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Highly stereoselective addition of silylphosphines to chiral aldehydes

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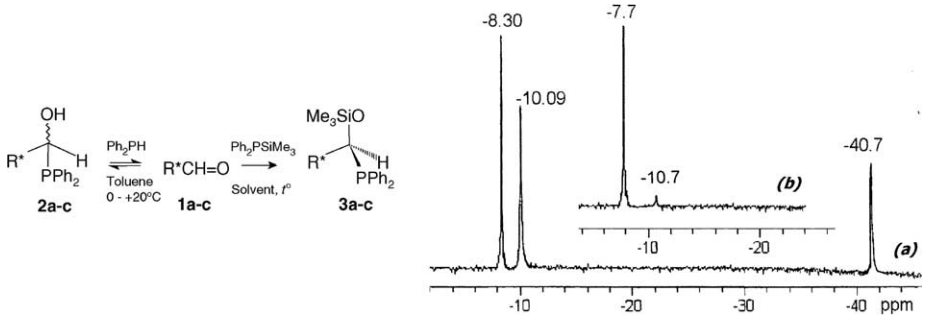
Abstract—The reaction between diphenyl(trimethylsilyl)phosphine and chiral aldehydes proceeds with high stereoselectivity to give diastereomerically pure tertiary α-trimethylsiloxyalkylphosphines. The diastereomeric purity of the addition products was 90–100%. The products were purified via the formation of borane–phosphine complexes. The reaction of bis(trimethylsilyl)phenylphosphine with acetonide (*R*)-glyceraldehyde provides tertiary bis(glyceryl)phosphines.

Chiral organophosphorus compounds are an important subject of investigation due to widespread use of these compounds as ligands in transition metal complexes, biologically active substances or drugs.[1–3] Therefore, the development of stereoselective methods for the synthesis of organophosphorus compounds is an important and challenging goal of contemporary synthetic organic chemistry.

In the present work, which is a part of our ongoing research program, we have studied the reactions of silylphosphines with chiral aldehydes leading to the formation of optically active tervalent phosphorus derivatives. In contrast to the reaction of dialkylphosphites with aldehydes (the Abramov reaction), which has been extensively studied, the diastereoselective addition of silylphosphines to aldehydes has not been reported.[1,2] Previously, only the achiral variant of this reaction was described.[4a–d]

First, we examined the reaction of diphenylphosphine with the chiral aldehyde **1a** and found that the reaction was reversible giving a mixture of the initial compounds and the addition product **2a** with low stereoselectivity (dr 45:55, Scheme 1). On the contrary, the reaction of diphenyl(trimethylsilyl)phosphine with aldehydes **1a–c**



Scheme 1. Reactions of chiral aldehydes **1a–c** with Ph_2PH and Ph_2PSiMe_3 and the ^{31}P NMR spectra of the reactions of aldehyde **1a** with Ph_2PH (a) and Ph_2PSiMe_3 (b).

Keywords: Stereoselectivity; Silylphosphines; Chiral aldehydes; Chiral α-trimethylsiloxyalkylphosphines.
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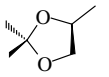
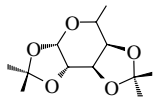
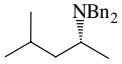
Table 1. Synthesis of tertiary phosphines **3a–c**

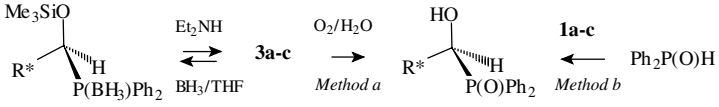
Entry	Compd	R*	Solvent	*T* (°C)	Yield (%)	dr[a]
1	**3a**		THF	−20	85	95:5
2	**3b**		Toluene	−20 to 0	90	∼100:0
3	**3c**		Toluene	−20 to +20	60	90:10

[a] Diastereomeric ratio (dr) was determined by ^{31}P and ^{1}H NMR spectroscopy.

resulted in the formation of products **3a–c** in good yields and high stereoselectivity. The optical purity of newly formed stereogenic center of compounds **3a–c** was 90–99% ee (Table 1). Evidently the reaction of silylphosphines with aldehydes is irreversible, since the adducts **3** possess strong Si–O bonds unlike adducts **2**, which possess a weak H–O bond, which can dissociate easily to regenerate the starting compounds.

Compounds **3**, on reaction with borane in THF solution were transformed into borane complexes **4**, which were purified by column chromatography on silica gel. The structures and purities of the borane complexes were confirmed by nuclear magnetic resonance and elemental analysis. Decomplexation of compounds **4** with a large excess of an amine such as diethylamine led to the formation of chemically and stereochemically pure tertiary phosphines **3a–c**. Aerial oxidation of the compounds **3a–c** provides the phosphine oxides **5a–c** in high yields (∼90%), (method *a*, Scheme 2). Compounds **5a–c** were isolated as colorless crystalline substances, the structure and purity of which were confirmed by elemental analysis and spectroscopic studies.[5] To confirm the structure of compounds **5a–c** we also prepared them by an alternative reaction from diphenylphosphine oxide and aldehydes **1a–c** (method *b*, Scheme 2). This reaction proceeded with moderate stereoselectivity (∼75% de) to afford addition products, which were identical to compounds **5a–c** prepared by method *a*.

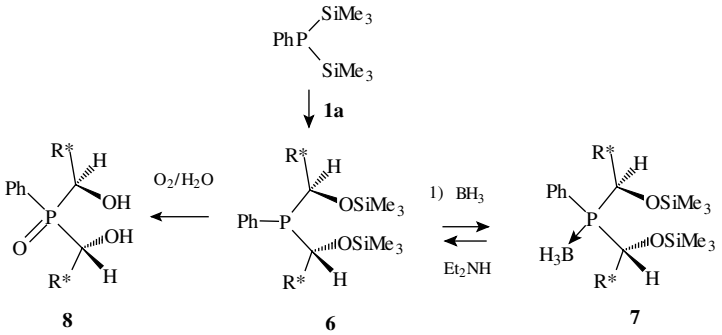
The reaction of bis(trimethylsilyl)phenylphosphine with aldehyde **1a** also proceeded with good stereoselectivity (Scheme 3). Despite the fact that product **6** contains four stereogenic centers and can exist as a mixture of several diastereomers, the reaction led to the formation of predominantly only one diastereomer. Subsequent treat-



4a-c **5a-c**

Compd	Yield (%) (method *a*)	*de* (%) (method *a*)	Yield (%) (method *b*)	*de* (%) (method *b*)
5a	90	95	60	70
5b	50	98	70	80
5c	40	98	40	70

Scheme 2. Synthesis of tertiary phosphine oxides **5a–c** via methods a and b.



Scheme 3. Reaction of the aldehyde **1a** with the phenyl-bis(trimethylsilyl)phosphine.

ment of the compound **6** with borane resulted in the optically pure borane complex **7**, which constitutes a new chiral ligand.[6] Compound **7** is stable to oxidation and hydrolysis by air, can be kept without racemization, and can be purified by column chromatography on silica gel. The co-ordinated BH_3 of complex **7** was removed on treatment with diethylamine to give the diastereomerically pure tertiary phosphine **6**. Compound **6** was oxidized to the corresponding tertiary phosphine oxide **8**, which was isolated as crystalline product. The structure and purity of compounds **6**–**8** have been confirmed by elemental analysis and NMR spectroscopy.[5]

The configuration of the newly formed stereogenic center of compounds **3**–**5** was determined to be *S* by NMR spectroscopy, the large value of the $^3J_{HH}$ constant and the small value of the $^2J_{HP}$ constant of compounds **3**–**5** indicating the *anti*-conformation of the H–C^1–C^2–H and O=P–C^1–H bonds.[7] The stereochemistry of this reaction is probably kinetically controlled. Nucleophilic attack of silylphosphines to the less shielded (*Si*) face of the carbonyl group provides, preferentially, the (S)-**3** diastereomer according to Cram's rule.

In conclusion, we have found that the reaction between silylphosphines and chiral aldehydes proceeds with good stereoselectivity to give addition products in high chemical yields. The reaction can be applied to asymmetric synthesis of new chiral organophosphorus compounds.

Acknowledgement

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References and notes

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5. All new compounds shown in Schemes 1–3 gave satisfactory analytical data and NMR spectra consistent with their structures. Some physical characteristics are reported below.
General procedure for the reaction of aldehyde **1a** with Ph_2PSiMe_3: To a solution of **1a** (1.1 mmol) in 5 mL of THF (or toluene) was added Ph_2PSiMe_3 (1.0 mmol) at −20 °C. The solution was left at this temperature overnight. Then the temperature was raised to +20 °C and after 1 h the solvent was evaporated to give tertiary phosphine **3a**. To a solution of **3a** in THF (3 mL) was added a solution of borane in THF (1.1 mmol) at −20 °C. The reaction mixture was left at 0 °C for 6–12 h. The solvent was evaporated and the residue was chromatographed on a silica gel column (hexane–ethyl acetate = 6:1) to give **4a**: Yield 80%. R_f 0.42 (hexane–ethyl acetate = 6:1). $[\alpha]_D$ +41.6 (*c* 1.5, ethyl acetate). ^{1}H NMR ($CDCl_3$), δ, ppm (*J*, Hz): −0.16 (9H, s, $SiMe_3$); 0.18–1.40 (3H, m, BH_3); 1.25 [3H, s, $(CH_3)_2C$]; 1.33 [3H, s, $(CH_3)_2C$]; 3.23 [1H, dd *J* 8, *J* 1(CH_2O)]; 3.43 [1H, dd, *J* 7.5, *J* 1 (CH_2O)]; 4.53 (1H, m, C*H*CH_2O); 5.00 (1H, dd, *J* 4.5, *J* < 1, PCH); 7.66 (6H, m, C_6H_5); 7.93 (4H, m, C_6H_5). ^{31}P NMR ($CHCl_3$): δ_P 21.60 ppm, d J_{PB} 57 Hz. The borane complex **4a** was dissolved in excess diethylamine and left for 12 h. The volatiles were evaporated in vacuum and the residue was extracted with hexane, which was filtered off under argon. **3a**: $[\alpha]_D^{20}$ −7 (*c* 4, toluene). ^{1}H NMR ($CDCl_3$), δ, ppm (*J*, Hz): −0.02 (s, CH_3Si); 1.33 (s, CH_3); 4.33 (m, OC*H*$_2$CH); 4.49 (m, OC*H*$_2$CH); 4.72 (m, CH_2C*H*O); 4.99 (m, PC*H*); 7.50 (m, C_6H_5); 7.90 (m, C_6H_5). ^{31}P NMR ($CHCl_3$): δ_P −7.69; −10.62 ppm (ratio ~11:1). The tertiary phosphines **3b** and **3c** and the borane complexes **4b** and **4c** were obtained analogously. **3b**: ^{31}P NMR (toluene), ppm: δ_P 4.4. **4b**: Yield 64%. R_f 0.35, $[\alpha]_D$ −71.8 (*c* 3, $CHCl_3$). ^{31}P NMR ($CHCl_3$): δ_P 25.30 ppm. **3c**: Yield 60%.^{31}P NMR (toluene): δ_P −10.50; −11.30 ppm (ratio 9:1). **5a**: mp 167 °C (toluene), $[\alpha]_D^{20}$ +11 (*c* 2, $CHCl_3$). ^{1}H NMR ($CDCl_3$), δ, ppm (*J*, Hz): 1.17 (3H, s, Me_2C^a); 1.20 (3H, s, Me_2C^b); 3.88 (1H, d, *J* 2 C^aH_2); 3.897 (1H, d, *J* 1.5 C^bH_2); 4.39 (1H, dt, *J* 6.5, *J* 2 OC*H*CH_2); 4.59 (1H, dd, *J* 5, *J* 0.9, PCH); 4.40 (1H, m, OH); 7.80 (6H, m, 4H, C_6H_5); 7.49 (4H, m, C_6H_5). ^{31}P NMR ($CHCl_3$): δ_P 30.87 ppm. **5b**: mp 156 °C, $[\alpha]_D^{20}$ −59 (*c* 3, $CHCl_3$). ^{31}P NMR ($CHCl_3$): δ_P 32 ppm. **5c**: mp 121 °C, $[\alpha]_D^{20}$ −30 (*c* 2, $CHCl_3$). ^{31}P NMR ($CHCl_3$): δ_P 29.4 ppm. The compounds **6** and **7** were prepared analogously to **3a** and **4a**. **6**: ^{31}P NMR ($CHCl_3$), ppm: δ_P −10.68. **7**: R_f 0.37 (hexane–ethyl acetate 3:1). $[\alpha]_D^{20}$ +23.6 (*c* 3, $CHCl_3$). ^{1}H NMR ($CDCl_3$), δ, ppm: −0.17 (9H, s, $SiMe_3$); −0.20 (9H, s, $SiMe_3$); 0.60–1.30 [3H, m, BH_3); 1.11 [3H, s, $(CH_3)_2C$]; 1.20 [3H, s, $(CH_3)_2C$]; 1.33 [3H, s, $(CH_3)_2C$]; 1.36 [3H, s, $(CH_3)_2C$]; 4.59 (1H, m, CHC*H*CH_2); 4.53 (1H, m, CHC*H*CH_2); 3.64 (1H, dt, OCH_2); 3.77 (1H, dt, OCH_2); 3.90 (1H, dt, OCH_2); 4.11 (1H, dt, OCH_2); 5.16 (1H, dd, *J* 9, *J* < 1, PCH); 7.20 (3H, m, C_6H_5); 7.80 (2H, m, C_6H_5). ^{31}P NMR ($CHCl_3$): δ_P 27.40 ppm.
6. Studies of compounds **6**–**8** as ligands in transition metal complexes are currently in progress.
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