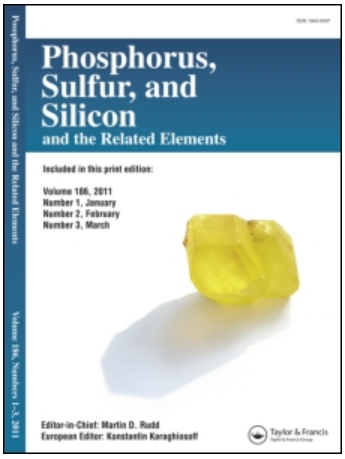

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New Approach to the Synthesis of Phosphorodichloridites, Phosphorochloridites, and Trialkyl Phosphites

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New Approach to the Synthesis of Phosphorodichloridites, Phosphorochloridites, and Trialkyl Phosphites

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Different trivalent organophosphorus esters such as phosphorodichloridites, phosphorochloridites, and mixed trialkyl phosphites have been easily synthesized in good yields using a HCl-catalyzed reaction of the corresponding chlorophosphine and alkoxytrimethylsilane by mutual exchange of the alkoxy and chlorine ligand ($P^{III}Cl/ROSiR'_3$; exchange reaction). Chemoselectivity of the exchange reaction with primary and secondary alkoxytrimethylsilanes, as well as with alkoxytrimethylsilanes and thioalkoxytrimethylsilanes, respectively, has also been examined. It has been also found that the substitution reaction of chlorophosphines with secondary amine occurs more rapidly than the exchange reaction with $ROSiR'_3$.

Keywords Mixed trialkyl phosphites; phosphorochloridites; phosphorodichloridites

INTRODUCTION

Trivalent organophosphorus esters, including phosphorodichloridites, phosphorochloridites, and trialkyl phosphates, are usually formed in the reactions of organophosphorus chlorides with the equimolar amount of the appropriate alcohol in the presence of a tertiary amine.[1] Another methodology consists in the exchange reaction of the chlorine atom of a chlorophosphine with alkoxy groups of alkoxytrimethylsilanes ($P^{III}Cl/ROSiR'_3$). However the latter route has not been widely used for synthesis.[2]

It is also known that the exchange reaction ($P^{III}Cl/R^1OSiR_3$) is sometimes more useful than the substitution reaction ($P^{III}Cl/R^1OH/HNR^2_3$). For example, *O*-alkyl 2-chloro-cycloalkylphosphorochloridites cannot

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Dedicated to Professor Marian Mikołajczyk from the CBMiM PAN in Łódź, Poland, on the occasion of his 70th birthday.

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be obtained from the reaction of 2-chloro-cycloalkylphosphorochloridites and an alcohol in the presence of a tertiary amine; the exchange reaction between 2-chlorocycloalkylphosphorochloridite and the respective alkoxysilane affords good yields, however.[3] Moreover the monomethoxylation at the P^{III} atom of (dichlorophosphinyl) methylamine is possible only via the exchange reaction.[4]

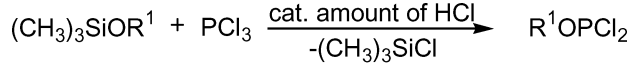
However, in some cases, the exchange reaction with alkoxytrimethylsilanes requires very harsh conditions. It has been found that the replacement of all chlorine atoms in PCl_3 by the exchange reaction is rather difficult. For example, treatment of phosphorus trichloride with an excess of butoxytrimethylsilane easily affords the phosphorochloridite via the formation of the corresponding phosphorodichloridite,[5] but the efficient replacement of the last chlorine atom is difficult, and the reaction must be performed at high temperatures and in the presence of [PyH]Cl as a catalyst.[6,7] Attempts to accelerate the exchange reaction between phosphorus trichloride and alkoxysilanes in the presence of $ZnCl_2$ as catalyst have failed.[8]

The aim of our work was to elaborate mild conditions for the exchange reaction and thus to find a convenient approach to different functional trivalent organophosphorus esters including phosphorodichloridites, phosphorochloridites, and mixed trialkylphosphites. We also examined the chemoselectivity of the exchange reaction of the *P*-chlorine ligand with alkoxy groups of primary and secondary alkoxytrimethylsilanes as well as with alkoxy and thioalkoxy groups of alkoxytrimethylsilanes and thioalkoxytrimethylsilanes, respectively. We have also compared the reactivity of the $P^{III}Cl$ moiety in the exchange reaction with $ROSiR'_3$ and in the substitution reaction with a secondary amine in order to predict whether the exchange reactions with suitable alkoxytrimethylsilanes bearing amine functionality might occur.

RESULTS AND DISCUSSION

Hydrogen Chloride as a Catalyst for the Exchange Reaction ($P^{III}Cl/ROSiR'_3$)

In our preliminary experiments, we have found that treatment of PCl_3 with $(CH_3)_3SiOC_2H_5$ under dry argon atmosphere at room temperature affords diethylphosphorodichloridite in satisfactory yield (80–85 mol % after 48 h, ^{31}P NMR analysis of the crude reaction mixture). However, when the reaction was carried out in the presence of argon, which was not additionally dried, the product was formed almost quantitatively.



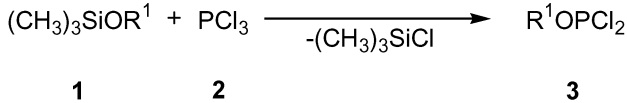
SCHEME 1

This observation suggests that the exchange reaction (Scheme 1) is facilitated by the presence of catalytic amounts of HCl derived from the reaction of PCl_3 with traces of water. This methodology seems to be especially useful in the preparation of different trivalent phosphorus esters.

Synthesis of Dichlorides 3

In order to test the synthetic applicability of the exchange reaction, a number of simple trimethylsilylated alcohols containing different functionalities have been used, including methoxytrimethylsilane (**1a**), ethoxytrimethylsilane (**1b**), trimethyl (propoxy)silane (**1c**), trimethyl (buthoxy)silane (**1d**), benzyloxytrimethylsilane (**1e**), 3-(trimethyl-siloxy)propane-nitrile (**1f**), trimethyl(2,2,2-trichloroethoxy)silane (**1g**), decyloxytrimethylsilane (**1h**), ethyl (*RS*)-2-(tri-methylsililoxy) propionoate (**1i**), *N*-palmitoyletanolamine trimethylsilyl ether (**1j**), and *N-boc*-etanolamine trimethylsilylether (**1k**).

These compounds have been treated with PCl_3 in methylene chloride solution under mild conditions (see the Experimental section) to achieve monomethoxylation at the P^{III} atom. The exchange reaction effectively led to the corresponding phosphorodichloridites **3** according to Scheme 2a.



R^1 = **a**) CH_3; **b**) C_2H_5; **c**) n-C_3H_7; **d**) n-C_4H_9; **e**) $C_6H_5CH_2$; **f**) NCC_2H_4; **g**) Cl_3CCH_2; **h**) $CH_3(CH_2)_8CH_2$; **i**) $C_2H_5OC(O)CHCH_3$; **j**) $C_{15}H_{31}C(O)NHCH_2CH_2$; **k**) $(CH_3)_3COC(O)NHCH_2CH_2$.

SCHEME 2a

The yields and physical constants of the products are presented in Table I.

TABLE I Dichlorophosphoridites $ROPCl_2$ 3

3	R	Yield[a,b] [%]	Bp. [°C]/Torr	^{31}P-NMR [δ, ppm]	Lit. or Mol. Formula[g] (Mol. Weight)
a	CH_3	70	40/85	181.5	[21]
b	C_2H_5	85	36–40/65	177.9	[22]
c	*n*-C_3H_7	69	65–68/65	178.6	[23]
d	*n*-C_4H_9	79	63–64/50	178.5	[24]
e	$C_6H_5CH_2$	71	80–83/3	177.8	[9,25]
f	NCC_2H_4	72	78–80/5	179.6	[25]
g	Cl_3CCH_2	75	47–49.5/2	178.6	[26]
h	$CH_3(CH_2)_8CH_2$	65	132–135/6	175.5	$C_{10}H_{21}Cl_2OP$ (259.16)
i	$C_2H_5OC(O)CHCH_3$	*c*	*d*	178.5	[27]
j	$C_{15}H_{31}C(O)NHCH_2CH_2$	*c*	*d*	177.8[e] 179.8	$C_{18}H_{36}Cl_2NO_2P$ (384.36)
k	$(CH_3)_3COC(O)NHCH_2CH_2$	*c*	*d*	180.0[f]	$C_7H_{14}Cl_2NO_3P$ (262.07)

[a]Yield of distilled products.

[b]Reaction time: **a–d** 24 h, **e–i** 1 week, **f–h**, **j** two weeks, **k** 1 h; the reaction is carried out in the presence of stoichiometric amount of pyridine.

[c]Crude oil contains 96–98 mol % of product.

[d]Reaction mixture was filtered, then evaporated and kept 15 min under vacuum (40 °C / 2 Torr).

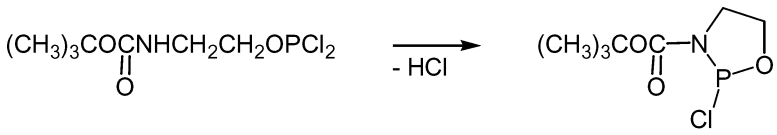
[e]Two rotamers.

[f] Product is unstable at room temperature forming during one week cyclic chlorophosphoroamidite, (**3l**), (^{31}P NMR, $\delta = 153.9$ ppm, ref. [10]).

[g]Satisfactory microanalyses obtained: C $\pm$ 0.35, H $\pm$ 0.25, P $\pm$ 0.30. All new compounds shown IR (film) absorption bands characteristic for a POC moiety: broad bands between 1170–1105 cm^{-1}, ref. [28].

As shown in Table I, the simple dichloridites (**b–d**), as well as those containing the most commonly used protecting groups (methyl, 2,2,2-trichloroethyl, 2-cyanoethyl and benzyl[9]), are formed in good yields (**a**, **e–g**).

It is also worth noting that mild conditions of the exchange procedure allow obtaining dichlorides, which contain carboester and carboamide functional groups, in excellent yields (**i–k)**. However, dichloridites **3j**,**k** appear to be unstable, and cyclic chlorophosphoroamidites have been formed. It has been found that the phosphorodichloridite **3k**, formed as a primary product of the exchange reaction, gave quantitatively the cyclic chlorophosphoroamidite **3l**[10] after 7 days (^{31}P NMR) (Scheme 2b). The dichloridite **3j** was found to be stable at room temperature.

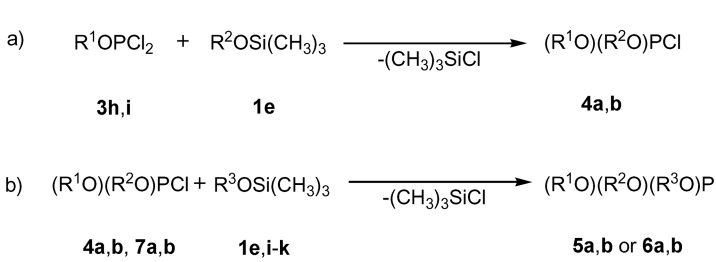


3k **3l**

SCHEME 2b

Synthesis of Mixed Alkyl Chloridites 4, Mixed Trialkyl Phosphites 5, and Their Derivatives 6

The successful application of the exchange method to the synthesis of phosphorodichloridites encouraged us to attempt the preparation of mixed dialkylphosphorochloridites **4** and mixed trialkylphosphites **5**. These compounds have been obtained according to Scheme 3. Dichloridites **3h**,**i**, as well as 2-chloro-(1,3,2)dioxaphospholane (**7a)** and the trimethylsilylated alcohols **1e**, **i**–**k**, have been used to produce the mixed chloridites **4a**,**b** and the mixed trialkylphosphites **5a**,**b**. 2-Chlorobenzo(1,3,2)dioxophosphinin-4-one (**7b**) was also used as a phosphitylating agent giving the trialkylphosphites **6a**,**b** in the reaction with **1j** and **1k**.



1e: $R^2 = C_6H_5CH_2$; **1i**: $R^2 = C_2H_5OC(O)CHCH_3$; **1j**: $R^2 = C_{15}H_{31}C(O)NHCH_2CH_2$;
1k: $R^2 = (CH_3)_3COC(O)NHCH_2CH_2$;
3h: $R^1 = CH_3(CH_2)_8CH_2$; **3i**: $R^1 = C_2H_5OC(O)CHCH_3$;
4a: $R^1 = CH_3(CH_2)_8CH_2$, $R^2 = C_6H_5CH_2$; **4b**: $R^1 = C_2H_5OC(O)CHCH_3$, $R^2 = C_6H_5CH_2$;
5a: $R^1 = C_2H_5OC(O)CHCH_3$, $R^2 = R^3 = C_6H_5CH_2$; **5b**: $R^1 = R^2 = -CH_2CH_2-$, $R^3 = CH_3(CH_2)_8CH_2$;
6a: $R^1 = R^2 =$ -o-$C_6H_4C(O)$-, $R^3 = (CH_3)_3COC(O)NHCH_2CH_2$;
6a: $R^1 = R^2 =$ -o-$C_6H_4C(O)$-, $C_{15}H_{31}C(O)NHCH_2CH_2$.

SCHEME 3

Yields, physical constants, and some spectroscopic data of **4**, **5**, and **6** are shown in Table II.

TABLE II Chlorophosphoridites (R^1O) (R^2O)PCl, 4, Trialkylphosphites (R^1O)(R^2O)(R^3O)P, 5, and Their Analogues 6

Starting Materials		Products							
Silylated alcohol Z = $OSi(CH_3)_3$	Chlorophosphine		R^1	R^2	R^3	Yield[a] %	B.p. [°C]/Torr	^{31}P NMR Δ(ppm)	Lit. or Mol. formula[f] (Mol. Weight)
$C_6H_5CH_2Z$ **1e**	$CH_3(CH_2)_8CH_2OPCl_2$ **3h**	**4a**	$CH_3(CH_2)_8CH_2$-	$C_6H_5CH_2$-		*b*	*d*	167.0	$C_{17}H_{28}ClO_2P$ (330.82)
$C_6H_5CH_2Z$ **1e**	$C_2H_5OC(O)CH(CH_3)OPCl_2$ **3i**	**4b**	$C_2H_5OC(O)CHCH_3$	$C_6H_5CH_2$-		*c*	*d*	165.8	$C_{12}H_{16}ClO_4P$ (290.68)
$C_6H_5CH_2Z$ **1e**	$C_2H_5OC(O)CH(CH_3)OPCl_2$ **3i**	**5a**	$C_2H_5OC(O)CHCH_3$	$C_6H_5CH_2$-	$C_6H_5CH_2$-	*d, e*	*d*	139.2	$C_{18}H_{23}O_5P$ (362.35)
$C_2H_5O(CO)CHCH_3Z$ **1i**	X-PCl-Y XY = -OCH_2CH_2O- **7a**	**5b**	-CH_2CH_2-		$C_2H_5OC(O)C(CH_3)CH$-	89	70–73/0.2 69–74/02[29]	136.2	[29]
$(CH_3)_3COC(O)NH(CH_2)_2Z$ **1k**	X-PCl-Y XY = -o-$OC_6H_4C(O)O$- **7b**	**6a**	-o-$C_6H_4C(O)$-		$(CH_3)_3COC(O)NHCH_2CH_2$-	*e*	*d*	125.3	$C_{14}H_{18}NO_6P$ (327.27)
$C_{15}H_{31}C(O)NHCH_2CH_2Z$ **1j**	X-PCl-Y XY = -o-$OC_6H_4C(O)O$- **7b**	**6b**	-o-$C_6H_4C(O)$-		$C_{15}H_{31}C(O)NHCH_2CH_2$-	*e*	*d*	124.9	$C_{25}H_{40}NO_5P$ (465.56)

[a]Reaction time: **4a**,**b**, **5a** 14 days; **5b** 24 h, **6a**,**b** 3 d; in case of **5a** two equivalents of silylated alcohol were used.

[b]Crude oil contains 95 mol % of product and 5 mol % of $CH_3(CH_2)_8CH_2OP(OCH_2C_6H_5)_2$.

[c]Crude oil contains 97–98 mol % of product and $(C_6H_5\text{-}CH_2O)_2PCl$.

[d]Unstable at elevated temperature.

[e]Crude oil contains 95–97 mol % of product.

[f] Satisfactory microanalyses obtained: C ± 0.35, H ± 0.25, P ± 0.30. All compounds show IR (film) absorption bands characteristic for the POC moiety: broad bands between 1170–1105 cm^{-1}.[28]

All compounds **4–6** are unstable at higher temperatures and could not be distilled even at low pressure, with exception of **5a**, which was obtained in 89% yield by vacuum distillation.

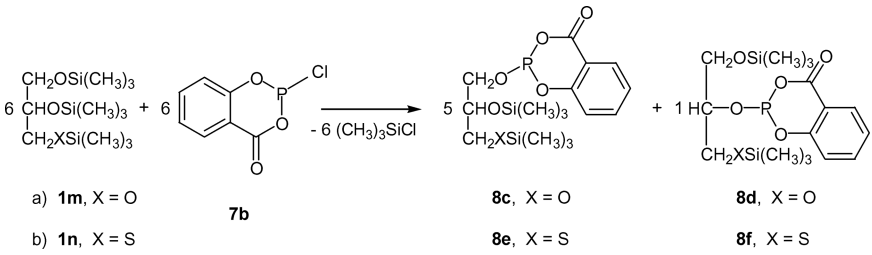
The mixed chloridites **4a**,**b**, the mixed trialkyl phosphite **5b**, and the analogs **6a**,**b** containing rather large alkyl substituents were obtained as oils in high yields (more than 95%, see Table II). Their stability at room temperature is presumably connected with the low ability of the two different bulky alkoxy substituents to undergo mutual exchange between two molecules of the mixed chloridites or mixed trialkylphosphites, respectively.

Chemoselectivity

Careful attention has been paid to investigate the chemoselectivity of the exchange reaction ($P^{III}Cl/ROSiR'_3$) of the *P*-chlorine ligand with:

a) Alkoxy groups of primary and secondary alkoxytrimethylsilanes
b) Alkoxy groups and thioalkoxy groups of alkoxytrimethylsilanes and thioalkoxy-trimethylsilanes. Chemoselectivity was studied by examining two model reactions:

a) 2-chlorobenzo-(1,3,2)-dioxaphosphinin-4-one (**7b**) with tris-*O*, *O*, *O*-trimethylsilyl-glycerol (**1m**), Scheme 4 (a)
b) 2-chlorobenzo-(1,3,2)-dioxaphosphinin-4-one (**7b**) with tris-*S*, *O*, *O*-trimethylsilylthio-glycerol (**1n**), Scheme 4 (b)



SCHEME 4

The results are given in Table III. In each case, two trivalent organophosphorus esters **8c**,**d** and **8e**,**f** were formed in almost quantitative yields. The structures of **8c**,**d** and **8e**,**f** and their molar ratios have been determined from spectral data (^1H, ^{31}P NMR, Experimental section, see also hydrolyses of the esters). It was found that in the first model reaction (Scheme 4a), the ester **8c** possessing phosphitylated

TABLE III Reaction of 2-Chlorobenzo(1,3,2)dioxaphosphinin-4-one (7b) with Tris-*O,O,O*-trimethylsilylglycerol (1m) and Tris-*S,O,O*-trimethylsilylthioglycerol (1n)

Starting Silylated Alcohol	Products[a] XY = - o-$OC_6H_4C(O)O$-	^{31}P-NMR δ(ppm)	Isomers ratio
$(CH_3)_3SiOCH_2$ CH[$OSi(CH_3)_3$] $CH_2OSi(CH_3)_3$ **1m**	$(CH_3)SiOCH_2$ CH[$OSi(CH_2)_3$] $CH_2OP(XY)$ **8c**	125.5	**8c:8d** (5:1)[b]
	$(CH_3)_3SiOCH_2$ $CH(OPXY)CH_2OSi(CH_3)_3$ **8d**	125.6	
$(CH_3)_3SiSCH_2$ CH[$OSi(CH_3)_3$] $CH_2OSi(CH_3)_3$ **1n**	$(CH_3)_3SiSCH_2$ CH[$OSi(CH_3)_3$] $CH_2OP(XY)$ **8e**	124.9	**8e:8f** (5:1)[b]
	$(CH_3)_3SiSCH_2CH(OPXY)$ $CH_2OSi(CH_3)_3$ **8f**	125.4	

[a]Crude oil contains 96–98 mol % of product; the isomer mixture has not been subjected to elemental microanalysis; reaction time in each case 24 h at –65°C and then 4 h at 20°C.

[b]The ratio of the isomers has been confirmed chemically. The exchange products were hydrolyzed to $HOCH_2CH(OH)CH_2OP(O)H(OH)$ (**9c**) and $(HOCH_2)_2CHOP(O)H(OH)$ (**9d**), as well as $HSCH_2CH(OH)CH_2OP(O)H(OH)$ (**9e**) and $HSCH_2CH[OP(O)H(OH)]CH_2OH$ (**9f**), respectively, and their molar ratio has been determined by ^{1}H and ^{31}P NMR spectroscopy. The ratio was 5:1 in each case (see the Experimental section). There is no evidence for the formation of thiophosphitylated esters.

hydroxy group at a primary carbon atom was the major product. Molar ratio of **8c:8d** was **5:1**. In the second reaction (Scheme 4b), two esters possessing phosphitylated hydroxy group at primary (**8e**) and secondary (**8f**) carbon atoms were also formed in molar ratio **8e:8f** = 5:1. In the latter case, *S*-phosphitylatet ester has not been found among the reaction products (see the Experimental section). On the basis of our results, it can be concluded that the exchange rate of chlorine atom of chlorophosphine by alkoxy and thioalkoxy group is as follows:

$$R^{I}OSi(CH_3)_3 > R^{II}OSi(CH_3)_3 \gg RSSi(CH_3)_3$$

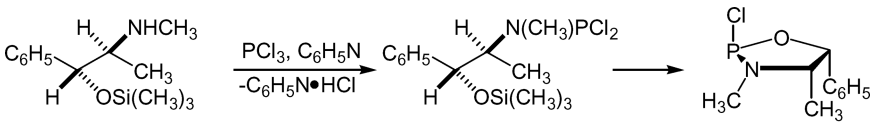
R^{I} – primary alkyl group, R^{II} – secondary alkyl group

It might be expected that the higher reactivity of alkoxy groups containing a primary carbon atom in the exchange reaction is due to the different steric requirements of the alkoxy ligands. However, the higher reactivity of the alkoxy group compared to that of the tioalkoxy

group in the exchange reaction should depend on different nature and reactivity of the C-O-Si and C-S-Si bonds in these reagents.

Comparison of PCl Reactivity Towards Trimethylsilyl Alcohols (Exchange Reaction, $P^{III}Cl/ROSiR'_3$) and Towards Secondary Amines (Substitution Reaction, $P^{III}Cl/HNR_2$)

The rate of exchange reaction between the PCl group and silyloxy moiety of alkoxytrimethylsilanes and the rate of the substitution reaction of PCl moiety by secondary amines have been investigated using model reaction between PCl_3 and *O*-tri-methylsilyl-(-)-ephedryne (**1l**) in the presence of pyridine (Scheme 5). The course of this reaction has been monitored by ^1H, ^{13}C, and ^{31}P NMR spectroscopy. It has been found that the primary product of this reaction—the enantiomeric phosphoroamidodichloridite **10**—was transformed into the optically pure cyclic chlorophosphoroamidite, (2*R*,4*S*,5*R*)-2-chloro-3,4-dimethyl-5-phenyl-(1,3,2)oxazaphospholidine (**11**),[11a,b] during 24 h at room temperature. The assignment of *trans* configuration between the chlorine atom and the substituents of the oxazaphospholidine ring in **11** is based on the value of $^3J_{PH}$ between the phosphorus atom and the hydrogen atom connected to the benzyl carbon atom.[11c]



(*1R*,*2S*)-**1l** **10** (*2R*,*4S*,*5R*)-**11**

SCHEME 5

Our results show that the substitution of chlorophosphine by the secondary amine proceeds faster than the exchange reaction between the PCl moiety and alkoxytrimethylsilane. Of course the final products are the result of the internal exchange reaction of the $P^{III}Cl$ and $ROSi(CH_3)_3$ moieties of **10**.

CONCLUSION

Phosphorodichloridites, mixed phosphorochloridites, and mixed phosphites are easily prepared by HCl-catalyzed exchange reaction of the chlorine atoms of the corresponding chlorophosphine and alkoxy ligands of an alkoxytrimethylsilane ($P^{III}Cl/ROSiR'_3$).

The exchange reaction is chemoselective, and in the case of primary and secondary alkoxytrimethylsilanes, the former are more reactive. The exchange reaction is also chemoselective with alkoxy and thioalkoxy ligands. The alkoxy ligands are more reactive than the thioalkoxy ones.

It was also established that the substitution of the PCl moiety by a secondary amine proceeds faster then the exchange reaction between the PCl moiety and an alkoxy ligand of alkoxytrimethylsilane.

EXPERIMENTAL

All reactions were carried out in atmosphere of argon not additionally dried. IR spectra were recorded using a Specord 71 IR C Zeiss spectrophotometer.

NMR spectra were obtained with a 250 Bruker Avance Spectrometer. Chemical shifts are reported as δ values using TMS as internal standard or 85% H_3PO_4 as an external standard. Solvents were obtained from commercial suppliers and used after typical purification and drying using molecular sieves.

All alcohols and thiols were obtained commercially with the exception of *N*-palmytoil etanolamine, which was prepared according to the literature procedure.[12] Commercially unavailable trimethylsilyl derivatives of alcohols, **1**, were obtained by the reaction of the alcohols (thiols) with trimethylchlorosilane/triethylamine or pyridine in ether: 3-(trimethylsilyloxy)propenenitryle (**1f**),[13] trimethyl(2,2,2-trichloroethoxy)silane (**1g**),[14] decyloxytrimethylsilane (**1h**) [15], ethyl (*R*, *S*)-2-(trimethylsilyloxy)propionate (**1i**) [16], *N*-palmitoylethanolamine trimethylsilyl ether (**1j**),[17] *N-boc*-etanolamine trimethylsilyl ether (**1k**), trimethylsilyl-(-)ephedrin (**1l**),[18] tris-*O*, *O*, *O*-trimethylsilyl glycerol (**1m**),[19,20] and tris-*S*, *O*, *O*-trimethylsilyl thioglycerol (**1n**).

1j: ^{1}H NMR ($CDCl_3$): $\delta = 0.12$ [s, 9H, $(CH_3)_3Si$], 0.87 (t, $^3J_{HH} = 6.5$ Hz, 3H, CH_3), 1.20–1.32 [m, 24H, $(CH_2)_{12}$], 1.60[m, $^3J_{HH} = 6.5$ Hz, 2H, $C\underline{H}_2CH_2C(O)$], 2.16 [t, $^3J_{HH} = 6.5$ Hz, 2H, $C\underline{H}_2C(O)$], 3.70 (m, $^3J_{HH} = 5.2$ Hz, 2H, CH_2N), 3.63 (t, $^3J_{HH} = 5.2$ Hz, 2H, CH_2O), 5.8 (1H, bs, NH).

1k: ^{1}H NMR ($CDCl_3$): $\delta =$ 0,03 [s, 9H, $(CH_3)_3Si$], 1.37 [s, 9H, $(CH_3)_3C$], 3.21 (m, 2H, CH_2N), 3.92 (m, 2H, CH_2O), 4.70 (m, 1H, NH), 7.00-8.23 (4H, arom-H).

1n: ^{1}H NMR ($CDCl_3$): $\delta =$ 0.21 [s, 9H, $(CH_3)_3Si$], 0.31 [s, 9H, $(CH_3)_3Si$], 0.36 [s, 9H, $(CH_3)_3Si$], 2.72, 2.89 (2H, AB system, $^3J_{AB} = 12.5$ Hz, $^3J_{HH} = 6.0$ Hz, CH_2S), 3.73, 3.81 (2H, AB system, $J_{AB} = 10.2$ Hz, $^3J_{HH} = 5.5$ Hz, $^3J_{HH} = 4.7$ Hz, CH_2O), 3.90 – 4.01 (m, $^3J_{HH} = 6.0$ Hz, $^3J_{HH} = 5.5$ Hz, $^3J_{HH} = 4.7$ Hz, 1H, CH).

1m: ^{1}H NMR (C_6D_6): $\delta = 0.19$ [s, 18H, $(CH_3)_3Si$], 0.27 [s, 9H, $(CH_3)_3Si$], 3.71, 3.79 (AB system, $J_{AB} = 10.2$ Hz, $^3J_{HH} = 5.7$ Hz, $^3J_{HH} = 4.8$ Hz, 4H, CH_2O), 3.93 (m, $^3J_{HH} = 5.7$ Hz, $^3J_{HH} = 4.8$ Hz, 1H, CHO).

Dichlorophosphoridites $ROPCl_2$ (3), Chlorophosphoridites $(R^1O)(R^2O)PCl$ (4), and Trialkylphosphites $(R^1O)(R^2O)(R^3O)P$ (5), as Well as Their Analogs (6): General Procedure

The trivalent phosphorus compound containing a P-Cl bond (0.01 mol) in methylene chloride (15 mL) was treated with the equimolar amount of alkoxytrimethylsilane under argon at –65°C. The tube was sealed and kept at –65°C for 3 h and then at room temperature for the time indicated in Tables I and II. After evaporation of the solvent and trimethylchlorosilane, the crude product was distilled under reduced pressure or kept under vacuum (45 °C, 0.5 h, 0.01 Torr). The results including yields, some physical and spectral properties are summarized in Tables I and II.

3h: ^{1}H NMR ($CDCl_3$): $\delta = 0.90$ (t, $J_{HH} = 6.5$ Hz, 3H, CH_3), 1.29 [m, 14H, $(CH_2)_7$], 1.72 (q, $J_{HH} = 6.5$Hz, 2H, $C\underline{H}_2CH_2O$), 4.25 (m, $^3J_{HH} = 6.5$ Hz, $^3J_{PH} = 7.7$ Hz, 2H, CH_2O).

3i: ^{1}H NMR ($CDCl_3$): $\delta = 1.25$ (t, $^3J_{HH} = 7.0$ Hz, 3H, CH_3), 1.55 (m, $^3J_{HH} = 7.0$ Hz, $^4J_{PH} = 0.5$ Hz, 3H, $C\underline{H}_3CH$), 4.19 (q, $^3J_{HH} = 7.0$ Hz, 2H, CH_2O), 5.10 (m, $^3J_{PH} = 13.5$ Hz, $^3J_{HH} = 7.0$ Hz, 1H, CHOP).

3j: ^{1}H NMR ($CDCl_3$): $\delta = 0.92$ (t, $^3J_{HH} = 6.7$ Hz, 3H, CH_3), 1.30 [m, 24H, $(CH_2)_{12}$], 1.70 (m, 2H, CH_2), 1.85 (m, 2H, CH_2), 3.51 (m, 2H, CH_2N), 4.14 (m, 2H, $CH_2O\underline{P}$), 5.31 (m, 1H, NH).

3k: ^{1}H NMR ($CDCl_3$): $\delta = 1.45$ (s, 9H, CH_3), 1.59 (s, 1H, NH), 3.40 (t, $^3J_{HH} = 5.0$ Hz, 2H, CH_2N), 4.25 (dt, $^3J_{HH} = 5.0$ Hz, $^3J_{PH} = 8.3$ Hz, 2H, CH_2OP), 5.1 (m, 1H, NH).

4a: ^{1}H NMR ($CDCl_3$): $\delta = 0.81$ (t, $^3J_{HH} = 6.5$ Hz, 3H, CH_3), 1.20 [m, 14H, $(CH_2)_7$], 1.68 (q, $J_{HH} = 6.5$ Hz, 2H, $C\underline{H}_2CH_2O$), 3.94 (m, $^3J_{HH} = 6.5$ Hz, $^3J_{HH} = 7.5$ Hz, 2H, CH_2O), 4.98 (d, $^3J_{PH} = 7.5$ Hz, 2H, CH_2Ar), 7.27–7.30 (5H, arom-H).

4b: ^{1}H NMR ($CDCl_3$): $\delta = 1.26$ (t, $^3J_{HH} = 7.0$ Hz, 3H, $CH_2C\underline{H}_3$), 1.28 (d, $^3J_{HH} = 7.0$ Hz, 3H, $CHC\underline{H}_3$), 4.19 (q, $^3J_{HH} = 7.0$ Hz, 2H, $CH_2OC{=}O$), 4.91 (q, $^3J_{HH} = 7.0$ Hz, 1H, CHOP), 7.35–7.38 (5H, arom-H).

5a: ^{1}H NMR ($CDCl_3$): $\delta = 0.81$ (t, $^3J_{HH} = 6.5$ Hz, 3H, CH_3), 1.20 [m, 14H, $(CH_2)_7$], 1.68 (q, $^3J_{HH} = 6.5$ Hz, 2H, $C\underline{H}_2CH_2O$), 4.07 (q, $^3J_{HH} = 6.5$ Hz, $^3J_{PH} = 6.5$ Hz, 4H, $CH_2C\underline{H}_2O$), 4.81 (d, $^3J_{PH} = 7.5$ Hz, 4H, CH_2Ph), 7.29–7.30 (10H, arom-H).

6a: ^{1}H NMR ($CDCl_3$): $\delta = 1.38$ [s, 9H, $(CH_3)_3C$], 3.21 (m, 2H, CH_2N), 3.92 (m, 2H, CH_2O), 4.70 (m, 1H, NH), 7.00–8.23 (4H, arom-H).

6b: ^{1}H NMR ($CDCl_3$): $\delta = 0.94$ (t, $^3J_{HH} = 6.7$ Hz, 3H, CH_3), 1.32 [m, 24H, $(CH_2)_{12}$], 1.64 [m, $^3J_{HH} = 6.7$ Hz, 2H, $C\underline{H}_2CH_2C(O)$], 2.14 [t, $^3J_{HH} = 6.7$ Hz, 2H, $CH_2C(O)$], 3.44–3.55 (m, 2H, CH_2N), 4.08 (m, 2H, CH_2O), 6.0 (br s, 1H, NH), 7.00–8.23 (4H, arom-H).

Reaction of 2-Chlorobenzo(1,3,2)dioxaphosphinin-4-one (7b) With Tris-*O,O,O*-trimethylsilylglycerol (1m) and Tris-*S,O,O*-trimethylsilylthioglycerol (1n)

The reaction was carried out as described above in the general procedure. The reaction time in each case was 25 h at –65°C and then 4 h at 20°C. The crude product obtained after filtration and evaporation of the solvent and trimethylchlorosilane has been kept under vacuum (45 °C, 0.5 h, 0.01 Torr). The results are summarized in Table III.

Isomers **8c** and **8d**: ^{1}H NMR ($CDCl_3$): $\delta = 0.12$, 0.13, 0.30 [s, 9H, $(CH_3)_3Si$], 3.75–4.07 (m, 5H, CH_2CHCH_2), 6.95–8.07 (4H, arom-H). ^{31}P NMR ($CDCl_3$): $\delta = 125.5$ (**8c**), 125.6 (**8d**), **8c**:**8d** = 5:1.

Hydrolysis of **8c** and **8d** gave 3-hydroxyphosphinyloxypropane-1,2-diol (**9c**) and 2-hydroxyphosphinyloxypropane-1,3-diol (**9d**).[29]

Isomers **9c** and **9d**: ^{1}H NMR (D_2O): $\delta = 3.50$–4.05 (m, 5H, CH_2-CH-CH_2 of **9a** and **9b**), 6.60 (d, $^1J_{PH} = 643$ Hz, 1H, **9a**), 6.73 (d, $^1J_{PH} = 640$ Hz, 1H, **9b**). ^{31}P NMR (D_2O): $\delta = 66.4$ (**9b**), 67.6 (**9a**), **9a**:**9b** = 5:1.

Isomers **8e** and **8f**: ^{1}H NMR ($CDCl_3$): $\delta = 0.21$, 0.32, 0.41, [s, 9H, $(CH_3)_3$)Si], 2.40–2.75 (m, 2H, CH_2S), 3.55–4.09 (m, 3H, CH-CH_2), 7.00–7.45 (4H, arom-H); ^{31}P NMR ($CDCl_3$): $\delta = 124.9$ (**8e**), 125.4 (**8d**), **8e**:**8d** = 5:1.

Hydrolysis of isomers **8e** and **8f** gave 3-hydroxyphosphinyloxy-2-hydroxy-1-thiol (**9e**) and 2-hydroxyphosphinyloxy-3-hydroxypropane-1-thiol (**9f**).

Isomers **9e** and **9f**: ^{1}H NMR (D_2O): $\delta = 2.30$–2.65 (m, 2H, CH_2S of **9e** and **9f**), 3.61–4.15 (m, 3H, CH-CH_2 of **9e** and **9f**), 6.65 (d, $^1J_{PH} = 6.6$ Hz, 14H, **9e**), 6.78 (d, $J_{PH} = 6.6$ Hz, 1H, **9f**). ^{31}P NMR (D_2O): $\delta = 6.9$ (**9f**), 8.0 (**9e**), **9e**:**9f** = 5:1.

Reaction of Trimethylsilyl-(-)-ephedrine with PCl_3 in the Presence of Pyridine

To a cooled (–65°C) chloroform-d solution (0.6 mL) of trimethylsilyl-(-)-ephedryne (**1l**) (0.19 g, 0.8 mmol) and pyridine (0.06 g, 0.8 mmol) in a NMR tube, was added in atmosphere of argon phosphorus trichloride (0.11 g, 0.8 mmol), and the mixture was kept at –65°C for 2 h. Then the mixture was allowed to warm up to 20°C and was kept at

that temperature for 24 h. During that period, the reaction mixture was analyzed qualitatively and quantitatively by means of ^{1}H and ^{31}P NMR spectroscopy at definite time intervals. The mixture consists of phosphoroamidodichloridite (**10**) and oxazaphospholidine (**11**). The molar ratio **10:11** changes with time as follows: 15:85 at 1 h, 35:65 at 5 h, 68:32 at 10 h, and 85:15 at 18 h. After 24 h, only compound **11** was observed. After evaporation of the solvent, hexane (2 mL) was added to the residue, and the mixture was filtered. The filtrate was evaporated to give analytically pure **11** as oil. Yield 99.5%.

When a similar experiment was interrupted at the point when the temperature of the reaction mixture had reached 20°C, it was possible in an analogous manner to isolate the phosphoroamidodichloridite **10** contaminated with the oxazaphospholidine **11** (7 mol %). Yield 98.2%.

10: ^{1}H NMR ($CDCl_3$): $\delta = 0.00$ [s, 9H, $(CH_3)Si$], 1.26 (m, $^{3}J_{HH} = 7.5$ Hz, $^{4}J_{PH} = 2.5$ Hz, 3H, $CHC\underline{H}_3$), 2.70 (d, $^{3}J_{PH} = 5.0$ Hz, 3H, NCH_3), 3.70 (m, $^{3}J_{PH} = 16.2$ Hz, $^{3}J_{PH} = 7.5$ Hz, $^{3}J_{HH} = 5.0$ Hz, 1H, CHN), 4.60 (d, $^{3}J_{HH} = 5.0$ Hz, 1H, CHO), 7.20–7.41 (5H, arom-H). ^{13}C NMR ($CDCl_3$): $\delta = -0.33$ [s, $Si(CH_3)_3$], 14.2 (d, $^{3}J_{PC} = 9.9$ Hz, $CH\underline{C}H_3$), 29.2 (d, $^{2}J_{PC} = 1.7$ Hz, NCH_3), 63.5 (d, $^{2}J_{PC} = 38.6$ Hz, $N\underline{C}H_3$), 77.0 (d, $^{3}J_{PC} = 5.7$ Hz, $\underline{C}HOSiMe_3$), 126.4, 127.4, 127.8, 127.9 (s, arom-C). ^{31}P NMR ($CDCl_3$): $\delta = 162.7$.

11: ^{1}H NMR ($CDCl_3$): $\delta = 0.68$ (d, $^{3}J_{HH} = 6.5$ Hz, 3H, $CHC\underline{H}_3$), 2.66 (dd, $^{3}J_{PH} = 16.0$ Hz, $^{4}J_{HH} = 2.7$ Hz, 3H, NCH_3), 3.62 (m, $^{3}J_{HH} = 6.5$ Hz, $^{3}J_{HH} = 8.0$ Hz, $^{3}J_{PH} = 7.0$ Hz, 1H, $C\underline{H}CH_3$), 5.78 (dd, $^{3}J_{HH} = 8.0$ Hz, $^{3}J_{PH} = 1.0$ Hz, 1H, CHO), 7.19–7.32 (5H, arom-H). ^{13}C NMR ($CDCl_3$): $\delta = 14.0$ (d, $^{3}J_{PC} = 5.3$ Hz, $CH\underline{C}H_3$), 28.5 (d, $^{2}J_{PC} = 14.0$ Hz, NCH_3), 57.5 (d, $^{2}J_{PC} = 6.7$ Hz, $N\underline{C}H_3$), 87.3 (d, $^{2}J_{PC} = 9.1$, CHO), 126.5, 127.0, 127.8, 127.9 (s, arom-C). ^{31}P NMR ($CDCl_3$): $\delta = 171.6$.

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