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Synthesis and Reactivity of Substituted Alkoxymethylphosphonites and Their Derivatives

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ABSTRACT: *Alkoxy-substituted methylphosphonites and their derivatives are prepared using an organomagnesium method of synthesizing the organophosphorus compounds and alkoxymethylation of various PH acids and their derivatives. Also, certain properties of these promising compounds as important precursors of new functionalized organophosphorue compounds with alkoxymethyl fragments are presented.* © 2012 Wiley Periodicals, Inc. Heteroatom Chem 23:281–289, 2012; View this article online at wileyonlinelibrary.com. DOI 10.1002/hc.21015

INTRODUCTION

The functionalized organophosphorus compounds with the various hydroxyl- or alkoxymethyl fragments and their derivatives containing tetracoordinated phosphorus have been intensively investigated in recent years; rather convenient methods of synthesis of these compounds have been proposed and their properties have been studied in detail [1–3]. Interesting biological activity of these compounds was found, so the well-known 1,2-epoxypropylphosphonic acid, also called phosphonomycin (fosfomycin), is a low molecular weight cell wall active antibiotic [2,4], and the substituted derivatives of hydroxymethylphosphonic acid, including the fragments of adenine (tenofovir, truvada, and viread) and cytosine (cidofovir), are effective antiviral drugs [3,5]. Also, various derivatives of substituted alkoxy- or hydroxymethyl phosphonites and their analogs present great interest as effective polydentate ligands and organophosphorus biomimetics of hydroxyl-substituted carboxylic acids [1–3]. Recently, we have proposed convenient methods for synthesis of the series of functionalized trimethylsiloxymethylphosphonites [6] and tris(alkoxymethyl)phosphines [7]. The present paper is devoted to the synthesis and study of the reactivity of substituted alkoxymethylphosphonites and their analogs, which are not available and almost unknown (cf. [1]).

RESULTS AND DISCUSSION

Following our previous investigations of dialkoxymethylation of some PH acids and their derivatives [8], we have studied the alkoxymethylation of PH acids by acetals of various structures, which have not previously been brought into this interaction [1]. We found that dialkoxymethanes, even on heating to 160–200°C, do not react with dibutyl and dibutoxyphosphines, or with dialkylphosphites. For dialkoxymethane activation, we used catalytic quantities of boron trifluoride etherate—a traditional reagent for generation of highly reactive alkoxycarbonium ions [8–12]. It was shown that

Dedicated to Professor Ivan F. Lutsenko (1912–1993).

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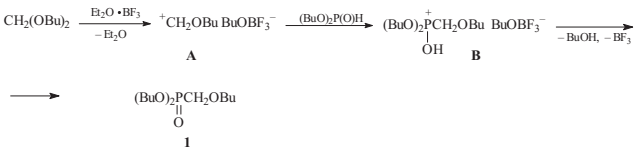
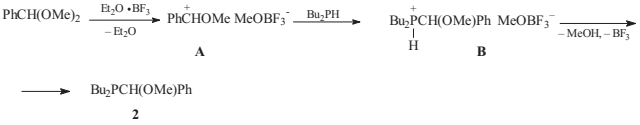
only dibutylphosphite enters into reaction with dibutoxymethane up to 180–200°C to yield butoxymethylphosphonate **1**. Apparently, the scheme of this interaction is similar to the Arbuzov reaction (Eq. (1)). The reaction begins with attack of an electrophilic complex **A** on the tricoordinated phosphorus atom of dibutylphosphite with formation of a phosphonium complex, the decomposion of which leads to butoxymethylphosphonate **1**.



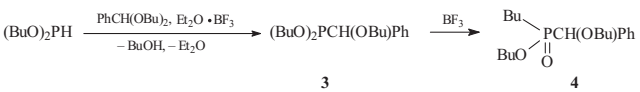
(1)

Under similar conditions, dibutylphosphine practically does not react with dibutoxymethane, whereas dibutoxyphosphine decomposes to tributylphosphite and polymer. Acetals of aliphatic aldehydes react with dialkylphosphites under these conditions to form a complex mixture of products, which is due to the instability of the intermediate alkyl-substituted alkoxycarbenium ions, which under the conditions of the reaction may be transformed to vinyl esters [12]. Much more active in the reactions with various PH acids are acetals of benzaldehyde and its derivatives. Thus, the highly nucleophilic dibutylphosphine reacts smoothly with dimethylacetal of benzaldehyde even at 100°C in the presence of boron trifluoride etherate to form methoxy(benzyl)phosphine **2** (Eq. (2)).



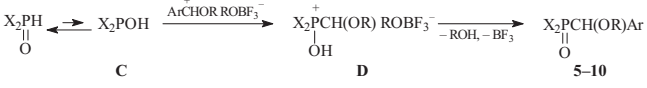
(2)

The reaction of dibutoxyphosphine with benzaldehyde dibutylacetal takes place under the same conditions; however, as a result of the reaction, in addition with phosphonite **3** we also obtained the product of its isomerization in the presence of boron trifluoride–phosphinate **4** (Eq. (3)).



(3)

The reaction of PH acids of trivalent phosphorus with acetals of benzaldehyde and its derivatives in the presence of boron trifluoride etherate takes place under more severe conditions (150–170°C) than for phosphines, which is due to the lower nucleophilicity and the low concentration of the reactive tautomer **C** with a tricoordinated phosphorus atom (Eq. (4)), (cf. Eq. (1)). The corresponding compounds **5–10** are obtained in high yields.

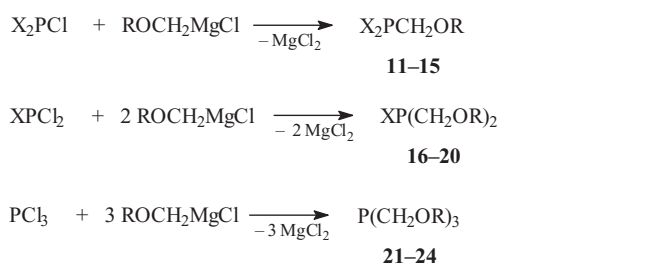


X = MeO (**5**), EtO (**6-9**), i-PrO (**10**); R = Me (**5,10**), Et (**6–9**);

Ar = Ph (**5,6,10**), 4-MeC_6H_4 (**7**), 4-$MeOC_6H_4$ (**8**), 4-ClC_6H_4 (**9**).

(4)

Note the compounds of this type may be synthesized in the absence of catalyst; however, in this case prolonged heating of the mixture (180–210°C) in a sealed ampul is required [1], due to the low electrophilicity of starting acetals as compared with intermediate complexes of the type **D**. Thus, the reaction of acetals of aromatic aldehydes with PH acids in the presence of boron trifluoride etherate as a catalyst is a convenient method of synthesizing alkoxymethylphosphonites and their derivatives. Also, for the first time, we have suggested the organometallic method of synthesis of several organophosphorus compounds with alkoxymethyl fragments using available alkoxymethylmagnesium chlorides, which are easily formed in high yields on the reaction of chloromethyl alkyl esters with magnesium in tetrahydrofuran (THF) at a temperature of the mixture of about −25°C [13–15]. Note that dialkoxymethyl compounds of magnesium have not been reported [16]; therefore, the possibilities of the organometallic method for the synthesis of (dialkoxymethyl)phosphonites and their derivatives are extremely limited (cf. [8]). So, the reaction of alkoxymethylmagnesium chlorides with various chlorophosphines proceeds under cooling to −70°C in THF in the presence of pyridine and leads to alkoxymethylphosphines and their derivatives **11–24** of various structures (Eq. (5)).



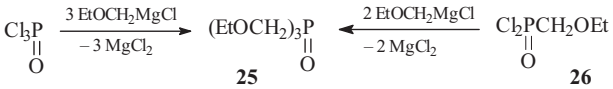
X = i-Pr (**11**), t- Bu (**16,17**), Ph (**12,18**), EtO (**19**), BuO (**13**), Me_2N (**14**), Et_2N (**15,20**);

R = Me (**12-14,16,18,21**), Et (**11,15,17,19,20,22**), Pr (**23**), Bu (**24**).

(5)

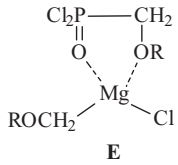
Note that tris(alkoxymethyl)phosphines **21–24** were yet obtained by using more expensive

tris(trimethylsilyl)phosphine (cf. [7]). Since alkoxymethylmagnesium chlorides are stable at temperature below −20°C, they cannot be introduced into a reaction with low activity phosphorus acids chlorides for which substitution of the chlorine atom takes place slowly and requires heating. So, on the reaction of di-*tert*-butylchlorophosphine with alkoxymethylmagnesium chlorides, formation of the corresponding alkoxymethylphosphine was not observed by ^{31}P NMR even in the reaction mixture, and the original chlorophosphine was returned in a yield of 90%. On the reaction with alkoxymethylmagnesium chlorides, acid chlorides of tetracoordinated phosphorus form in low yields (5%–10%); the corresponding oxides of alkoxymethylphosphines are strongly contaminated by oligomeric products of decomposition of the starting organomagnesium compounds. At the same time, it is interesting to note the different yields of oxide of tris(ethoxymethyl)phosphine **25**, which is formed on the reaction of ethoxymethylmagnesium chloride with phosphorus oxychloride (yield 13%) and dichloro ethoxymethyl phosphonate **26** (yield 44%) (Eq. (6)).



(6)

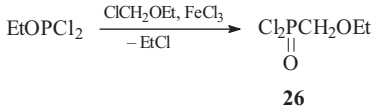
The significant increase in the yield of phosphine oxide in the latter case is apparently related to the formation of an intermediate complex **E** with participitation of the alkoxy and phosphoryl groups of the starting phosphonate **26**, in which there may be an increase in the reaction capacity of the alkoxymethylmagnesium chloride (Eq. (7)).



E

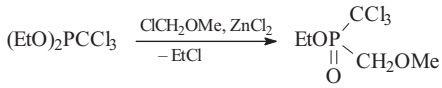
(7)

Thus, the organomagnesium method may successfully be used basically for the synthesis of alkoxymethylphosphines and their derivatives **11–25**. Note that dichlorophosphonate **26** was specially obtained by us via the interaction of highly reactive chloromethyl ethyl ether with dichloro ethyl phosphite in the presence of iron(III) chloride as a catalyst under heating to 90°C (cf. [1]) (Eq. (8)).



(8)

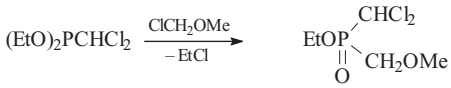
The unique reactivity of chloromethyl alkyl esters was used by us for preparing several functionalized organophosphorus compounds with alkoxymethyl fragments (see [8]). So it was reported previously that trichloromethylphosphonite **F** does not enter into the Arbuzov reaction [17]. We succeeded in rearrangement of phosphonite with chloromethyl methyl ether in the presence of zinc chloride, that is, under conditions of generation of a highly reactive methoxycarbenium ion, and the corresponding phosphinate **27** was obtained in high yield (Eq. (9)).



F **27**

(9)

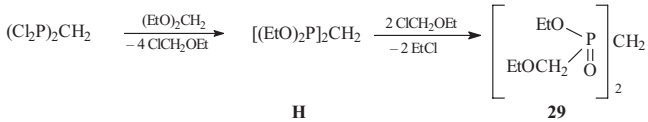
The more nucleophilic dichloromethylphosphonite **G** slowly reacts with chloromethyl methyl ether even when the mixture is boiled in the absence of catalyst to give phosphinate **28** (Eq. (10)).



G **28**

(10)

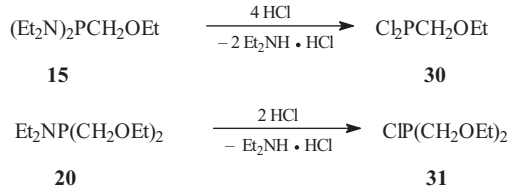
Also, for using chloromethyl ethyl ether as intermediate, the reaction of bis(dichlorophosphino)methane with an excess of diethoxymethane was carried out by us. The first step of this reaction is an exchange of chloro and ethoxy groups with formation of the bisphosphonite **H** and chloromethyl ethyl ether as intermediates, which were completely transformed under boiling of mixture into bisphosphinate **29** (cf. [8,18]), (Eq. (11)).



H **29**

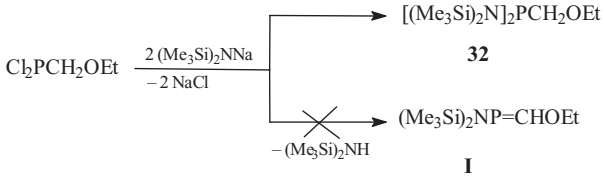
(11)

In contrast to dialkoxymethylphosphonites (cf. [8]), the high stability of the P—C bond in alkoxymethylphosphonites permits one to prepare chlorine-substituted alkoxymethylphosphines **30**, **31** via the treatment of the corresponding amino derivatives **15**, **20** with an excess of hydrogen chloride under mild conditions (Eq. (12)).



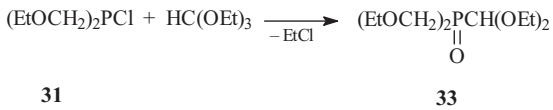
(12)

It is interesting to note that in distinction from dihalogen(halogenmethyl)phosphines, which reacts with 2 equiv of sodium bis(trimethylsilyl)amide to form halogen-substituted phosphaethylenes [19,20], dichloro(ethoxymethyl)phosphine **30** reacts under analogous conditions by the path of double nucleophilic substitution of the chlorine atom to form diamino(ethoxymethyl)phosphonite **32** but not the expected ethoxy-substituted phosphaethylene **I** (Eq. (13)).



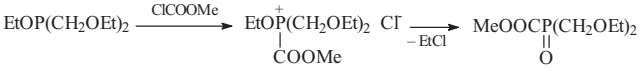
(13)

The impossibility of the dehydrochlorination reaction in this case and the formation of phosphaethylene **I** are due to the low CH acidity of the methylene component of the ethoxymethyl group (cf. [21]). Chlorophosphine **31** reacts with an excess of triethyl orthoformate via usual direction (cf. Eq. (11)) forming substituted phosphine oxide **33** in high yield (Eq. (14)), (cf. [8,22]).



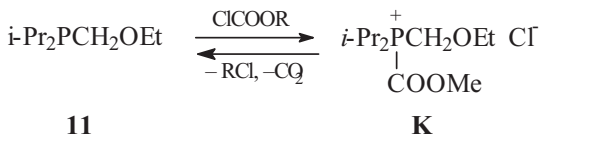
(14)

In contrast to dialkoxymethylphosphonites (cf. [8]), the interaction of bis(ethoxymethyl)-phosphinite **19** with methoxy chloroformate proceeds under mild conditions with retention of P—C bonds giving methoxycarbonylphosphine oxide **34**. So, the increase in the strength of the P—C bond and the decrease in the electrophilicity of the central carbon atom in the ethoxy group in the quasiphosphonium compound **J** lead to the usual direction of the Arbuzov reaction—dealkylation with the formation of phosphine oxide **34** (Eq. (15)).



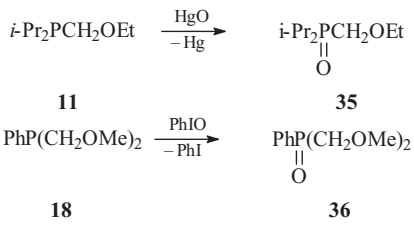
(15)

The reaction of diisopropyl(ethoxymethyl)-phosphine **11** with alkoxy chloroformates takes place in an unusual manner. Even at 20°C, one observes rapid liberation of a gas and the original phosphine remains in the reaction mixture, that is, the reaction amounts to decomposition of the alkoxy chloroformates to alkyl chloride and carbon dioxide. Consequently, the decomposition of quasiphosphonium compound **K** takes place with attack of a chlorine anion on the electrophilic carbon atom in the radical of the alkoxycarbonyl group with breakage of the labile P—C bond. A similar decomposition of alkoxy chloroformates is also observed in the presence of catalytic quantities of tertiary phosphines under 20°C, whereas in the presence of triethylamine the decomposition takes place on heating of the mixture to 40–60°C, which is in agreement with the data in the literature on the stability of alkoxy chloroformates [23] (Eq. (16)).



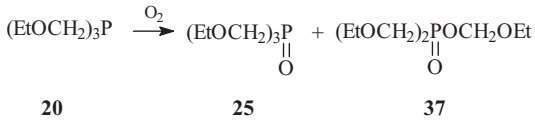
(16)

On the basis of alkoxymethyl derivatives of trivalent phosphorus using standard methods of oxidation and addition of sulfur, we suggested new unknown or alkoxymethyl compounds of phosphorus that are available with difficulty, including phosphoryl or thiophosphoryl groups. So, yellow mercury oxide and iodosobenzene smoothly oxidize alkoxymethylphosphines **11**, **18** to the corresponding oxides **35**, **36** on boiling in benzene (Eq. (17)).



(17)

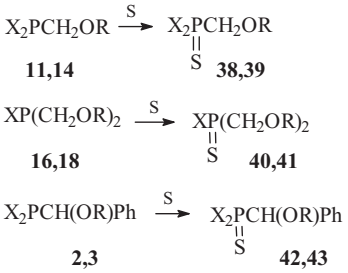
Note that oxidation of tris(ethoxymethyl)-phosphine **20** by dry atmospheric oxygen, even under moderate conditions, leads to a mixture of phosphine oxide **25** and phosphinate **37** formed due to insertion of oxygen in the P—C bond in a ratio 4:1 (Eq. (18)).



Phosphinate **37**, fragment $POCH_2$: δ_P 41.72 s; δ_H 5.12 d, $^3J_{PH}$ 12.

(18)

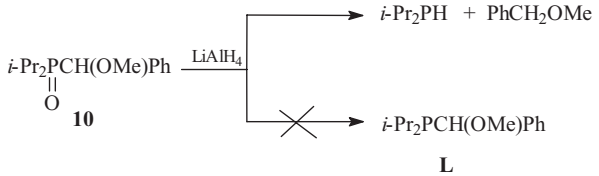
Sulfur is smoothly added to alkoxymethylphosphines during boiling in diethyl ether or benzene with formation of thiooxides **38–43** in high yields (Eq. (19)).



X = i-Pr (**11,38**), Bu (**2,42**), t-Bu (**16,40**), Ph (**18,41**), BuO (**3,43**), Me_2N (**14,39**); R = Me (**2,14,16,18,39-42**), Et (**11,38**), Bu (**3,43**).

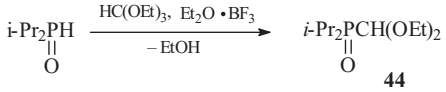
(19)

The reduction of the phosphine oxide **10** with an excess of lithium aluminum hydride results in the breakage of the P—C bond and formation of diisopropylphosphine and methylbenzyl ether, but not the expected phosphine **L** (Eq. (20)).



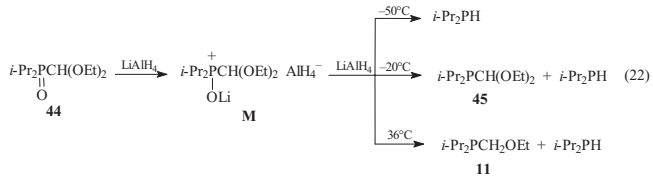
(20)

Also, we observed the lability of the P—C bond on the similar reduction or diethoxymethylphosphine oxide **44**, which was specially prepared via the interaction of diisopropylphosphine oxide and triethyl orthoformate in the presence of boron trifluoride diethyl etherate as a catalyst under heating to 150°C (cf. [8]) (Eq. (21)).



(21)

So, the direction of this reaction with an excess of lithium aluminum hydride is greatly dependent on the temperature conditions under which it is carried out. Under cooling to −50°C, the only product of the reaction is diisopropylphosphine—a product of breakage of the P—C bond in the intermediate compound **M** by the hydride anion (cf. [8]). When the reaction is carried out at −20°C, diisopropyl(diethoxymethyl)phosphine **45**—a product of usual reduction—was obtained with a yield of 30%. When the reaction mixture is boiled in ether (36°C), diisopropyl(ethoxymethyl)phosphine **11**—a product of the reduction of both the phosphoryl group and the diethoxymethyl fragment of the starting oxide 44—was obtained with a yield of 31%; in both cases, diisopropylphosphine was also found (Eq. (22)).



It should be noted that lithium aluminum hydride does not react with diisopropyl-(diethoxymethyl)phosphine **45** on boiling in diethyl ether, which shows the possibility of reduction of the diethoxymethyl fragment only at the stage of the complex **M** with the more electrophilic central carbon atom of the dialkoxymethyl group (cf. [8]).

Thus, in the present investigation, we found preparative methods for obtaining of alkoxy-substituted methylphosphonites and their derivatives; in addition, the detailed investigations of the reactivity of these promising compounds were carried out.

The structures of compounds **1–45** were confirmed by the ^1H, ^{13}C, and ^{31}P NMR spectra, which show characteristic signals of the central PCH_2O and other fragments by the tri- or tetracoordinated,

phosphorus (see Table 1). According to the NMR spectra, the compounds **4** and **29** are the mixtures of the stereoisomers. Their ratio was determined from the ^{1}H NMR and ^{31}P spectra. The elemental analysis data of synthesized compounds is summarized in Table 2.

EXPERIMENTAL

The ^{1}H, ^{13}C, and ^{31}P NMR spectra were registered on a Bruker Avance-400 spectrometer (400, 100, and 162 MHz, respectively), in $CDCl_3$ or C_6D_6 (**1–45**) against tetramethylsilane (TMS) (^{1}H and ^{13}C) and 85% H_3PO_4 in D_2O (^{31}P). All reactions were performed under dry argon in anhydrous solvents. Starting organic derivatives of trivalent phosphorus were prepared according to the procedures described in [24].

*O,O-Dibutyl Butoxymethylphosphonate (**1**)*

A mixture of dibutyl phosphite, 9.7 g, dibutoxymethane, 8 g, and boron trifluoride diethyl etherate, 0.3 g, was heated at 180–200°C for 1.5 h with the distillation of butanol. The residue was distilled to give 4.5 g of phosphonate **1**.

The compounds **2–10**, **44** were obtained similarly.

*Diisopropyl(ethoxymethyl)phosphine (**11**)*

A solution of 9.5 g pyridine in 10 mL of diethyl ether was added dropwise to a solution of 15.3 g of diisopropyl(chloro)phosphine in 100 mL of diethyl ether under stirring and cooling to −70°C; then a solution of ethoxymethylmagnesium chloride, which was cooled to −40°C and prepared from 3.1 g of magnesium and 12.3 g of chloromethyl ethyl ether in 80 mL of THF under cooling to −30°C, was added dropwise. The mixture was stirred with slow heating to room temperature, then diethyl ether, 100 mL, and a saturated solution of sodium bicarbonate, 50 mL, were added to the mixture. The organic part was separated and dried with magnesium sulfate, the solvents were removed, and the residue was distilled to give 11.2 g of phosphine **11**.

The compounds **12–25** were obtained similarly.

*O-Ethyl(trichloromethyl)-methoxymethylphosphinate (**27**)*

The mixture of diethyl trichloromethylphosphonite, 8.1 g, chloromethyl methylether, 5.4 g, and zinc chloride, 0.1 g, was refluxed for 1.5 h, and then it was distilled to give 8 g of phosphinate **27**.

The compounds **26–29** were prepared in a similar way.

*Dichloro(ethoxymethyl)phosphine (**30**)*

Dry hydrogen chloride, 16 g, which was obtained from 27 g of ammonium chloride, and excess of concentrated sulfuric acid was bubbled into a solution of 23.4 g of bis(diethylamino)ethoxymethylphosphine **15** in 250 mL of pentane with stirring and cooling to −40°C. The mixture was slowly heated to room temperature and was diluted with 200 mL of pentane. The precipitate was separated, the solvent was removed, and the residue was distilled to give 10.4 g of phosphine **30**.

Phosphine **31** was prepared similarly.

*Bis[bis(trimethylsilyl)amino]-ethoxymethylphosphine (**32**)*

A solution of 1 M sodium bis(trimethylsilyl)amide in diethyl ether, 100 mL, was added to a solution of 7.5 g of dichloro(ethoxymethyl)phosphine **30** under stirring and cooling to −70°C, The mixture was left for 2 h and then was diluted with 100 mL of pentane. The precipitate was separated, the solvents were removed, and the residue was distilled to obtain 9.8 g of phosphine **32**.

*Diethoxymethylbis(ethoxymethyl)phosphine Oxide (**33**)*

Chlorobis(ethoxymethyl)phosphine **31**, 5.2 g, was added by stirring to triethyl orthoformate, 5.3 g; and the obtained mixture was heated under 100°C for 1 h and was distilled to give 6.5 g of oxide **33**.

*Methoxycarbonylbis(ethoxymetyl)phosphine Oxide (**34**)*

Methoxy chloroformate, 3.4 g, was added to a solution of 6.8 g of phosphinite **19** in 15 mL of benzene. The mixture was heated to boil, the solvent was removed, and the residue was distilled to give 6.7 g of oxide **34**.

The Interaction of Diisopropyl(ethoxymethyl)phosphine **11** *with Butoxycarbonyl Chloroformate*

Butoxy chloroformate, 4.1 g, was added to 5.3 g of phosphine **11**. The formation of a gas was observed, which was bubbled through a solution of calcium chloride in water with precipitation of calcium carbonate. The mixture was stirred for 1 h and then was

TABLE 1 Yields, Product Constants, and NMR Spectral Data (δ, ppm, J, Hz) for the PC^1H_nO Fragments of Compounds **1–45**[a]

No.	*Yield (%)*	*B.p. (°C), (p, mm Hg)*	n_D^{20}	$\delta_H C^1 Hd$	$^2J_{PH}$	δ (C^1) d	$^1J_{PC}$	δ_P, s^b
1	32	122 (1)	1.4345	3.60	8.0	64.69	110.1	21.12
2	87	104 (1)	[c]	4.42	1.5	78.49	4.3	−13.49
3	18	120 (1)	[c]	4.28	1.5	80.03	12.8	163.94
4	28	180 (1)	1.51.42	4.33	10.3	79.02	110.5	38.81
				4.38	10.1	77.85	108.1	38.03
				4.80	12.3	77.16	116.5	36.21
				4.88	12.0	78.43	109.2	38.78
5	85	118 (1)	1.5085	4.42[d]	16.2	80.12	112.1	20.61
6	83	121 (1)	1.4886	4.45	16.0	81.30	115.2	19.26
7	60	130 (1)	1.4892	4.38	16.1	79.18	114.3	18.75
8	54	155 (1)	1.4965	4.33	16.0	78.97	114.9	19.59
9	71	132 (1)	1.4995	4.35	16.3	79.96	115.5	17.66
10	78	128 (1)	1.5273	4.58	14.0	73.26	108.1	51.52
11	63	66 (8)	1.4565	3.75	5.4	72.65	5.2	0.11
12	80	133 (1)	1.6085	4.05	5.0	71.04	4.9	−21.64
13	72	60 (1)	[c]	3.51	8.5	70.65	10.9	165.30
14	38	53 (1)	1.4695	3.73	9.0	74.85	22.3	82.57
15	55	71 (1)	1.4685	3.73	9.0	73.57	21.1	77.74
16	35	55 (1)	[c]	3.67	5.0	68.24	7.2	−16.33
17	62	68 (1)	[c]	3.72	5.0	67.92	6.8	−15.85
18	64	94 (1)	[c]	[e]	[e]	68.96	6.4	−33.10
19	54	51 (1)	[c]	[f]	[f]	69.23	8.1	110.72
20	58	60 (1)	1.4600	[f]	[f]	71.42	9.1	37.03
21	59	74 (8)	[c]	3.75	4.8	68.15	7.5	−42.28
22	54	78 (1)	[c]	3.68	4.8	68.20	6.8	−42.08
23	61	104 (1)	[c]	3.70	5.0	74.65	5.0	−40.69
24	68	130 (1)	[c]	3.71	4.9	72.74	5.8	−41.11
25	44	104 (1)	1.4515	3.87	5.0	69.30	64.30	36.35
26	74	81 (10)	[c]	4.11	22.1	77.77	116.6	19.96
27[g]	86	92 (1)	1.4845	4.17	3.3	67.73	92.6	32.42
28[g]	86	94 (1)	1.4712	3.93	6.2	67.28	94.1	34.69
29[g]	43	142 (1)	1.4620	[f]	[f]	66.83	116.6	41.17
				[f]	[f]	67.64	117.2	40.60
30	65	51 (15)	[c]	3.90	18.2	79.87	56.8	166.68
31	67	39 (1)	[c]	3.98	10.4	74.09	39.9	75.13
32	51	122 (1)	1.4925	3.98	12.6	75.47	25.5	97.65
33[g]	84	105 (1)	1.4475	3.81	5.2	64.35	67.9	34.28
34[g]	85	115 (1)	1.4558	3.89	5.0	65.62	64.8	27.60
35	87	70 (1)	1.4560	3.65	7.1	68.95	65.3	49.74
36	86	130 (1)	1.5375	3.88	5.2	69.03	63.5	28.92
38	86	75 (1)	1.5035	3.78	6.2	69.94	64.7	64.30
39	84	68 (1)	1.5090	3.92	5.9	71.76	105.5	79.14
40	79	87 (1)	1.5107	3.92	4.2	75.61	66.7	54.91
41	85	140 (1)	1.5817	3.95	4.0	72.08	65.9	34.93
42[g]	87	143 (1)	1.5477	4.48	10.2	81.26	62.9	54.81
43	83	141 (1)	1.4980	4.50	13.0	104.10	108.7	88.83
44	76	86 (1)	1.4543	4.62	6.2	102.28	101.7	48.92
45	30	70 (2)	1.4572	5.02	2.3	106.55	3.3	−6.87

[a]All signals of alkyl, aryl, and trimethylsilyl fragments are in the standard area. The ratio of stereoisomers of compounds, %: **4**, 35:30:20:15; **29**, 55:45. Compound **37** was observed only in the mixture.
[b]Data of $^{31}P–\{^1H\}$ spectra.
[c]Because of the ease of oxidation and hydrolysis, the refractive index of this compound was not measured.
[d]In ^1H NMR spectrum for fragment $(MeO)_2P(O)$: δ_H 3.52 d, $^3J_{PH}$ 10.4, and 3.57 d, $^3J_{PH}$ 10.4.
[e]m ABX, δ (H_A) 4.05, δ (H_B) 3.95, ^2J (H_AH_B) 11.8, ^2J (H_AP) 4.3, and ^2J (H_BP) 6.5.
[f] Overlapping multiplets.
[g]Fragment for compounds: CCl_3, **27**, δ_C 98.12 d, $^1J_{PC}$ 107.5; $CHCl_2$, **28**, δ_H 6.02 d, $^2J_{PH}$ 2.1, δ_C 62.03 d, $^1J_{PC}$ 101.2; PCH_2P, **29**, δ_H 2.61 t, $^2J_{PH}$ 16.9 and 2.4–2.8 m ABXY, δ_C 25.83 t, $^1J_{PC}$ 79.9 and 25.15 t, $^1J_{PC}$ 81.0; PCHO, **33**, δ_H 4.80 d, $^2J_{PH}$ 8.1, δ_C 99.83 d, $^1J_{PC}$ 104.5; PC═O, **34**, δ_C 167.81 d, $^1J_{PC}$ 158.7; $(PrCH_2)_2P(S)$, **42**, δ_C 26.80 d, $^1J_{PC}$ 49.4 and 25.49 d, $^1J_{PC}$ 48.2.

TABLE 2 Elemental Analyses Data of Compounds[a]

			Calcd. (%)		Found (%)	
No	*Empirical Formula*	*Formula Weight*	*C*	*H*	*C*	*H*
2	$C_{16}H_{27}OP$	266.36	72.15	10.22	71.86	10.03
3	$C_{19}H_{33}O_3P$	340.44	67.03	9.77	66.85	9.59
4	$C_{19}H_{33}O_3P$	340.44	67.03	9.77	66.91	9.62
10	$C_{14}H_{23}O_2P$	254.31	66.12	9.12	65.83	8.91
11	$C_9H_{21}OP$	176.24	61.34	12.01	60.85	11.52
12	$C_{14}H_{15}OP$	230.24	73.03	6.57	72.78	6.52
13	$C_{10}H_{23}O_3P$	222.26	54.15	10.37	54.04	10.43
14	$C_6H_{17}N_2OP$	164.19	43.89	10.45	43.68	10.37
15	$C_{11}H_{27}N_2OP$	234.32	56.38	11.61	56.21	11.55
16	$C_8H_{19}O_2P$	178.21	53.92	10.75	54.20	10.62
17	$C_{10}H_{23}O_2P$	206.27	58.21	11.25	58.07	11.13
18	$C_{10}H_{15}O_2P$	198.20	60.60	7.63	60.42	7.55
19	$C_8H_{19}O_3P$	194.21	49.48	9.86	49.31	9.80
20	$C_{10}H_{24}NO_2P$	221.28	54.28	10.93	54.43	10.85
21	$C_6H_{15}O_3P$	166.16	43.37	9.10	43.11	8.98
22	$C_9H_{21}O_3P$	208.24	51.91	10.17	52.07	10.09
23	$C_{12}H_{27}O_3P$	250.32	57.58	10.87	57.35	10.65
24	$C_{15}H_{33}O_3P$	292.40	61.62	11.38	61.42	11.10
25	$C_9H_{21}O_4P$	224.24	48.21	9.44	48.03	9.28
26	$C_3H_7Cl_2O_2P$	176.97	20.36	3.99	20.20	3.91
27	$C_5H_{10}Cl_3O_3P$	255.47	23.50	3.94	23.69	3.90
28	$C_5H_{11}Cl_2O_3P$	221.02	27.16	5.01	27.48	5.07
29	$C_{11}H_{26}O_6P_2$	316.27	41.77	8.29	41.49	8.07
30	$C_3H_7Cl_2OP$	160.97	22.39	4.38	22.15	4.29
31	$C_6H_{14}ClO_2P$	184.60	39.04	7.64	39.31	7.54
32	$C_{15}H_{43}N_2OPSi_4$	410.83	43.85	10.55	43.59	10.47
33	$C_{11}H_{25}O_5P$	268.29	49.24	9.39	49.58	9.27
34	$C_8H_{17}O_5P$	224.19	42.86	7.64	42.49	7.56
35	$C_9H_{21}O_2P$	192.24	56.23	11.01	56.18	11.07
36	$C_{10}H_{15}O_3P$	214.20	56.07	7.06	56.38	7.13
38	$C_9H_{21}OPS$	208.30	51.90	10.16	52.23	10.07
39	$C_6H_{17}N_2OPS$	196.25	36.72	8.73	36.69	8.63
40	$C_8H_{19}O_2PS$	210.27	45.70	9.11	45.59	9.07
41	$C_{10}H_{15}O_2PS$	230.26	52.16	6.57	52.27	6.48
42	$C_{16}H_{27}OPS$	298.42	64.40	9.12	64.23	9.01
43	$C_{19}H_{33}O_3PS$	372.50	61.26	8.93	61.03	8.87
44	$C_{11}H_{25}O_3P$	236.29	55.91	10.66	55.90	10.75
45	$C_{11}H_{25}O_2P$	220.29	59.97	11.44	60.22	11.70

[a]The constants of compounds **1**, **5–9** are in agreement with the reported values [1,25,26]. Compound **37** was observed only in the mixture with compound **25**.

distilled to give 4.9 g starting phosphine **11**, yield 93%.

*Diisopropyl(ethoxymetyl)phosphine Oxide (**35**)*

The mixture of 3.4 g of phosphine **11**, 4.2 g of yellow mercury(II) oxide, and 10 mL of benzene was refluxed for 4 h. Then the organic solution was decanted, the solvent was removed, and the residue was distilled to give 3.2 g of oxide **35**.

Phosphine oxide **36** was obtained similarly using iodosobenzene.

*Diisopropyl(ethoxymetyl)phosphine Thiooxide (**38**)*

The mixture of 4.2 g of phosphine **11**, 0.8 g of sulfur, and 10 mL of benzene was refluxed for 0.5 h, then the solvent was removed, and the residue was distilled to give 4.3 g of thiooxide **38**.

The thiooxides **39–43** were synthesized similarly.

*The Interaction of Phosphine Oxide **10** with Lithium Aluminum Hydride*

A solution of 7.1 g of phosphine oxide **10** in 40 mL of diethyl ether was added under stirring to a mixture

of 1.1 g of lithium aluminum hydride and 50 mL of ether. The mixture was refluxed for 1 h and left for 1 day, and then an excess of lithium aluminum hydride was neutralized by moisture ether and water. The organic solution was separated and dried with magnesium sulfate; the solvent was removed and entrapped in low-temperature traps. The residue was distilled to give 2.7 g of methyl benzyl ether, yield 79%, bp 60°C (10 mmHg), n_D^{20} 1.5020. In ^{1}H NMR spectra, δ_H: 3.18 s (OMe), 4.28 s (OCH_2), 7.1–7.2 m (C_6H_5). The distillation of the trap contents gives 2 g of diisopropylphosphine, yield 61%, bp 60°C (120 mmHg), δ_P: 17.3 d, $^1J_{PH}$ 193.

The interaction of diisopropyl(diethoxymethyl)-phosphine oxide **44** with lithium aluminum hydride was carried out similarly, and the following results were obtained depending on the temperature of the reaction mixture: this interaction was carried out under −50°C to give only diisopropylphosphine, yield 64%; under −20°C: diisopropylphosphine, yield 59%, and diisopropyl(diethoxymethyl)phosphine **45**, yield 30%; under 36°C :diisopropyl(ethoxymethyl)phosphine **11**, yield 31%.

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