scheme 1). In the case of PCl_3, the predominant formation of 3-hexyl-1-ethylphospholane oxide was observed.[4] Product **2a** is formed as a mixture of *syn*- and *anti*-isomers in a 1:1 ratio.



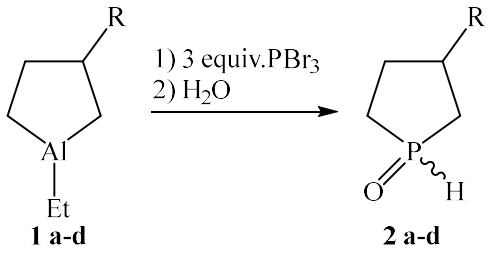
Scheme 1. Reaction of 1-ethyl-3-hexylaluminacyclopentane **1a** with 1 eq. PBr_3.

Selective formation of 1*H*-phospholanoxide **2a** was observed using three equivalents of PBr_3 with a yield of 78% (Scheme 2).

The yield of reaction product **2a** depends on the reaction time. Thus, two hours after the addition of PBr_3, the yield of **2a** was only 30%. The main product was 3-methylnonane, a decomposition product of **1a**. When the reaction time was increased to 10 h, the yield of **2a** increased to 78%. The optimal solvent for the reaction is methylene chloride.

Under the developed conditions (CH_2Cl_2, 20–22 °C, 8–10 h), 3-butyl-1H-phospholanoxide **2b**, 3-octyl-1H-phospholanoxide **2c**, and 3-benzyl-1H-phospholanoxide **2d** were synthesized in yields of 54–78%. Isolated products **2b-d** are a mixture of *syn*/*anti* isomers in a 1:1 ratio (Scheme 2).

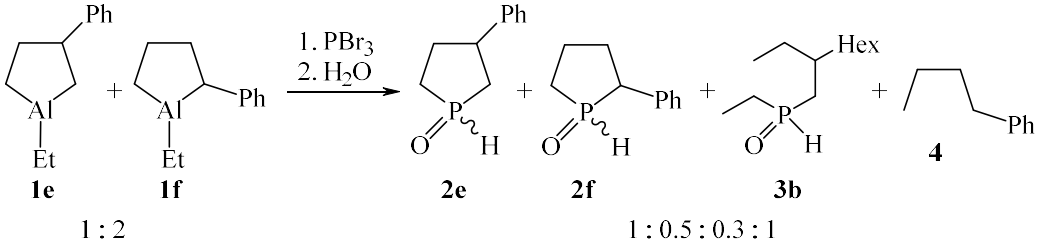
The structure of the obtained compounds was confirmed by mass spectrometry and ^{1}H, ^{13}C, ^{31}P NMR spectroscopy.



R = *n*-C_6H_{13} (78%) (**a**), *n*-C_4H_9 (72%) (**b**), *n*-C_8H_{17} (81%) (**c**), -CH_2-Ph (54%) (**d**).

Scheme 2. Synthesis of 3-substituted 1*H*-phospholane oxides **2 a-d**.

A mixture of 3-phenyl-1-ethylaluminacyclopentane **1e** and 2-phenyl-1-ethylaluminacyclopentane **1f**, formed by the reaction of styrene with Et_3Al in the presence of Cp_2ZrCl_2 in a ratio of 1:2, reacts with PBr_3 to form a mixture of products. The composition of the products indicates that 3-substituted aluminolane is successfully transformed under the action of PBr_3, while the yield of 2-substituted phospholane oxide under the reaction conditions is low.



Scheme 3. Reaction of a mixture of 3-phenyl-1-ethylaluminocyclopentane **1e** and 2-phenyl-1-ethylaluminocyclopentane **1f** with PBr_3.

To extend this method to more complex cyclic and polycyclic olefins, we investigated the interaction of PBr_3 with an alumolane obtained by cycloalumination of nor-

bornene (bicyclo [2.2.1]hept-2-ene). However, the only reaction product was 3-ethylnorbornane, a decomposition product of aluminolane, which indicates that the replacement of the aluminum atom with a phosphorus atom does not occur.

3. Conclusions

An alternative one-pot method for the synthesis of 3R-substituted 1*H*-phospholanoxides by reacting substituted aluminolane with phosphorus tribromide is proposed. The yield of 2R-substituted 1*H*-phospholanoxides is quite low. Norborneannelated aluminolanes do not react with PBr_3. The reaction of aluminolane with PBr_3 takes longer compared to PCl_3. The synthesized 3-substituted 1*H*-phospholane oxides are promising as ligands for the synthesis of new catalysts for homogeneous catalysis [6,7] and as antiseptics, fungicides, and insecticides.

4. Experimental Part

^1H, ^{13}C and ^{31}P NMR spectra were acquired in $CDCl_3$ on a Bruker Avance-400 spectrometer (100.58 MHz for ^{13}C, 400.00 MHz for ^1H and 161.92 MHz for ^{31}P). The ratio of products was determined by the integrated intensity of the signals in the ^{31}P NMR spectrum. Reactions with organometallic compounds were carried out in a flow of dry argon. The solvents were dried and used freshly distilled. We used commercially available Cp_2ZrCl_2, phosphines (Acros company) and Et_3Al (92%) (Redkinsky Experimental Plant).

3-Substituted 1H-phospholane oxides 2a–f. General procedure. A round-bottomed flask in a dry argon atmosphere was charged successively with stirring at 0 °C with Cp_2ZrCl_2 (0.073 g, 0.25 mmol), alkene (5 mmol), and Et_3Al (0.75 mL, 5 mmol). 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, CH_2Cl_2 (7 mL) and phosphorus tribromide (15 mmol, 3 equiv.) was added. The mixture was stirred at room temperature for 10 h. 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–f** as colourless oils.

3-Butyl-1*H*-phospholane oxide (**2b**) (*syn*:*anti* ≈ 1:1). ^1H NMR ($CDCl_3$): δ 0.54–0.61 (m, 6H, CH_3); 0.94–1.05 (m, 10H, CH_2); 1.07–1.19 (m, 3H, CH_2); 1.25–1.30 (m, 2H, (C-4)H_2); 1.43–1.55 (m, 2H, (C-2)H_2, CH); 1.57–1.65 (m, 1H, (C-5)H_2); 1.67–1.80 (m, 2H, (C-2)H_2, (C-4)H_2); 1.82–1.91 (m, 2H, (C-4)H_2, CH); 1.94–2.10 (m, 4H, (C-2)H_2, (C-5)H_2); 7.15 (d, 1H, PH, $^1J_{PH}$ = 460 Hz); 7.17 (d, 1H, PH, $^1J_{PH}$ = 460 Hz). ^{13}C NMR ($CDCl_3$): δ 13.77 (CH_3); 22.40 ($\underline{C}H_2CH_3$); 25.43 (d, C-5, $^1J_{CP}$ = 64.4 Hz); 26.98 (d, C-5, $^1J_{CP}$ = 63.4 Hz); 29.30 (d, C-4, $^2J_{CP}$ = 8.0 Hz); 29.52 (d, C-4, $^2J^{CP}$ = 6.0 Hz); 29.69 ($\underline{C}H_2CH_2CH_3$); 31.99 (d, C-2, $^1J_{CP}$ = 65.4 Hz); 32.80 (d, C-2, $^1J_{CP}$ = 64.4 Hz); 35.32 (d, CH$\underline{C}H_2$, $^3J_{CP}$ = 13.1 Hz); 35.54 (d, CH$\underline{C}H_2$, $^3J_{CP}$ = 12.1 Hz); 36.83 (d, C-3, $^2J_{CP}$ = 10.1 Hz); 38.10 (d, C-3, $^2J_{CP}$ = 7.6 Hz). ^{31}P NMR ($CDCl_3$): δ 47.35 (J_{PH} = 456 Hz), 47.79 (J_{PH} = 458 Hz), Mass spectrum (HRMS), m/z 161.1093 ($[M+H]^+$ calcd 161.1090).

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