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Dedicated to the 115th anniversary of B.A. Arbuzov's birth

Synthesis of 4-(Dibromomethyl)benzaldehyde by Catalytic Debromophosphoryl- and Phosphonyloxylation of 1,4-Bis(dibromomethyl)benzene with Phosphorus(IV) Acid Methyl Esters and Its Properties

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Abstract—A new procedure has been developed for the simultaneous preparation of terephthalaldehyde and 4-(dibromomethyl)benzaldehyde by catalytic debromophosphoryl- and phosphonyloxylation of 1,4-bis-(dibromomethyl)benzene with P(IV) acid methyl esters. The reaction of 4-(dibromomethyl)benzaldehyde with ortho esters in the presence of sulfuric acid gave the corresponding acetals, whereas in the presence of $ZnCl_2$ terephthalaldehyde bis-acetals were formed. 4-(Dibromomethyl)benzaldehyde and its acetal were converted to methyl 4-(dibromomethyl)- and 4-(dimethoxymethyl)benzoates which were phosphorylated by the action of chlorophosphines, as well as by successive treatment with phosphorus(III) chloride and P(III) esters.

Keywords: 1,4-bis(dibromomethyl)benzene, four-coordinate phosphorus acid methyl esters, phosphorylation

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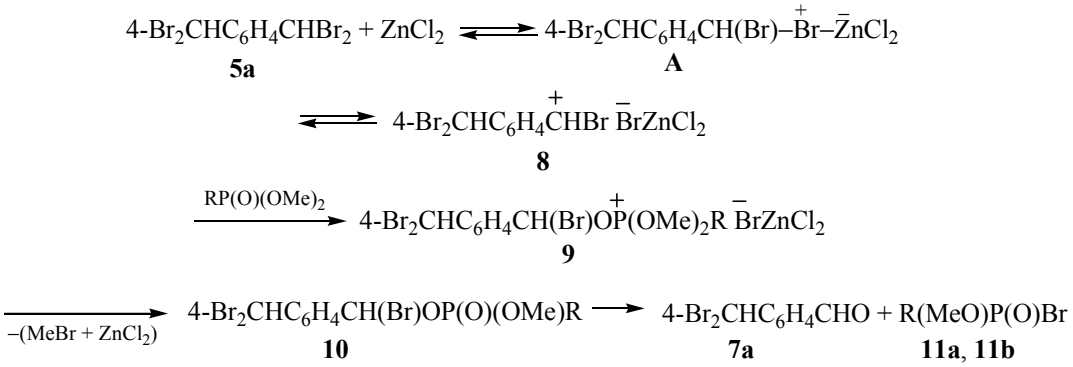
We previously described a new reaction of dimethyl phosphonates $RP(O)(OMe)_2$ **1** with benzylidene halides **2**, which afforded aromatic aldehydes and pyro phosphorus compounds $[R(MeO)P(O)]_2$ **3** or $[RP(O)O]_3$ **4** [1, 2]. This reaction has recently been extended to a compound containing two dibromomethyl groups, 1,4-bis(dibromomethyl)benzene (**5a**) [3–5]. For this purpose, dimethyl methylphosphonate (**1a**) and trimethyl phosphate (**1b**) were used. The thermally induced reaction was carried our at 170–180°C, and the products were terephthalaldehyde (**6**) and previously unknown 4-(dibromomethyl)benzaldehyde (**7a**). It should be noted that, among isomeric (dibromomethyl)benzaldehydes **7a**–**7c**, only 3-(dibromomethyl)-benzaldehyde (**7b**) has been reported. It was synthesized by reaction of 1,3-bis(dibromomethyl)-benzene (**5b**) with *N*,*N*-dimethylformamide at a temperature exceeding 140°C. However, neither experimental details nor characteristics of the product were given in [6]. We have developed a procedure ensuring simultaneous synthesis of compounds **6** and **7a**, the isolated yield of **7a** being 43% [3–5].

The main drawback of the noncatalytic version of this reaction is elevated temperature. In order to reduce the reaction temperature and shorten the reaction time we tried Lewis acids such as $AlCl_3$, $FeCl_3$, and $ZnCl_2$ to catalyze the process. Positive results were obtained only with the use of $ZnCl_2$; in this case, the reaction temperature was reduced from 180 to 130°C, and the reaction time was significantly shortened, from 8 to 3–4 h. Compounds **7a** and **6** were isolated by column chromatography in 53.5 and 7.5% yield, respectively. Thus, 4-(dibromomethyl)benzaldehyde described for the first time by us in [3–5] can be obtained with the best yield (53.5%) by the catalytic version of the reaction with the use of trimethyl phosphate which is the cheapest among P(IV) acid methyl esters.

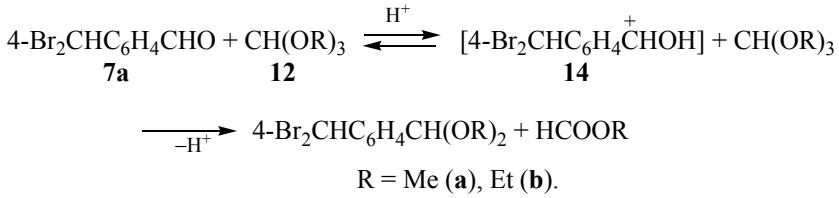
In keeping with the mechanism of activation of low reactive C_{sp^3}–Hlg bonds by Lewis acids [7], zinc chloride is likely to react with bromine of one dibromomethyl group with the formation of donor–acceptor complex **A** (Scheme 1) which is transformed to dipolar ion **8**. The positively charged CH carbon

Scheme 1.



R = Me (**a**), OMe (**b**).

Scheme 2.



R = Me (**a**), Et (**b**).

atom of **8** is then attacked by the phosphoryl oxygen atom of phosphonic (phosphoric) acid ester. The resulting quasiphosphonium salt **9** is converted to labile phosphoryloxy derivative **10** according to the second stage of the Michaelis–Arbuzov reaction, and compound **10** at elevated temperature (130°C) decomposes into aldehyde **7a** and bromophosphate **11a** or bromophosphonate **11b**. Reactions of the latter with the initial phosphorus ester (**1**) give rise to pyrophosphorus compounds **3** and **4**.

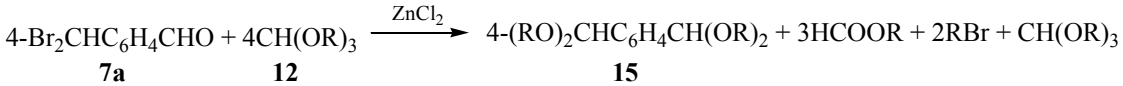
4-(Dibromomethyl)benzaldehyde (**7a**) is a heterofunctional compounds and it can be used as intermediate product for the synthesis of various polyfunctional organic compounds. Initially, we studied acetalization of **7a** with trialkyl orthoformates **12** in the presence of both Brønsted (sulfuric acid) and Lewis acids (zinc chloride). In the first case, the reaction involved only the aldehyde group to produce the corresponding acetals, 1-(dialkoxymethyl)-4-(dibromomethyl)benzenes **13a** and **13b** (Scheme 2). Presumably, the ortho ester reacted directly with protonated aldehyde **14**.

When the reaction was catalyzed by zinc chloride, the product was terephthalaldehyde bis-acetal **15** since $ZnCl_2$ is capable of activating not only the aldehyde group but also low reactive C–Br bond (Scheme 3). Excess ortho ester is necessary to avoid elimination of alkyl bromide from the intermediate α-bromo ether 4-$(RO)_2CHC_6H_4CH(OR)Br$ (**16**).

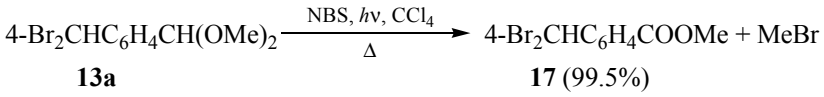
Aldehyde **7a** and acetal **13a** were oxidized with *N*-bromosuccinimide (NBS) (Scheme 4). Acetal **13a** was thus converted to the corresponding ester, methyl 4-(dibromomethyl)benzoate (**17**). Aldehyde **7a** reacted with NBS to give 4-(dibromomethyl)benzoyl bromide (**18**) which was isolated in the pure state. Bromide **18** readily reacted with trimethyl orthoformate to afford, depending on the reactant ratio, ester **17** (1 : 1) or **19** (1 : 5). Compound **19** was also obtained by acetalization of geminal dibromide **17** with trimethyl orthoformate in the presence of $ZnCl_2$.

Acetals **13** and **19** were used to synthesize new organophosphorus compounds (Scheme 5). They were readily phosphinylated with chlorophosphines **20** to obtain compounds **23** and **24**. The reaction is likely to

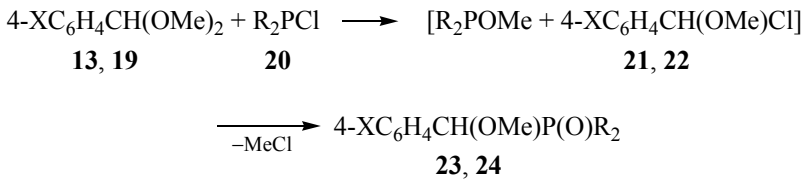
Scheme 3.



Scheme 4.



Scheme 5.



X = 4-Br_2CH (**13, 21**), COOMe (**19, 22**); X = $CHBr_2$, R = Ph (**23a**), Et (**23b**); X = COOMe, R = Ph (**24a**), Et (**24b**).

involve intermediate formation of α-chloro ethers **21** and **22**. The formation of the latter was confirmed experimentally by reacting acetals **13** with PCl_3 in the cold (Scheme 6). The structure of **21** was proved by ^1H NMR, as well as by reaction with P(III) esters **25** (after removal of excess PCl_3 and alkyl phosphorodichloridite from the reaction mixture).

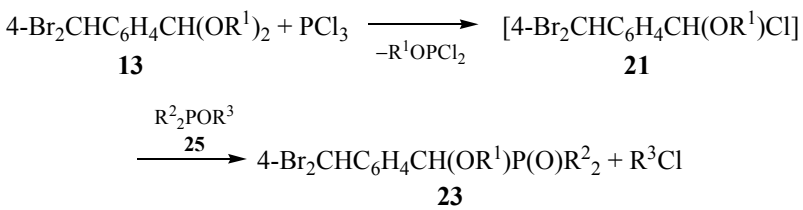
Phosphoryl derivatives **23** were converted to new benzaldehydes **26** containing a phosphorus atom in the side chain (Scheme 7). Compounds **23** reacted with pyridine to give solid dipyridinium salts **27**, and hydrolysis of the latter afforded aldehydes **26**.

In summary, we have developed a catalytic procedure for the simultaneous synthesis of terephthaldehyde and 4-(dibromomethyl)benzaldehyde, which allows significant reduction of the reaction temperature and shortening of the reaction time. 4-(Dibromomethyl)benzaldehyde is a promising intermediate product for organic synthesis, and it can be used to obtain new polyfunctional organic compounds.

EXPERIMENTAL

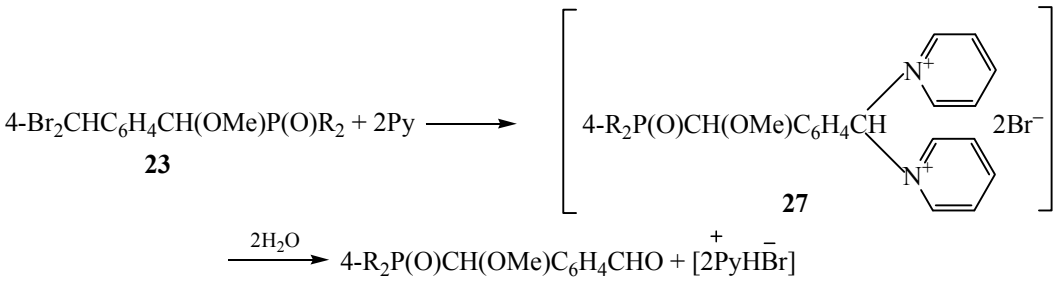
The ^1H and ^{13}C NMR spectra were recorded on Tesla BS–567A (100 MHz for ^1H) and Bruker Avance 400WB spectrometers (400.13 MHz for ^1H and 100.61 MHz for ^{13}C) using $CDCl_3$ as solvent. The ^{31}P NMR spectra were recorded on a Bruker Avance 400WB instrument at 161.98 MHz. The mass spectra

Scheme 6.



R^1 = Me (**21a**), Et (**21b**); R^1 = Me, R^2 = Ph (**23a**), Et (**23b**), OMe (**23c**), OEt (**23d**); R^1 = Et, R^2 = Ph (**23e**), OMe (**23f**).

Scheme 7.



R = Ph (**a**), Et (**b**).

were obtained on a Thermo Electron Corporation DFS GC/MS instrument (Germany); electron impact, 70 eV; ion source temperature 250°C; SGE BPX5 capillary column, 50 cm × 0.32 mm; carrier gas helium (ion peaks corresponding to the most abundant isotopes, in particular ^{79}Br, are given below).

Reaction of 1,4-bis(dibromomethyl)benzene (5a) with dimethyl methylphosphonate (1a). *a. Reactant ratio 1:1.* A mixture of 8.44 g (0.02 mol) of tetrabromide **5a** and 2.48 g (0.02 mol) of phosphonate **1a** was heated for 8 h at 170°C on an oil bath. The mixture was extracted with boiling isooctane (3 × 20 mL) by heating each time for 20 min under reflux and separating the isooctane solution by decanting. After cooling, crystals of a mixture of **5a**, **7a**, and **6** precipitated. By column chromatography with benzene as eluent we isolated 2.39 g (43%) of of 4-(dibromomethyl)benzaldehyde (**7a**) as colorless crystals with mp 89–90°C. ^1H NMR spectrum, δ, ppm: 6.66 s (1H, $CHBr_2$), 7.73 d and 7.89 d (4H, C_6H_4, $^3J_{HH}$ = 8.4 Hz), 10.02 s (1H, CHO). ^{13}C NMR spectrum, δ_C, ppm: 39.49 ($CHBr_2$), 127.35 and 130.06 (CH_{arom}), 137.04 and 147.39 (C_{arom}), 191.11 (CHO). Mass spectrum, *m*/*z* (I_{rel}, %): 247 (0.13) $[M - CHO]^+$, 197 (91.3) $[M - Br]^+$, 168 (7.8) $[M - CHO - Br]^+$, 89 (100.0) $[C_7H_5]^+$, 63 (77.5) $[C_5H_3]^+$, 50 (20.4) $[C_4H_2]^+$. Found, %: C 34.36; H 2.12; Br 57.41. $C_8H_6Br_2O$. Calculated, %: C 34.57; H 2.18; Br 57.50.

b. Reactant ratio 1:1; in the presence of $ZnCl_2$. A mixture of 8.44 g (0.02 mol) of tetrabromide **5a**, 2.48 g (0.02 mol) of phosphonate **1a**, and 0.27 g (0.002 mol) of anhydrous zinc chloride was heated for 3 h at 130°C. Extraction with boiling isooctane, followed by column chromatography with benzene as eluent, gave 0.97 g (11.5%) of unreacted compound **5a**, 2.23 g (45.3%) of aldehyde **7a** (mp 89–90°C), and 0.32 g (13.5%) of terephthalaldehyde (**6**) as colorless crystals with mp 115–116°C [8] (the yields were calculated on the reacted tetrabromide **5a**).

c. Reactant ratio 1.0:2.1; in the presence of $ZnCl_2$. A mixture of 8.44 g (0.02 mol) of compound **5a**, 5.21 g (0.042 mol) of phosphonate **1a**, and 0.27 g (0.002 mol) of zinc chloride was heated for 4 h at 130°C. The mixture was treated with hot isooctane (3 × 20 mL), the solvent was removed from the extract, the residue was dissolved in 40 mL of benzene, and the solution was washed with water (3 × 20 mL), dried over $MgSO_4$, and concentrated under reduced pressure. The residue was subjected to column chromatography using benzene as eluent to isolate 2.62 g (47.1%) of **7a** and 0.33 g (12.3%) of **6**.

Reaction of 1,4-bis(dibromomethyl)benzene (5a) with trimethyl phosphate (1b). *a. Reactant ratio 1.0:1.5.* A mixture of 4.22 g (0.010 mol) of compound **5a** and 2.10 g (0.015 mol) of ester **1b** was heated for 5.5 h at 180°C. The mixture was extracted with hot isooctane, the solvent was removed from the extract, and the residue was subjected to column chromatography using benzene as eluent to isolate 1.17 g (42.1%) of **7a** and 0.32 g (23.9%) of **6**.

b. Reactant ratio 1.0:2.1; in the presence of $ZnCl_2$. A mixture of 4.22 g (0.01 mol) of tetrabromide **5a**, 2.94 g (0.021 mol) of phosphate **1b**, and 0.14 g (0.001 mol) of zinc chloride was heated for 4 h at 130°C. The mixture was extracted with hot isooctane, the extract was washed with water, the solvent was removed, and the residue was subjected to column chromatography using benzene as eluent to isolate 0.06 g (1.4%) of unreacted **5a**, 1.47 g (53.5%) of **7a**, and 0.10 g (7.5%) of **6** (the yields were calculated on the reacted tetrabromide **5a**).

1-(Dibromomethyl)-4-(dimethoxymethyl)benzene (13a). One drop of sulfuric acid was added to a

mixture of 2.00 g (0.0072 mol) of compound **7a** and 3.06 g (0.0288 mol) of trimethyl orthoformate (**12a**). The reaction was accompanied by evolution of heat. The mixture was left to stand for 24 h at room temperature, and volatile components were removed under reduced pressure. Yield 2.22 g (98%), colorless oil. ^{1}H NMR spectrum, δ, ppm: 3.28 s (6H, Me), 5.40 s (1H, CHO_2), 6.62 s (1H, $CHBr_2$), 7.42 d and 7.55 d (4H, C_6H_4, $^3J_{HH}$ = 8.4 Hz). ^{13}C NMR spectrum, δ_C, ppm: 40.77 ($CHBr_2$), 52.81 (OMe), 102.37 (CHO_2), 126.48 and 127.11 (CH_{arom}), 139.94 and 142.02 (C_{arom}). Mass spectrum, *m/z* (I_{rel}, %): 247 (0.26) [*M* – $CH(OMe)_2]^+$, 199 (96.5) [*M* – OMe – Me – Br]$^+$, 168 (8.6) [*M* – $CH(OMe)_2$ – Br]$^+$, 89 (100.0) $[C_7H_5]^+$, 63 (80.9) $[C_5H_3]^+$, 50 (21.7) $[C_4H_2]^+$. Found, %: C 36.84; H 3.65; Br 49.21. $C_{10}H_{12}Br_2O_2$. Calculated, %: C 37.06; H 3.74; Br 49.32.

1-(Dibromomethyl)-4-(diethoxymethyl)benzene (13b) was synthesized in a similar way from 1.00 g (0.0036 mol) of aldehyde **7a** and 3.20 g (0.0216 mol) of triethyl orthoformate (**12b**). Yield 1.23 g (97%), colorless oil. ^{1}H NMR spectrum, δ, ppm: 1.23 t (6H, CH_2**Me**, $^3J_{HH}$ = 7.1 Hz), 3.54 q (4H, C**H**$_2$Me, $^3J_{HH}$ = 7.1 Hz), 5.50 s (1H, CHO_2), 6.63 s (1H, $CHBr_2$), 7.60 d and 7.69 d (4H, C_6H_4, $^3J_{HH}$ = 8.7 Hz). Found, %: C 40.71; H 4.43; Br 45.31. $C_{12}H_{16}Br_2O_2$. Calculated, %: C 40.91; H 4.55; Br 45.45.

1,4-Bis(dimethoxymethyl)benzene (15a). A mixture of 1.00 g (0.00360 mol) of compound **7a**, 1.53 g (0.01440 mol) of orthoeester **12a**, and 0.05 g (0.00036 mol) of zinc chloride was heated for 2 h at 80°C. Volatile components were removed under reduced pressure, and the residue was extracted with hot isooctane to isolate 0.80 g (98.8%) of 1,4-bis (dimethoxymethyl)benzene (**15a**) as colorless crystals with mp 53°C [9]. ^{1}H NMR spectrum, δ, ppm: 3.13 s (12H, OMe), 5.23 s (2H, CHO_2), 7.26 s (4H, C_6H_4). ^{13}C NMR spectrum, δ_C, ppm: 52.08 (OMe), 102.32 (CHO_2), 126.54 (CH_{arom}), 138.07 (C_{arom}).

1,4-Bis(diethoxymethyl)benzene (15b) was synthesized in a similar way from 1.00 g (0.00360 mol) of aldehyde **7a**, 2.13 g (0.01440 mol) of ortho ester **12b**, and 0.05 g (0.00036 mol) of zinc chloride. Yield 1.00 g (99%), colorless oil [10]. ^{1}H NMR spectrum, δ, ppm: 1.17 t (12H, OCH_2**Me**, $^3J_{HH}$ = 7.0 Hz), 3.49 q (8H, OCH_2, $^3J_{HH}$ = 7.0 Hz), 5.44 s (2H, CHO_2), 7.37 s (4H, C_6H_4).

Methyl 4-(dibromomethyl)benzoate (17). A solution of 2.03 g (0.0063 mol) of 1-(dibromomethyl)-4-(dimethoxymethyl)benzene (**13a**) and 1.12 g (0.0063 mol) of NBS in 10 mL of carbon tetrachloride was refluxed for 1 h in an inert atmosphere under irradiation. The precipitate of succinimide was filtered off, and the solvent was removed to isolate 1.93 g (99.5%) of compound **17** as colorless crystals with mp 70–71°C (from pentane). ^{1}H NMR spectrum, δ, ppm: 3.93 s (3H, COOMe), 6.63 s (1H, $CHBr_2$), 7.62 d and 8.03 d (4H, C_6H_4, $^3J_{HH}$ = 8.4 Hz). ^{13}C NMR spectrum, δ_C, ppm: 39.55 ($CHBr_2$), 52.24 (COO**Me**), 126.60 and 130.02 (CH_{arom}), 131.33 and 146.06 (C_{arom}), 165.65 (CO). Found, %: C 34.88; H 2.49; Br 51.81. $C_9H_8Br_2O_2$. Calculated, %: C 35.06; H 2.60; Br 51.95.

4-(Dibromomethyl)benzoyl bromide (18) was synthesized in a similar way from 5.00 g (0.018 mol) of 4-(dibromomethyl)benzaldehyde (**7a**) using 4.45 g (0.025 mol) of NBS; reaction time 4 h. Yield 4.25 g (66.1%), colorless crystals, mp 97–99°C (from CCl_4). ^{1}H NMR spectrum, δ, ppm: 6.63 s (1H, $CHBr_2$), 7.70 d and 8.10 d (4H, C_6H_4, $^3J_{HH}$ = 8.4 Hz). ^{13}C NMR spectrum, δ_C, ppm: 38.45 ($CHBr_2$), 127.14 and 132.25 (CH_{arom}); 126.74, 130.65, 135.92, and 148.44 (C_{arom}); 164.06 (CO). Found, %: C 26.67; H 1.31; Br 67.12. $C_8H_5Br_3O$. Calculated, %: C 26.89; H 1.40; Br 67.23.

Reaction of 4-(dibromomethyl)benzoyl bromide (18) with trimethyl orthoformate (12a). *a. Reactant ratio 1:1.* Ortho ester **12a**, 0.30 g (0.00280 mol), and zinc chloride, 0.04 g (0.00028 mol), were added to a solution of 1.00 g (0.00280 mol) of compound **18** in 5 mL of chloroform, and the mixture was heated for 30 min at 50°C. Removal of the solvent and volatile components under reduced pressure left 0.85 g (98.8%) of methyl 4-(dibromomethyl)benzoate (**17**) as colorless crystals with mp 70–71°C (from pentane).

b. Reactant ratio 1:5. A mixture of 3.00 g (0.00840 mol) of compound **18**, 4.46 g (0.04200 mol) of trimethyl orthoformate (**12a**), and 0.11 g (0.00084 mol) of zinc chloride was heated for 10 h at 80°C. Volatile components were removed under reduced pressure to leave 1.75 g (99.2%) of methyl 4-(dimethoxymethyl)benzoate (**19**) as colorless oil [11].

Methyl 4-(dimethoxymethyl)benzoate (19). A mixture of 0.63 g (0.0020 mol) of compound **17**, 0.85 g (0.0080 mol) of ortho ester **12a**, and 0.03 g (0.0002 mol) of zinc chloride was heated for 2 h at 80°C. Volatile components were removed under reduced pressure, and the residue was extracted with hot isooctane to isolate 0.34 g (81%) of ester **19** as colorless oil [11]. ^{1}H NMR spectrum, δ, ppm: 3.21 s

(6H, OMe), 3.84 s (3H, COOMe), 5.35 s (1H, CHO_2), 7.43 d and 7.94 d (4H, C_6H_4, $^3J_{HH}$ = 8.2 Hz). ^{13}C NMR spectrum, δ_C, ppm: 51.90 (COO**Me**), 52.12 (OMe), 101.82 (CHO_2), 126.79 and 129.46 (CH_{arom}); 126.53, 130.14, 130.76, and 142.81 (C_{arom}); 166.31 (CO).

{[4-(Dibromomethyl)phenyl](methoxy)methyl}diphenylphosphine oxide (23a). 1-(Dibromomethyl)-4-(dimethoxymethyl)benzene (**13a**), 2.02 g (0.0062 mol), was added dropwise with stirring to a solution of 1.37 g (0.0062 mol) of chloro(diphenyl)phosphine (**20a**) in 10 mL isooctane at such a rate that the temperature did not exceed 30°C. The mixture was then refluxed for 1.5 h and left to stand for 24 h at room temperature. The crystalline solid was filtered off and dried. Yield 2.45 g (80.1%), colorless crystals, mp 146–148°C (from isooctane). ^1H NMR spectrum, δ, ppm: 3.37 s (3H, OMe), 5.02 d (1H, PCH, $^2J_{PH}$ = 13.3 Hz), 6.56 s (1H, $CHBr_2$), 7.15–8.05 m (14H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 40.68 ($CHBr_2$), 58.97 d (OMe, $^2J_{PC}$ = 12.5 Hz), 83.08 d (PCH, $^1J_{PC}$ = 86.5 Hz); 126.37, 128.09, 128.16, 128.51, 128.63, 131.68, 131.76, 132.20, 132.54, 132.62 (CH_{arom}); 128.78, 128.76, 130.36, 130.87, 135.54, 141.67, 141.69 (C_{arom}). ^{31}P NMR spectrum (CCl_4): δ_P 28.2 ppm. Found, %: C 50.81; H 3.77; P 6.14. $C_{21}H_{19}Br_2O_2P$. Calculated, %: C 51.04; H 3.88; P 6.27.

{[4-(Dibromomethyl)phenyl](methoxy)methyl}diethylphosphine oxide (23b) was synthesized from 0.80 g (0.0064 mol) of chloro(diethyl)phosphine (**20b**) and 2.07 g (0.0064 mol) of compound **13a**. Yield 2.01 g (78.8%), colorless crystals, mp 147–149°C (from isooctane). ^1H NMR spectrum, δ, ppm: 0.97 d.t and 1.26 d.t (3H, PCH_2**Me**, $^3J_{HH}$ = 7.6, $^3J_{PH}$ = 15.2 Hz), 1.43–1.57 m (2H, PC**H**$_2$Me), 1.81–1.89 m (2H, PC**H**$_2$Me), 3.41 s (3H, OMe), 4.61 d (1H, PCH, $^2J_{PH}$ = 13.2 Hz), 6.61 s (1H, $CHBr_2$), 7.37 d and 7.56 d (4H, C_6H_4, $^3J_{HH}$ = 7.6 Hz). ^{13}C NMR spectrum, δ_C, ppm: 5.22 d and 5.48 d (PCH_2**Me**, $^2J_{PC}$ = 5.5 Hz), 16.84 d and 18.15 d (P**C**H$_2$Me, $^1J_{PC}$ = 65.4 Hz), 40.18 s ($CHBr_2$), 59.15 d (OMe, $^3J_{PC}$ = 11.6 Hz), 80.45 d (PCH, $^1J_{PC}$ = 78.3 Hz); 126.84, 126.96, 127.00 (CH_{arom}); 135.95 and 141.71 (C_{arom}). ^{31}P NMR spectrum (CCl_4): δ_P 50.8 ppm. Found, %: C 38.96; H 4.71; Br 39.97; P 7.64. $C_{13}H_{19}Br_2O_2P$. Calculated, %: C 39.21; H 4.82; Br 40.14; P 7.79.

{[4-(Dibromomethyl)phenyl](ethoxy)methyl}diphenylphosphine oxide (23e) was synthesized in a similar way from 1.32 g (0.006 mol) of phosphine **20a** and 2.11 g (0.006 mol) of acetal **13b**. Yield 2.65 g (86.9%), colorless crystals, mp 136–138°C (from isooctane). ^1H NMR spectrum, δ, ppm: 1.15 t (3H, OCH_2**Me**, $^3J_{HH}$ = 7.2 Hz), 3.35 q and 3.57 q (2H, OC**H**$_2$Me, $^3J_{HH}$ = 7.2 Hz), 5.13 d (1H, PCH, $^2J_{PH}$ = 13.2 Hz), 6.55 s (1H, $CHBr_2$), 7.15–7.93 m (14H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 15.27 (OCH_2**Me**), 40.53 ($CHBr_2$), 66.99 d (O**C**H$_2$Me, $^2J_{PC}$ = 11.2 Hz), 81.48 d (PCH, $^1J_{PC}$ = 86.4 Hz); 126.26, 127.74, 127.78, 127.88, 128.00, 128.27, 128.39, 131.72, 131.81, 131.91, 131.97, 132.50, 132.59 (CH_{arom}); 129.07, 130.30, 131.31, 131.42, 136.22, 141.47 (C_{arom}). ^{31}P NMR spectrum (CCl_4): δ_P 26.9 ppm. Found, %: C 51.71; H 4.03; P 5.95. $C_{22}H_{21}Br_2O_2P$. Calculated, %: C 51.99; H 4.17; P 6.10.

Methyl 4-[(diphenylphosphinyl)(methoxy)methyl]benzoate (24a). Methyl 4-(dimethoxymethyl)benzoate (**19**), 1.76 g (0.0084 mol), was added dropwise with stirring in inert atmosphere to a solution of 1.85 g (0.0084 mol) of phosphine **20a** in 3 mL of isooctane. The reaction was accompanied by evolution of heat. The mixture was refluxed for 2 h and left to stand for 24 h at room temperature. The solvent and volatile components were removed under reduced pressure to leave 2.93 g (91.8%) of compound **24a** as thick oil. ^1H NMR spectrum, δ, ppm: 3.18 s (3H, OMe), 3.69 s (3H, COOMe), 5.01 d (1H, PCH, $^2J_{PH}$ = 16.0 Hz), 7.03–7.76 m (14H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 51.99 (COO**Me**), 58.93 d (OMe, $^2J_{PC}$ = 12.5 Hz), 83.07 d (PCH, $^1J_{PC}$ = 86.4 Hz); 127.80, 127.84, 127.99, 128.11, 128.50, 128.61, 129.14, 131.73, 131.82, 132.23, 132.53, 132.62 (CH_{arom}); 128.18, 128.31, 128.39, 129.47, 131.33, 131.43, 131.61, 138.72 (C_{arom}); 166.62 (CO). ^{31}P NMR spectrum (CCl_4): δ_P 27.6 ppm. Found, %: C 69.25; H 5.41; P 8.08. $C_{22}H_{21}O_4P$. Calculated, %: C 69.47; H 5.53; P 8.16.

Methyl 4-[diethylphosphinyl(methoxy)methyl]benzoate (24b) was synthesized in a similar way from 0.92 g (0.0074 mol) of phosphine **20b** and 1.55 g (0.0074 mol) of ester **19**. Yield 2.01 g (95.7%), thick oil. ^1H NMR spectrum, δ, ppm: 0.86 d.t and 1.18 d.t (6H, PCH_2**Me**, $^3J_{HH}$ = 8.0, $^3J_{PH}$ = 16.0 Hz), 1.42–1.50 m and 1.80–1.90 m (4H, PC**H**$_2$Me), 3.30 s (3H, OMe), 3.80 s (3H, COOMe), 4.71 d (1H, PCH, $^2J_{PH}$ = 12.0 Hz), 7.39 d and 7.92 d (4H, C_6H_4, $^3J_{HH}$ = 8.0 Hz). ^{13}C NMR spectrum, δ_C, ppm: 5.14 d and 5.43 d (PCH_2**Me**, $^2J_{PC}$ = 5.0 Hz), 16.55 d and 17.79 d (P**C**H$_2$Me, $^1J_{PC}$ = 65.4 Hz), 51.83 (COO**Me**), 59.13 d (OMe, $^2J_{PC}$ = 11.8 Hz), 80.41 d (PCH, $^1J_{PC}$ = 78.5 Hz), 126.77 and 129.35 (CH_{arom}); 127.71, 129.29, 129.75, 129.92, 130.08, 139.08 (C_{arom}); 165.98 (CO). ^{31}P NMR spectrum (CCl_4): δ_P 52.8 ppm. Found, %: C 58.97; H 7.30; P 10.83. $C_{14}H_{21}O_4P$. Calculated, %: C 59.15; H 7.39; P 10.92.

1-[(Chloro)(methoxy)methyl]-4-(dibromomethyl) benzene (21a). In order to remove HCl impurity, 10 mL of PCl_3 was mixed with 0.75 g (0.0062 mol) of *N*,*N*-dimethylaniline at room temperature, and the mixture was distilled in a nitrogen atmosphere directly into the reaction flask. A solution of 2.00 g (0.0062 mol) of acetal **13a** in 1 mL of carbon tetrachloride was added dropwise to 1.70 g (0.0124 mol) of purified PCl_3, maintaining the temperature at –5 to 0°C. After 5 min, the mixture crystallized. Compound **21a** is thermally unstable, and it was identified without additional purification after removal of the solvent and volatile products in a high vacuum (0.05 mm) in the cold. ^{1}H NMR spectrum (5°C), δ, ppm: 3.68 s (3H, OMe), 6.43 s (1H, CHCl), 6.62 s (1H, $CHBr_2$), 7.42–7.62 m (4H, C_6H_4).

1-[(Chloro)(ethoxy)methyl]-4-(dibromomethyl)-benzene (21b) was synthesized in a similar way from 1.7 g (0.0124 mol) of PCl_3 and 2.0 g (0.0057 mol) of acetal **13b**. ^{1}H NMR spectrum (5°C), δ, ppm: 1.11–1.65 m (3H, OCH_2**Me**), 3.39–4.01 m and 4.01–4.62 m (2H, OC**H**$_2$Me), 6.45–6.83 m [2H, $CHBr_2$, CH(OEt)Cl], 7.41–7.82 m (4H, C_6H_4).

{[4-(Dibromomethyl)phenyl](methoxy)methyl}diphenylphosphine oxide (23a). Ethyl diphenylphosphinite, 0.87 g (0.0038 mol), was added dropwise to a solution of 1.25 g (0.0038 mol) of compound **21a** in 1 mL of diethyl ether on cooling to –5 to 5°C. The mixture was left to stand for 24 h at room temperature, and the solvent and volatile components were removed under reduced pressure. Yield 1.44 g (76.6%), colorless crystals, mp 146–148°C (from isooctane). The spectral characteristics of samples of **23a** synthesized by different methods were identical.

Dimethyl [4-(dibromomethyl)phenyl](methoxy)-methylphosphonate (23c) was synthesized in a similar way from 1.41 g (0.0043 mol) of compound **21a** and 0.53 g (0.0043 mol) of trimethyl phosphite. Yield 0.65 g (37.6%), colorless crystals, mp 95–96°C (from isooctane). ^{1}H NMR spectrum, δ, ppm: 3.40 s (3H, CHO**Me**), 3.70 d and 3.67 d (6H, POMe, $^3J_{PH}$ = 10.6 Hz), 4.49 d (1H, PCH, $^2J_{PH}$ = 16.0 Hz), 6.62 s (1H, $CHBr_2$), 7.15–7.70 m (4H, C_6H_4). ^{31}P NMR spectrum (CCl_4): δ_P 18.3 ppm. Found, %: C 32.64; H 3.62; P 7.58. $C_{11}H_{15}Br_2O_4P$. Calculated, %: C 32.86; H 3.77; P 7.70.

Diethyl [4-(dibromomethyl)phenyl](methoxy)-methylphosphonate (23d) was synthesized in a similar way from 2.00 g (0.0062 mol) of compound **21a** and 1.03 g (0.0062 mol) of triethyl phosphite. The product was isolated by column chromatography using ethyl acetate–benzene (3:2) as eluent. Yield 0.80 g (30%), colorless crystals, mp 64–66°C. ^{1}H NMR spectrum, δ, ppm: 1.23 d.t (6H, OCH_2**Me**, $^3J_{HH}$ = 6.8, $^4J_{PH}$ = 4.4 Hz), 3.38 s (3H, OMe), 3.95–4.07 m (4H, OC**H**$_2$Me), 4.48 d (1H, PCH, $^2J_{PH}$ = 16 Hz), 6.61 s (1H, $CHBr_2$), 7.40 d and 7.53 d (4H, C_6H_4, $^3J_{HH}$ = 8.0 Hz). ^{13}C NMR spectrum, δ_C, ppm: 16.47 d (OCH_2**Me**, $^3J_{PC}$ = 4.6 Hz), 40.30 ($CHBr_2$), 58.97 d (OMe, $^2J_{PC}$ = 14.2 Hz), 62.95 d and 63.14 d (O**C**H_2Me, $^2J_{PC}$ = 6.8 Hz), 80.04 d (PCH, $^1J_{PC}$ = 168.0 Hz); 126.58, 128.01, 128.07 (CH_{arom}); 126.45, 130.30, 136.54, 141.98 (C_{arom}). ^{31}P NMR spectrum (CCl_4): δ_P 18.3 ppm. Mass spectrum, *m*/*z* (I_{rel}, %): 428 (0.15) $[M]^+$, 293 (100.0) $[M - P(O)(OEt)_2 + 2H]^+$, 249 (19.6) $[M - CH(OMe)P(O)(OEt)_2 + 2H]^+$, 212 (68.3) $[M - P(O)(OEt)_2 - Br]^+$, 168 (26.8) $[M - CHBr_2 - 2OEt + H]^+$, 89 (31.8) $[C_7H_5]^+$. Found, %: C 36.05; H 4.34; Br 37.01; P 7.04. $C_{13}H_{19}Br_2O_4P$. Calculated, %: C 36.30; H 4.46; Br 37.16; P 7.20.

Dimethyl [4-(dibromomethyl)phenyl](ethoxy)-methylphosphonate (23f) was synthesized in a similar way from 2.00 g (0.0057 mol) of compound **21b** and 0.71 g (0.0057 mol) of trimethyl phosphite (**12a**). Yield 1.91 g (80.6%), thick oil. ^{1}H NMR spectrum, δ, ppm: 1.21 t (3H, OCH_2**Me**, $^3J_{HH}$ = 7.0 Hz), 3.15–3.85 m (2H, OC**H**$_2$Me, partially overlapped by the POMe signals), 3.62 d and 3.73 d (6H, POMe, $^3J_{PH}$ = 10.7 Hz), 4.60 d (1H, PCH, $^2J_{PH}$ = 16.4 Hz), 6.61 s (1H, $CHBr_2$), 7.38 d and 7.53 d (4H, C_6H_4, $^3J_{HH}$ = 8.5 Hz). ^{31}P NMR spectrum (CCl_4): δ_P 18.4 ppm. Found, %: C 34.43; H 4.02; P 7.31. $C_{12}H_{17}Br_2O_4P$. Calculated, %: C 34.64; H 4.13; P 7.44.

4-[(Diphenylphosphinyl(methoxy)methyl]benzaldehyde (26a). A mixture of 0.94 g (0.0019 mol) of phosphine oxide **23a** and 0.75 g (0.0095 mol) of pyridine was heated for 2 h at 100°C. The mixture was poured into 30 mL of ice-cold distilled water and extracted with diethyl ether (3×10 mL). The combined extracts were washed with water and dried over Na_2SO_4, and the solvent was removed under reduced pressure. Yield 0.33 g (49.6%), pale yellow crystals, mp 163–165°C (from hexane). ^{1}H NMR spectrum, δ, ppm: 3.36 s (3H, OMe), 5.11 d (1H, PCH, $^2J_{PH}$ = 12.8 Hz), 7.34–7.92 m (14H, H_{arom}), 9.96 s (1H, CHO). ^{13}C NMR spectrum, δ_C, ppm: 59.12 d (OMe, $^3J_{PC}$ = 12.1 Hz), 83.48 d (PCH, $^1J_{PC}$ = 85.2 Hz); 128.4, 128.06, 128.18, 128.33, 128.37, 128.55, 128.66, 129.43, 131.61, 131.69, 132.25, 132.45, 132.54 (CH_{arom}); 127.87, 128.84,

130.98, 131.96, 136.12, 140.87 (C_{arom}); 192.01 (CO). ^{31}P NMR spectrum (CCl_4): δ_P 27.4 ppm. Found, %: C 71.78; H 5.31; P 8.73. $C_{21}H_{19}O_3P$. Calculated, %: C 72.00; H 5.43; P 8.86.

4-[Diethylphosphinyl(methoxy)methyl]benzaldehyde (26b) was synthesized in a similar way from 1.00 g (0.0025 mol) of phosphine oxide **23b** and 0.99 g (0.0125 mol) of pyridine. Yield 0.25 g (39.4%), yellow oil. ^1H NMR spectrum, δ, ppm: 0.94 d.t and 1.22 d.t (3H, PCH_2**Me**, $^3J_{HH}$ = 7.6, $^3J_{PH}$ = 15.2 Hz), 1.45–1.62 m and 1.81–1.89 m (4H, PC**H**$_2$Me), 3.39 s (3H, OMe), 4.67 d (1H, PCH, $^2J_{PH}$ = 13.2 Hz), 7.55 d and 7.85 d (4H, C_6H_4, $^3J_{HH}$ = 7.6 Hz), 9.95 s (1H, CHO). ^{13}C NMR spectrum, δ_C, ppm: 5.03 d and 5.24 d (PCH_2**Me**, $^2J_{PC}$ = 5.0 Hz), 16.74 d and 18.12 d (P**C**H_2Me, $^1J_{PC}$ = 64.6 Hz), 59.12 d (OMe, $^3J_{PC}$ = 11.4 Hz), 80.51 d (PCH, $^1J_{PC}$ = 76.9 Hz), 127.32 and 128.09 (CH_{arom}); 126.60, 127.35, 135.97, 141.23 (C_{arom}); 191.24 (CO). ^{31}P NMR spectrum (CCl_4): δ_P 51.2 ppm. Found, %: C 61.17; H 7.34; P 12.06. $C_{13}H_{19}O_3P$. Calculated, %: C 61.42; H 7.48; P 12.20.

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CONFLICT OF INTERESTS

No conflict of interests was declared by the authors.

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