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Synthesis of β-ketophosphonates with electron rich β-aryl groups as useful organophosphorus reagents in lignans synthesis

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ABSTRACT

Investigation of the oxidation reaction of electron rich alkoxy substituted β-aryl β-hydroxyphosphonates to corresponding β-ketophosphonates, which may be utilized in syntheses of lignans with various oxidizing agents (PCC, PDC, SIBX, CAN, Oxone®, $KMNO_4/SiO_2$, $KMnO_4$/MS 4 Å, $KMnO_4/CuSO_4$, $KMnO_4/CuSO_4/Al_2O_3$, MnO_2, CrO_3/SiO_2, H_2O_2/salen) is described. The effect of oxidants and reaction conditions on the reaction efficiency and yield was also investigated.

1. Introduction

β-Ketophosphonates are useful compounds in organic chemistry, especially in the synthesis of biologically active and natural products as reagents introducing α,β-unsaturated carbonyl moieties and enabling modifications (e.g., by substitution in the α position or nucleophilic substitution at the carbonyl group) of the β-ketoalkyl chain.[1] Their attractiveness lies in the ease of anion formation in the α-position to the phosphoryl group, which enables further applications in Horner–Wittig olefinations.

Syntheses of β-aryl substituted β-ketophosphonates by the existing methods usually are not very practical and suffer from several drawbacks. The standard condensation of dialkyl 1-lithiomethylphosphonates with carboxylic acid esters usually proceeds in ca. 50% yield and half of the substrate is lost due to hydrogen exchange between the lithiated substrate and the product. The modified Arbuzov reaction of chloromethyl ketones, potassium iodide, and trialkyl phosphites in acetone/acetonitrile affords the desired phosphonates in good yields but in turn it is limited by a troublesome synthesis of the starting carbonyl compounds[2] as the reaction of labile aryloyl chlorides with dialkyl 1-lithiomethylphosphonates.[3]

Finally, a very convenient and general method constitutes the two-step synthesis involving formation and oxidation of β-hydroxymethylphosphonates. The latter can be obtained from the reaction of 1-lithio alkylphosphonates with aldehydes, which usually are commercially available and cheap. In most cases this step is very efficient and proceeds almost quantitatively.[4] However, in contrast to β-alkyl substituted β-hydroxyphosphonates, the oxidation step of the corresponding β-aryl analogs creates synthetic problems and there are few reports known on oxidation of the latter. The described methods are not general and concern oxidations of single compounds.[5] Among them, most constitute α,α′-difluoro substituted β-hydroxyphosphonates and the corresponding β-ketophosphonates,[5a] which cannot be further utilized in the Horner–Wittig olefination.

Electron rich alkoxy substituted β-aryl β-ketophosphonates constitute a peculiar subclass of β-ketophosphonates and in our investigations are utilized in syntheses of both natural and synthetic lignans.[6] However, the only known protocol of synthesis of electron rich dimethyl 2-(1,4-dimethoxy-2-methyl-3-naphthyl)-2-oxoethylphosphonate, using MnO_2 as an oxidant, remains incomplete, since the amount of the latter has not been given.[5b] Therefore, searching for new methods of synthesis of such electron rich substituted β-aryl β-ketophosphonates via oxidation of the corresponding secondary β-hydroxy derivatives is still open and it became a fragment of our investigations on the total syntheses of new classes of lignans, which are known from ancient times[6b] as a very rich class of plant isolated and biologically active compounds possessing polyalkoxy substituted aryls. Some representatives are shown in Scheme 1.

In this paper, we would like to report our results on synthesis of the polyalkoxy substituted β-aryl β-ketophosphonates, which may be utilized in various syntheses of lignans as organophosphorus reagents transferring the aryloylmethyl functionality.

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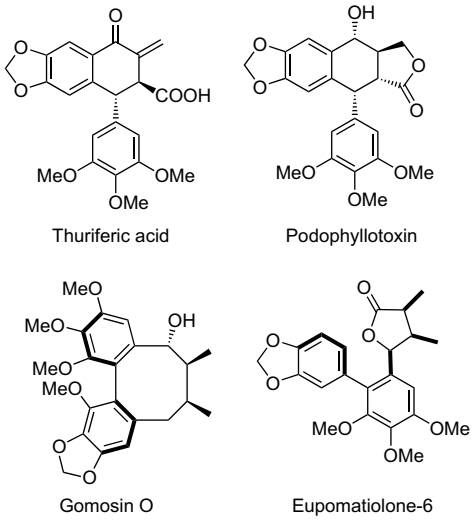
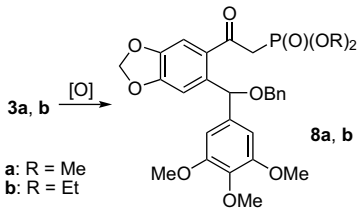


Scheme 1.

2. Results

We have synthesized a series of 2-aryl-2-hydroxymethylphosphonates **3a**, **3b**, **5a**, **5b**, **7** in the reaction of the corresponding aryl aldehydes **1**, **4a**, **4b**, **6** with dimethyl or diethyl 1-lithio-methylphosphonates in good yields (Scheme 2). In the case of phosphonates **3a** and **3b**, a mixture of two diastereoisomers was formed (ca. 1:1). These isomers were well visible in NMR spectra (^{1}H, ^{31}P, and ^{13}C) but were inseparable by column chromatography.

At the outset, 2-hydroxymethylphosphonate **3a** was oxidized to the β-ketophosphonate **8a** (Scheme 3, Table 1) using pyridinium chlorochromate (PCC).[7] Initially, an excess of PCC (1.2–1.5 equiv) in methylene chloride, as the standard solvent for this oxidant, was applied. It turned out that tuning of this reaction was rather difficult. The first experiment was carried out at 0 °C for 18 h in presence of 1.2 equiv of PCC (Table 1, entry 1). The ^{31}P NMR spectrum of the crude mixture indicated the formation of 53% of the keto compound **8a** and 30% of the unreacted substrate, however, the product could be isolated in 25% yield only. The oxidation of **3a** at elevated temperature (20 °C) in the presence of 1.2 equiv of PCC for 18 h (Table 1, entry 2) increased the yield up to 64% of the oxidized product **8a** and remaining 24% of the substrate (by ^{31}P NMR). Shortening of the reaction time to 2 h using the same reaction conditions (20 °C) gave **8a** in the unexpected 71% yield (by ^{31}P NMR) and 61% after isolation (Table 1, entry 3).



Scheme 3.

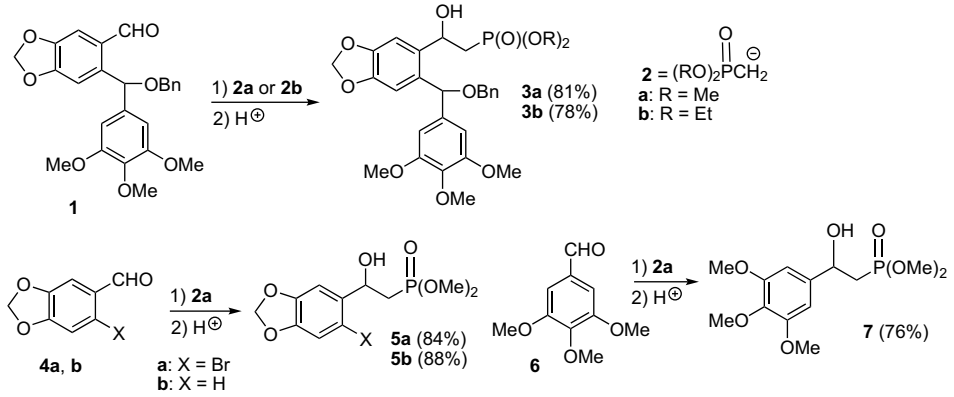
The unreacted substrate in these experiments (Table 1, entries 1-3) was exposed to additional portions of PCC. At first, **3a** was oxidized with 1.2 equiv PCC for 2 h at 20 °C (like in entry 3) and then the resulting mixture was reoxidized with an additional amount of PCC (0.3 equiv) for 18 h at the same temperature (Table 1, entry 4), unexpectedly isolating only 41% of the product **8a** (61% by NMR after water workup). The same result (37% isolated yield) was obtained in the oxidation of **3a** with 1.5 equiv PCC in one portion for 20 h at room temperature (60% in crude mixture after water workup). In the NMR spectra of crude mixtures (Table 1, entries 4 and 5), only traces of the unreacted substrate **3a** were observed in both cases indicating a hydrolysis of the labile dimethoxyphosphoryl moiety as the most probable side reaction.

The oxidation of **3a** in the presence of 2.0 equiv of PCC (Table 1, entry 7) for 1 h at higher temperature of 40 °C gave the crude **8a** in a similar 60% yield (after water workup). Replacement of methylene chloride for DMF or THF and use of even larger excess of the oxidating agent (3.0 equiv PCC) brought a further decrease in the yield of the product **8a** (only trace amounts).

Another standard oxidizing reagent for benzyl alcohols is pyridinium dichromate (PDC). This compound gave worse results than PCC. For instance, the oxidation of **3a** with 1.1 equiv of PDC in CH_2Cl_2 at room temperature overnight gave the keto product **8a** in 39% (conversion determined by NMR) and 36% isolated yield (Table 1, entry 10, compare with entry 2). A large excess of PDC (4.0 equiv), like with PCC, brought a complex mixture containing only 20% of the expected product **8a** after 3 h at 20 °C (Table 1, entry 11).

$KMnO_4$ a powerful oxidizing agent, which is widely used in organic synthesis for certain oxidation processes and may be activated by impregnation onto inorganic supports such as molecular sieves and silica gel.[8] However, oxidation of the β-hydroxyphosphonate **3a** using $KMnO_4$ under various conditions brought the keto product **8a** in low yields only (Table 1, entries 12–14).

Lee and Shaabani[9] reported that secondary alcohols were converted into the corresponding ketones by potassium permanganate mixed with copper sulfate pentahydrate (or a 20/80 mixture of copper sulfate and alumina) in good yields. For the



Scheme 2.

Table 1
Oxidation of 2-aryl-2-hydroxymethylphosphonates **3a**, **3b**, **5a**, **5b**, **7**

Entry	Substrate	Oxidating agent (equiv)	Conditions	Ratio[a] product/substrate	Isolated yield (%)
1	**3a**	PCC (1.2)	CH_2Cl_2, 18 h, 0 °C	53:30	25
2	**3a**	PCC (1.2)	CH_2Cl_2, 18 h, 20 °C	64:24	
3	**3a**	PCC (1.2)	CH_2Cl_2, 2 h, 20 °C	71:26	61
4	**3a**	PCC (1.2+0.3)	CH_2Cl_2, 2 h+18 h, 20 °C	61:4	36
5	**3a**	PCC (1.5)	CH_2Cl_2, 20 h, 20 °C	60:2	37
6	**3a**	PCC (1.2+0.5)	CH_2Cl_2, 18 h+2 h, 20 °C	78:22	46
7	**3a**	PCC (2.0)	CH_2Cl_2, 1 h, 40 °C	60:40	
8	**3a**	PCC (3.0)	DMF, 2.5 h, 20 °C	0:44	
9	**3a**	PCC (3.0)	THF, 1.5 h, 0 °C	4:87	
10	**3a**	PDC (1.1)	CH_2Cl_2, 18 h, 20 °C	39:32	36
11	**3a**	PDC (4.0)	CH_2Cl_2, 3 h, 20 °C	20:25	
12	**3a**	$KMnO_4$/MS 4 Å (10.0)	Benzene, 8.5 h, 80 °C	15:67	
13	**3a**	$KMnO_4$/MS 4 Å (3.0)	Benzene, 60 h, 80 °C	24:70	
14	**3a**	$KMnO_4/SiO_2$ (3.0)	Benzene, 8 h, 80 °C	13:66	
15	**3a**	$KMnO_4/CuSO_4 \cdot 5H_2O$ (10.0)	Neat, 2 h, 20 °C, 10 min, 50 °C	5:95	
16	**3a**	$KMnO_4/CuSO_4/Al_2O_3$ (10.0)	Neat, 2 h, 20 °C, 10 min, 50 °C	10:90	
17	**3a**	CrO_3/SiO_2 (10.0)	CH_2Cl_2, 18 h, 20 °C	0:0	
18	**3a**	H_2O_2/salen (10.0)	THF, 1 h, 20 °C	0:100	
19	**3a**	Oxone (2.0)	EtOAc/H_2O (1:1), 2 h, 20 °C	0:100	
20	**3a**	CAN (3.0)	CH_3CN/H_2O (9:1), 18 h, 20 °C	15:58	
21	**3a**	SIBX (1.2)	Toluene, 1.5 h, 80 °C	33:40	
22	**3a**	SIBX (1.2+1.2)	Toluene, 1.5 h+1.5 h, 80 °C	56:32	44
23	**3a**	SIBX (1.2)	THF, 0.5 h, 60 °C	*68:8*	*65*[b]
24	**3a**	SIBX (3.0)	CH_2Cl_2, 3 d, 20 °C	53:18	44
25	**3b**	PCC (1.2)	CH_2Cl_2, 2 h, 20 °C	86:14	27
26	**3b**	SIBX (1.2)	THF, 0.5 h, 60 °C	65:25	61
27	**3b**	SIBX (1.5)	Toluene, 2 h, 20 °C, 3 h, 80 °C	*76:22*	*69*[b]
28	**3b**	SIBX (3.0)	Toluene, 3 h, 80 °C	64:0	59
29	**5a**	PCC (1.1)	CH_2Cl_2, 3 h, 20 °C	56:34	
30	**5a**	PCC (1.1)	CH_2Cl_2, 1 h, 40 °C	75:25	
31	**5a**	PCC (1.5)	CH_2Cl_2, 2 h, 40 °C	78:22	
32	**5a**	PCC (2.0)	CH_2Cl_2, 2 h, 40 °C	*100:0*	*52*[b]
33	**5a**	$KMnO_4$/MS 4 Å (3.0)	Benzene, 6 h, 80 °C	63:47	
34	**5a**	$KMnO_4$/MS 4 Å (3.0)	Benzene, 10 h, 80 °C	68:32	
35	**5a**	MnO_2 (2.0)	$CHCl_3$, 4 h, 60 °C	5:90	
36	**5a**	MnO_2 (10.0)	$CHCl_3$, 10 h, 60 °C	83:17	
37	**5b**	PCC (1.5+1.5)	CH_2Cl_2, 1.5 h+1.5 h, 20 °C	*97:3*	*61*[b]
38	**5b**	$KMnO_4$/MS 4 Å (3.0)	Benzene, 10 h, 80 °C	80:20	47
39	**7**	PCC (1.5+1.5)	CH_2Cl_2, 1.5 h+1.5 h, 20 °C	90:10	36
40	**7**	PCC (1.5)	CH_2Cl_2, 1 h, 40 °C	91:0	39
41	**7**	$KMnO_4$/MS 4 Å (3.0)	Benzene, 13 h, 80 °C	*80:20*	*65*[b]

[a] By ^{31}P NMR.
[b] The best optimized yield.

hydroxyphosphonate **3a** only 5% and 10% conversions (by ^{31}P NMR) were observed at conditions reported in literature (Table 1, entries 15 and 16).

The other oxidant, for example, CrO_3 supported on silica gel[10] (Table 1, entry 17) was similarly unsuccessful. Most probably CrO_3 oxidized other functional groups in the substrate. Oxidation of **3a** by H_2O_2 in the presence of salen as a catalyst[11] or by Oxone®[12] gave no conversions (Table 1, entries 18 and 19). Another strong oxidant CAN[13] gave only 15% of the desired product **8a** (Table 1, entry 19).

Our continuing interest in the oxidation chemistry of β-hydroxyphosphonates led us to examine the behavior of **3a** in the presence of SIBX (Stabilized IBX—2-iodoxybenzoic acid) a new hypervalent iodine compound, which has been introduced by Quideau et al.[14] for mild oxidations of primary and secondary alcohols (mainly benzylic and allylic) to aldehydes and ketones, respectively. Authors reported that the best solvents for SIBX were toluene and THF. Initial attempt (Table 1, entry 21) to oxidize **3a** with 1.2 equiv of SIBX in toluene for 1.5 h at 80 °C led to the formation of **8a** in only 33% (by NMR). The crude mixture contained large quantities of the substrate (40%). Reoxidation of the remaining substrate by additional portion of 2-iodoxybenzoic acid (1.2 equiv) and heating for additional time (1.5 h) at the same temperature (Table 1, entry 22) brought only a little progress in formation of the expected product **8a**. NMR spectra indicated the formation of **8a** in 56% yield in the crude mixture and the isolated yield was 44%. The reaction of **3a** with SIBX performed in THF gave much better results. By the use of 1.2 equiv of SIBX in this solvent after only 0.5 h at 60 °C, **3a** was converted into **8a** in 68% yield. Isolated yield of **8a** was 65% and only traces of the substrate (8%) were observed in the crude mixture (Table 1, entry 23). Large excess of SIBX (3.0 equiv) in methylene chloride oxidized **3a** after 3 days at room temperature in 53% yield (by NMR). The β-ketophosphonate **8a** was isolated after a standard workup in 44% of yield (Table 1, entry 24).

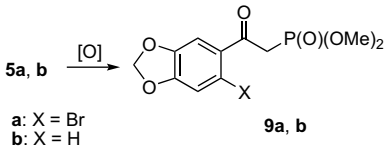
Since the lability of the dimethoxyphosphoryl group was most probably responsible for moderate yields of oxidation of **3a**, we synthesized the β-hydroxyphosphonate **3b** bearing a diethoxyphosphoryl group, which was known to be much more resistant to hydrolytic conditions and oxidized it with PCC, one of the best oxidant for **3a**. During oxidation with 1.2 equiv of PCC in methylene chloride at room temperature after 2 h, the conversion was better (86% by NMR) but the isolated yield was still unexpectedly very low (27%) (Table 1, entry 25) most probably due to oxidative debenzylation on silica gel.[15]

In the next experiment, **3b** (R=Et) was mixed with SIBX (1.5 equiv) in THF at 60 °C and after 0.5 h, the corresponding ketone **8b** was obtained in 65% yield (61% of isolated yield) (Table 1, entry 26). The oxidation of **3b** performed in toluene with 1.5 equiv SIBX

for 2 h at 20 °C and then for 3 h at 80 °C gave 69% of the ketone **8b** and 22% of the substrate (Table 1, entry 27). To reoxidize it, **3b** was treated with a large excess of SIBX (3.0 equiv) in toluene for 3 h at 80 °C (Table 1, entry 28). NMR spectra of the crude mixtures indicated no substrate and the product present in 64% yield. Standard isolation gave 59% of the desired ketone.

In a summary, the best oxidizing reagent for **3a** and **3b** was SIBX at elevated temperature. The best solvent for the first one was THF (2 h at 60 °C, Table 1, entry 23) and for the second one toluene (2 h at 20 °C, 3 h at 80 °C, Table 1, entry 27). Isolated yields for **3a** and **3b** were 65% and 69%, respectively.

The results concerning oxidation of another electron rich alkoxy substituted β-aryl β-ketophosphonate, i.e., dimethyl 2-(benzo[*d*][1,3]dioxol-5-yl)-2-hydroxyethyl phosphonate **5b** and its 6-bromo analog **5a** are summarized in Table 1 (Scheme 4).



Scheme 4.

The standard oxidation of **5a** by pyridinium chlorochromate (1.1 equiv) in methylene chloride at room temperature for 3 h gave the oxidized product in 56% yield. Elevation of the reaction temperature (CH_2Cl_2 at reflux) increased the yield up to 75% (after only 1 h). The use of 1.5 equiv of PCC in CH_2Cl_2 for 2 h, at reflux gave only a slight increase in yield (up to 78%) When 2.0 equiv of the same oxidizing agent was used, the 100% conversion (observed by ^{31}P NMR) was observed but the isolated yield was only 52% in this case.

Potassium permanganate on molecular sieves (3.0 equiv) in CH_2Cl_2 at reflux was able to convert **5a** in 63% of yield after 6 h. Prolongation of the reaction time to 10 h gave only a little increase in the yield up to 68% (32% of the substrate still remained in the crude mixture).

The use of active manganese dioxide[16] in chloroform at reflux for oxidation of **5a** gave a good result (83% yield), however, it was necessary to use a large excess of MnO_2—10.0 equiv. Additionally a long reaction time (10 h) was required. Using only 2 equiv of the same oxidant for a shorter time—4 h (in chloroform at reflux, too) gave only the 5% conversion (monitored by ^{31}P NMR).

Dimethyl 2-(benzo[*d*][1,3]dioxol-5-yl)-2-hydroxy ethylphosphonate **5b** was transformed into the corresponding β-aryl β-ketophosphonate **9b** with PCC (initially 1.5 equiv of the oxidant for 1.5 h and then additional 1.5 equiv for the next 1.5 h) in methylene chloride at room temperature in 61% of the isolated yield (97% by ^{31}P NMR). Typical oxidation of **5b** by $KMnO_4$ on molecular sieves (reflux, benzene, 10 h) provided the corresponding β-ketophosphonate **9b** in 47% isolated yield only (80% by ^{31}P NMR).

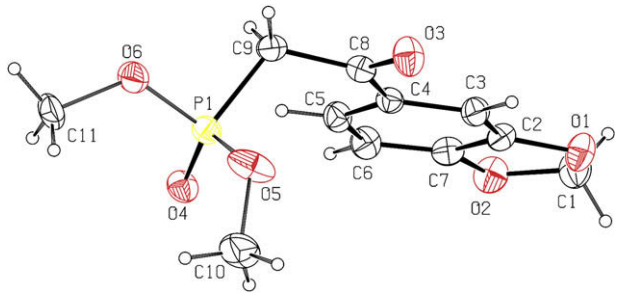


Figure 1. A plot of the molecule **9b**, showing the atom numbering scheme. Displacement ellipsoids are drawn at the 20% probability level and H atoms are shown as small spheres of arbitrary radii. The minor disorder component of the dimethoxyphosphoryl group has been omitted for clarity.

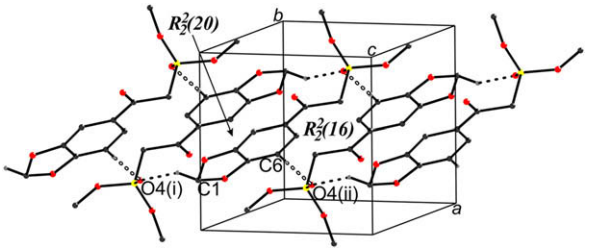
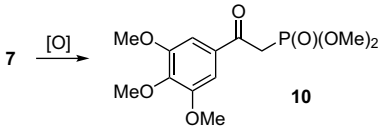


Figure 2. A part of the crystal structure of **9b**, showing the formation of a chain built from $R_2^2(16)$ and $R_2^2(20)$ rings. All H-atoms not involved in the intermolecular C–H···O hydrogen bonds (dashed lines) and the minor disorder component of the dimethoxyphosphoryl group, have been omitted for clarity. Symmetry codes: (i) 1−*x*, 2−*y*, 1−*z*; (ii) 1−*x*, 1−*y*, 1−*z*.

X-ray crystal structure of the molecule **9b** and its situation in the elemental cell are shown in Figures 1 and 2 (see also Experimental section).

Summarizing, optimum results for oxidations of **5a** and **5b** were obtained using standard oxidizing agents such as PCC and $KMnO_4$ on molecular sieves.

Our attempts to oxidize another electron rich alkoxy substituted β-aryl β-ketophosphonate, i.e., dimethyl 2-hydroxy-2-(3,4,5-trimethoxyphenyl)ethylphosphonate (**7**) are presented in Scheme 5 and in Table 1.



Scheme 5.

Oxidation of **7** under standard conditions by PCC (CH_2Cl_2 at room temperature for 3 h) and at elevated temperature (reflux in CH_2Cl_2 for 1 h) gave similar results, i.e., 90% and 91% (conversion indicated by NMR), respectively. The isolated yield in case of **10** was only 36% and 39% for PCC. Oxidation of **7** by $KMnO_4$ on 4 Å molecular sieves in boiling benzene (for 13 h) gave a lower conversion than that for PCC (80%, indicated by ^{31}P NMR spectra) but isolated yield was higher—65%. The crude mixture still contained 20% of the substrate.

In conclusion, in this work we presented general investigations on the effective oxidation of β-aryl-β-hydroxyphosphonates substituted in the aryl moiety by electron rich alkoxy substituents, for the first time touching this problem. The oxidation of this synthetically useful and sensitive subgroup of β-hydroxyphosphonates is usually troublesome unlike oxidation of their β-alkyl substituted analogs and can be achieved in every particular case by two steps: (1) a choice of appropriate oxidizing agent for a selected substrate and (2) a careful tuning of reaction conditions.

3. Experimental

3.1. General

The ^1H NMR (200.16 MHz), ^{31}P NMR (81.03 MHz), and ^{13}C NMR (50.33 MHz) spectra were recorded using a Bruker AC-200 spectrometer in C_6D_6 or in $CDCl_3$. Chemical shifts are given in parts per

million. The mass spectra of pure compounds were obtained using a Finnigan Mat 95 spectrometer. IR spectra were recorded using an ATI Mattson Infinity FTIR 60 spectrometer. Column chromatography was done using Merck silica gel (F_{254} 60, 70–230, and 270–400 mesh). Organic solvents were purified by standard procedures.

*3.1.1. Crystallographic data of **9b***

$C_{11}H_{13}O_6P$, M=272.18, monoclinic, $P2_1/c$, a=7.6521(5) Å, b=7.2978(4) Å, c=22.5690(12) Å, β=98.898(5)°, V=1245.16(13) Å, Z=4 molecules per unit cell, D_c=1.452 g/cm^3, $F(000)$=568, crystal size 0.28×0.15×0.06 mm. Diffraction data were collected at 290(2) K, using an Oxford Diffraction Xcalibur 3™ diffractometer with graphite-monochromated Mo Kα radiation. The structure was solved by direct methods and refined by full-matrix least-squares on F^2 with SHELXL-97.[18] During refinement, two methoxy groups in **9a** were found to be disordered over two sites with occupancies of 0.80(2) and 0.20(2). The C and O atoms of main component were refined anisotropically, while those belonging to the minor component were refined isotropically. All aromatic and methyl H atoms were positioned geometrically and constrained to ride on their parent atoms, with C–H distances of 0.93 and 0.96 Å, respectively, and with U_{iso}(H) values of 1.2 U_{eq}($C_{aromatic}$) and 1.5 U_{eq}(C_{methyl}). H atoms bonded to C1 and C9 atoms were located in difference maps and refined with U_{iso}(H) set at 1.5 U_{eq}(C), giving C–H distances in the range 0.87(4)–1.00(3) Å. $R[F^2>2\sigma(F^2)]$=0.0437, $wR(F^2)$=0.1273, S=1.026 for 2176 independent reflections [1383 reflections with $I>2\sigma(I)$] and 197 parameters. Further details on the crystal structure investigation have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 705171.

*3.1.2. Crystallographic discussion on **9b***

Compound **9b** crystallized in the monoclinic $P2_1/c$ space group with four molecules per unit cell. In the dimethoxyphosphoryl group region of this molecule, a disorder on atoms O5, O6, C10, and C11 was identified and refined over two positions with an occupancy of 0.80(2) for the major component for which only the geometric parameters will be presented. As can be seen from Figure 1, the benzene and dioxolane rings as a whole are essentially planar with the largest deviations from the best least-squares plane of 0.071(4) Å for atom C1, and the C8, C9, and O3 atoms are nearly coplanar, with deviations from the plane of 0.120(3), 0.291(3), and 0.112(2) Å, respectively. The phosphorus and oxygen atoms belonging to the dimethoxyphosphoryl group, i.e., P1, O4, O5, and O6, lie 1.244(1), 1.868(2), 2.104(6), and 0.670(9) Å below this plane, respectively, and the angle between the C9–P1 bond and the plane formed by benzene and dioxolane rings is 57.4(1)°. The crystal packing of **9b** is stabilized by two weak non-conventional intermolecular C–H···O hydrogen bonds. Atom C6 in benzene ring at (x, y, z) acts as hydrogen bond donor to atom O4 at (1−x, 1−y, 1−z), linking the two molecules into a dimer unit, so generating a centrosymmetric $R_2^2(16)$ ring[17] centered at (1/2, 1/2, 1/2). Moreover, the atom C1 in the dioxolane ring at (x, y, z) acts as a donor, via H1A, towards atom O4 at (1−z, 2−y, 1−z), generating a centrosymmetric $R_2^2(20)$ ring centered at (1/2, 1, 1/2). The combined effect of these two C–H···O hydrogen bonds is the formation of a chain running parallel to the [010] direction and build from the fused $R_2^2(16)$ and $R_2^2(20)$ rings (Fig. 2).

3.2. Synthesis of 2-aryl-2-hydroxymethylphosphonates 3a, 3b, 5a, 5b, 7

To a stirred solution of dialkyl methylphosphonate (**2a** or **2b**) (0.03 mmol) in anhydrous THF (50 mL), a solution of *n*-BuLi (1.2 M, 27.5 mL, 0.033 mmol, 1.1 equiv) was added at −78 °C. After 30 min, the temperature was raised to −30 °C and stirring was continued for 15 min. Then, the temperature was lowered again to −78 °C and an appropriate aldehyde (**1**, **4a**, **4b**, **6**) (1.2 equiv) in dry THF (20 mL) was added. The reaction mixture was stirred for 30 min at the same temperature and then was slowly warmed to −20 °C. Then, the mixture was cooled to −78 °C and saturated aqueous solution of NH_4Cl (20 mL) was added. The solvent was evaporated and the residue was partitioned between water (20 mL) and ethyl acetate (40 mL). The organic phase was washed with saturated aqueous NH_4Cl (10 mL), water (10 mL), dried ($MgSO_4$), filtered, and concentrated in vacuo to give the crude product, which was purified by column chromatography on silica gel using ethyl acetate/petroleum ether as the eluent.

*3.2.1. Dimethyl 2-(6-(benzyloxy (3,4,5-trimethoxyphenyl) methyl) benzo[d][1,3]dioxol-5-yl)-2-hydroxy ethylphosphonate (**3a**)*

A colorless oil; yield: 81%; R_f=0.50 (ethyl acetate); IR (thin film) ν/cm^{-1}: 3329 (br m, O–H), 2952 (m, O–CH_2–O), 2849 (m, OCH_3), 1591 (s), 1503 (s), 1482 (s), 1462 (s, C(O)–CH_2), 1420 (m), 1331 (m), 1233 (s, P=O), 1127 (s, CH–O–CH), 1065 (s, C–OH), 1036 (vs, P–O–C), 849 (m), 828 (m), 801 (w), 736 (m), 700 (m); ^{31}P NMR (C_6D_6): δ 32.48, 32.40 ppm (two diastereoisomers); ^{1}H NMR (C_6D_6): δ 2.05–2.17 (m, 2H, CH_2P(O)), 3.22 (d, J_{PH}=10.9 Hz, 6H, P(O)(OCH_3)$_2$), 3.34 (d, J_{PH}=11.0 Hz, 3H, P(O)OCH_3), 3.38 (d, J_{PH}=11.0 Hz, 3H, P(O)OCH_3), 3.44 (s, 6H, Ar(OCH_3)$_2$), 3.51 (s, 6H, Ar(OCH_3)$_2$), 3.82 (s, 3H, ArOCH_3), 3.84 (s, 3H, ArOCH_3), 4.54 (d_{AB}, J_{HH}=11.6 Hz, 1H, OCH_2Ph), 4.57 (s, 2H, OCH_2Ph), 4.72 (d_{AB}, J_{HH}=11.6 Hz, 1H, OCH_2Ph), 4.87 (s, OH), 5.06 (s, OH), 5.28–5.34 (m, 2H, OCH_2O), 5.34–5.38 (m, 2H, OCH_2O), 5.72–5.88 (m, 1H, C*H*OH), 5.87 (s, 1H, CHOBn), 5.92 (s, 1H, CHOBn), 6.86 (s, 2H, *o*-$C_6H_2(OCH_3)_2$), 6.89 (s, 2H, *o*-$C_6H_2(OCH_3)_2$), 7.04–7.18 (m, 3H, *m*-Ph, *p*-Ph), 7.09 (s, 1H, ArH), 7.15 (s, 1H, ArH), 7.34–7.39 (m, 2H, *o*-Ph), 7.40 (s, 1H, ArH), 7.46 (s, 1H, ArH); ^{1}H NMR ($CDCl_3$): δ 1.27–1.43 (m, 1H, CH_2P(O)), 1.53–1.66 (m, 1H, CH_2P(O)), 3.15 (br s, 1H, OH), 3.54–3.75 (m, 6H, P(O)(OCH_3)$_2$), 3.80 (s, 3H, *p*-$C_6H_2(OCH_3)_3$), 3.81 (s, 3H, 2×*m*-$C_6H_2(OCH_3)_3$), 3.84 (s, 3H, 2×*m*-$C_6H_2(OCH_3)_3$), 4.45–4.66 (m, 2H, OCH_2Ph), 4.67 (s, 2H, OCH_2Ph), 5.28–5.55 (m, 1H, CHOH), 6.61 (s, 1H, CHOBn), 5.92–5.96 (m, 2H, OCH_2O), 6.53 (s, 2H, *o*-$C_6H_2(OCH_3)_2$), 6.60 (s, 2H, *o*-$C_6H_2(OCH_3)_2$), 6.67 (s, 1H, Ar–H), 7.12 (s, 1H, Ar–H), 7.34–7.40 (m, 5H, Ph); ^{13}C NMR (C_6D_6): δ 33.72 (d, J_{PC}=135.0 Hz, CH_2P(O)), 34.34 (d, J_{PC}=135.4 Hz, CH_2P(O)), 52.04 (d, J_{PC}=6.5 Hz, P(O)OCH_3)), 52.54 (d, J_{PC}=6.5 Hz, P(O)OCH_3)), 55.93 (s, Ar(OCH_3)$_2$), 60.66 (s, ArOCH_3), 64.01 (d, J_{PC}=8.9 Hz, CHOH), 64.09 (d, J_{PC}=8.9 Hz, CHOH), 70.59 (s, OCH_2Ph), 70.78 (s, OCH_2Ph), 78.98 (s, CHOBn), 79.22 (s, CHOBn), 101.08 (s, OCH_2O), 104.07 (s, 2×*o*-$C_6H_2(OMe)_3$), 104.68 (s, Ar–H), 106.18 (s, Ar–H), 127.52 (s, *m*-Ph), 127.77 (s, *p*-Ph), 128.26 (s, *o*-Ph), 131.19 (s, *p*-$C_6H_2(OMe)_3$), 136.20 (s, C–CHO–), 136.42 (s, *ipso*-Ph), 137.30 (s, *ipso*-$C_6H_2(OMe)_3$), 137.85 (d, J_{PC}=7.1 Hz, C–CHOH), 146.82 (s, C–OCH_2O), 147.50 (s, C–OCH_2O), 153.21 (s, *m*-$C_6H_2(OMe)_2$); MS (CI) (*m*/*z*): 561 (1.5%, M^++H), 560 (2, M), 543 (8, M^++H(−H_2O)), 453 (100, M^++H(−BnOH)), 451 (52, M^++H(−P(O)$(OMe)_2$)), 435 (25, M^++H(−H_2O, −BnOH)). Anal. $C_{28}H_{33}O_{10}P$ requires: C, 60.00%; H, 5.93%. Found: C, 59.70%; H, 5.88%.

*3.2.2. Diethyl 2-(6-(benzyloxy (3,4,5-trimethoxyphenyl) methyl) benzo[d][1,3]dioxol-5-yl)-2-hydroxy ethylphosphonate (**3b**)*

A colorless oil; yield: 78%; R_f=0.53 (ethyl acetate); IR (thin film) ν/cm^{-1}: 3327 (br m, O–H), 2950 (m, O–CH_2–O), 2847 (m, O–CH_3), 1591 (s), 1510 (m), 1477 (m), 1460 (s), 1236 (s, P=O), 1126 (s, CH–O–CH), 1061 (s, C–OH), 1036 (vs, P–O–C), 960 (m), 789 (m), 801 (w), 736 (m), 700 (m); ^{31}P NMR (C_6D_6): δ 29.60, 29.91 ppm (1:1) (two diastereoisomers); ^{1}H NMR (C_6D_6): δ 0.88–1.09 (m, 6H, P(O)(OCH_2CH_3)$_2$), 1.90–2.26 (m, 2H, CH_2P(O)), 3.43 (s, 6H, 1 isomer 2×*o*-$C_6H_2(OCH_3)_3$), 3.50 (s, 6H, 2 isomer-2×*o*-$C_6H_2(OCH_3)_3$), 3.74–3.92 (m, 4H, P(O)(OCH_2CH_3)$_2$), 3.82 (s, 3H, 1 isomer *p*-$C_6H_2(OCH_3)_3$), 3.84 (s, 3H, 2 isomer-*p*-$C_6H_2(OCH_3)_3$), 4.52 (d_{AB}, J_{HH}=11.8 Hz, 1H, 2 isomer OCH_2Ph), 4.55 (d_{AB}, J_{HH}=9.8 Hz, 1H, 1 isomer OCH_2Ph), 4.58 (d_{AB}, J_{HH}=11.8 Hz, 1H, 2 isomer OCH_2Ph), 4.69 (d_{AB}, J_{HH}=9.8 Hz, 1H,

1 isomer OCH_2Ph), 4.47 (s, 1H, OH), 5.27–5.33 (m, 2H, 1 isomer OCH_2O), 5.33–5.36 (m, 2H, 2 isomer OCH_2O), 5.68–5.51 (m, 1H, CHOH), 5.52 (s, 1H, CHOBn), 6.87 (s, 2H, 2 isomer 2×*o*-$C_6H_2(OCH_3)_3$), 6.89 (s, 2H, 1 isomer 2×*o*-$C_6H_2(OCH_3)_3$), 7.05–7.17 (m, 3H, 2×*m*-, *p*-Ph), 7.37–7.43 (m, 2H, 2×*o*-Ph), 7.37 (s, 1H, 2 isomer Ar), 7.41 (s, 1H, 1 isomer Ar), 7.49 (s, 1H, 1 isomer Ar), 7.53 (s, 1H, 2 isomer Ar); ^{13}C NMR (C_6D_6): δ 17.08 (d, J=5.8 Hz, 2×P(O)$(OCH_2CH_3)_2$), 35.54 (d, J=32.1 Hz, 1 isomer $CH_2P(O)$), 38.21 (d, J=32.4 Hz, 2 isomer $CH_2P(O)$), 56.56 (s, 2×*m*-$C_6H_2(OCH_3)_3$), 61.13 (s, *p*-$C_6H_2(OCH_3)_3$), 62.11 (d, J=6.9 Hz, P(O)$(OCH_2CH_3)_2$), 62.69 (d, J=5.9 Hz, P(O)$(OCH_2CH_3)_2$), 65.43 (d, J=20.3 Hz, CHOH), 71.66 (s, OCH_2Ph), 80.43 (s, CHOBn), 101.87 (s, 2×*o*-$C_6H_2(OMe)_3$), 105.95 (s, 1 isomer OCH_2O), 106.55 (s, 2 isomer OCH_2O), 107.68 (s, 1 isomer Ar–H), 107.79 (s, 2 isomer Ar–H), 109.07 (s, Ar–H), 127.48 (s, *m*-Ph), 127.70 (s, *p*-Ph), 129.00 (s, *o*-Ph), 133.03 (s, 1 isomer *p*-$C_6H_2(OMe)_3$), 133.19 (s, 2 isomer *p*-$C_6H_2(OMe)_3$), 137.80 (s, 1 isomer C–CHO–), 138.15 (s, 2 isomer C–CHO–), 138.59 (s, *ipso*-Ph), 139.33 (s, *ipso*-$C_6H_2(OMe)_3$), 139.50 (s, 1 isomer C–CHOH), 139.81 (s, 2 isomer C–CHOH), 148.05 (s, 1 isomer C–OCH_2O), 148.37 (s, 2 isomer C–OCH_2O), 148.57 (s, 1 isomer C–OCH_2O), 148.71 (s, 2 isomer C–OCH_2O), 154.92 (s, 1 isomer *m*-$C_6H_2(OMe)_2$), 154.98 (s, 2 isomer *m*-$C_6H_2(OMe)_2$); MS (CI) (m/z): 571 (11%, M^++H(−H_2O)), 463 (100, M^++H(−H_2O, −BnOH)). Anal. $C_{30}H_{37}O_{10}P$ requires: C, 61.22%; H, 6.34%. Found: C, 61.37%; H, 6.47%.

3.2.3. Dimethyl 2-(6-bromobenzo[d][1,3]dioxol-5-yl)-2-hydroxy ethylphosphonate (**5a**)

A light-yellow oil; yield: 84%; R_f=0.52 (petroleum ether/acetone 1:1 v/v); IR (KBr) ν/cm^{-1}: 3312 (br s, O–H), 2957 (w), 2918 (w, O–CH_2–O), 2851 (w, O–CH_3), 1495 (m), 1478 (s), 1255 (m, P═O), 1224 (s), 1088 (m), 1033 (vs, P–O–C, C–OH), 930 (w), 869 (w), 829 (m); ^{31}P NMR ($CDCl_3$): δ 31.56; ^1H NMR ($CDCl_3$): δ 2.00 (ddd_{AB}, $^3J_{HH}$=10.5 Hz, $^2J_{PH}$=14.8 Hz, $^2J_{HH}$=15.3 Hz, 1H, $CH_2P(O)$), 2.30 (ddd_{AB}, $^3J_{HH}$=2.0 Hz, $^2J_{HH}$=15.3 Hz, $^2J_{PH}$=18.4 Hz, 1H, $CH_2P(O)$), 3.75 (d, J=11.2 Hz, 3H, P(O)OCH_3), 3.82 (d, J=11.2 Hz, 3H, P(O)OCH_3), 4.21 (br s, 1H, OH), 5.30 (ddd, $^3J_{HH}$=2.0 Hz, $^3J_{PH}$=10.4 Hz, $^3J_{HH}$=10.5 Hz, 1H, CH(OH)), 5.96 (s, 2H, OCH_2O), 6.94 (s, 1H, 5-Ar–H), 7.17 (s, 1H, 2-Ar–H); ^{13}C NMR ($CDCl_3$): δ 33.24 (d, J=135.0 Hz, $CH_2P(O)$), 52.63 (s, P(O)$(OCH_3)_2$), 67.57 (d, J=4.3 Hz, CH(OH)), 101.69 (s, OCH_2O), 107.06 (s, 2-Ar–H), 111.06 (s, C–Br), 112.28 (s, 5-Ar–H), 136.19 (d, J=17.9 Hz, 1-Ar), 147.56 (s, C–OCH_2O), 147.77 (s, C–OCH_2O); MS (CI) (m/z): 355 (6%, M^++H (^{80}Br)), 353 (5, M^++H (^{79}Br)), 337 (91, M^++H (^{80}Br)(−H_2O)), 337 (89, M^++H (^{79}Br)(−H_2O)), 273 (100, M^+(−Br)), 273 (27, M^+(−Br, −H_2O)); HRMS (CI) (m/z): calcd for $C_{11}H_{14}PBrO_6$: 351.971150, 353.969303, found: 353.97062.

3.2.4. Dimethyl 2-(benzo[d][1,3]dioxol-5-yl)-2-hydroxy ethylphosphonate (**5b**)

A colorless oil; yield: 88%; R_f=0.15 (hexane/ethyl acetate 1:1 v/v), 0.33 (hexane/ethyl acetate 1:4 v/v); IR (KBr) ν/cm^{-1}: 3320 (s, O–H), 3009 (w), 2960 (w, O–CH_2–O), 2914 (w, O–CH_3), 2855 (w, O–CH_3), 1505 (m), 1488 (m), 1440 (m), 1246 (m, P═O), 1229 (m), 1081 (m), 1034 (vs, P–O–C, C–OH), 838 (m), 811 (m); ^{31}P NMR (C_6D_6): δ 32.03; ^1H NMR (C_6D_6): δ 1.94 (ddd_{AB}, $^3J_{HH}$=3.2 Hz, $^2J_{PH}$=11.8 Hz, $^2J_{HH}$=18.0 Hz, 1H, $CH_2P(O)$), 2.03 (ddd_{AB}, $^3J_{HH}$=9.9 Hz, $^2J_{PH}$=15.3 Hz, $^2J_{HH}$=18.0 Hz, 1H, $CH_2P(O)$), 3.28 (d, J=10.9 Hz, 3H, P(O)OCH_3), 3.33 (d, J=10.8 Hz, 3H, P(O)OCH_3), 5.00 (bs, 1H, OH), 5.15 (ddd, $^3J_{HH}$=3.2 Hz, $^3J_{PH}$=10.1 Hz, $^3J_{HH}$=9.9 Hz, 1H, CH(OH)), 5.30 (s, 1H, OCH_2O), 5.31 (s, 1H, OCH_2O), 6.63 (d, J=7.9 Hz, 1H, 6-Ar–H), 6.73 (d, J=7.9 Hz, 1H, 5-Ar–H), 7.01 (s, 1H, 2-Ar–H); ^{13}C NMR (C_6D_6): δ 36.69 (d, J=135.1 Hz, $CH_2P(O)$), 52.31 (d, J=6.9 Hz, P(O)OCH_3), 52.93 (d, J=6.6 Hz, P(O)OCH_3), 69.31 (d, J=4.3 Hz, CHOH), 101.60 (s, OCH_2O), 107.39 (s, 2-Ar), 108.88 (s, 5-Ar), 119.82 (s, 6-Ar), 140.34 (d, J=16.5 Hz, 1-Ar), 147.93 (s, $COCH_2O$), 148.94 (s, $COCH_2O$); MS (CI) (m/z): 274 (18%, M^+), 257 (15, M^++H(−H_2O)); MS (EI) (m/z): 274 (21%, M^+), 256 (15, M+(−H_2O)), 164 (100, M^+(−HP(O)$(OCH_3)_2$)), 146 (24, M+(−HP(O)$(OCH_3)_2$, −H_2O)), 124 (37, HP(O)$(OCH_3)_2$); HRMS (EI) (m/z): calcd for $C_{11}H_{15}PO_6$: 274.060627, found: 274.06098.

3.2.5. Dimethyl 2-hydroxy-2-(3,4,5-trimethoxyphenyl) ethylphosphonate (7)

A colorless oil; yield: 76%; R_f=0.05 (hexane/ethyl acetate 1:1 v/v), 0.16 (hexane/ethyl acetate 1:4 v/v); IR (KBr) ν/cm^{-1}: 3393 (br m), 3292 (s, O–H), 3004 (m), 2941 (m, O–CH_2–O), 2842 (m, O–CH_2), 1592 (s), 1507 (m), 1463 (s), 1417 (s), 1339 (m), 1235 (s, P═O), 1217 (s), 1124 (vs, CH–O–CH), 1054 (s), 1026 (vs, P–O–C), 857 (m), 803 (m); ^{31}P NMR (C_6D_6): δ 32.13; ^1H NMR (C_6D_6): δ 2.05–2.18 (m, 2H, $CH_2P(O)$), 3.28 (d, J=11.1 Hz, 3H, P(O)OCH_3), 3.32 (d, J=10.9 Hz, 3H, P(O)OCH_3), 3.41 (s, 6H, 2×*m*-$C_6H_2(OCH_3)_3$), 3.85 (s, 3H, *p*-$C_6H_2(OCH_3)_3$), 4.68 (br s, 1H, OH), 5.21–5.33 (m, 1H, CH(OH)), 6.67 (s, 2H, 2×*o*-$C_6H_2(OCH_3)_3$); ^1H NMR ($CDCl_3$): δ 2.14–2.28 (m, 2H, $CH_2P(O)$), 3.77 (d, J=11.0 Hz, 3H, P(O)OCH_3), 3.80 (d, J=11.0 Hz, 3H, P(O)OCH_3), 3.83 (s, 3H, *p*-$C_6H_2(OCH_3)_3$), 3.87 (s, 6H, 2×*m*-$C_6H_2(OCH_3)_3$), 5.00–5.12 (m, 1H, CH(OH)), 5.30 (s, 1H, OH), 6.62 (s, 2H, 2×*o*-$C_6H_2(OCH_3)_3$); ^{13}C NMR (C_6D_6): δ 37.15 (d, J=135.9 Hz, $CH_2P(O)$), 52.32 (d, J=6.6 Hz, P(O)OCH_3), 53.15 (d, J=6.0 Hz, P(O)OCH_3), 56.54 (s, 2×*m*-$C_6H_2(OCH_3)_3$), 61.14 (s, *p*-$C_6H_2(OCH_3)_3$), 69.76 (d, J=4.2 Hz, CH(OH)), 104.08 (s, 2×*o*-$C_6H_2(OCH_3)_3$), 139.21 (s, *p*-$C_6H_2(OCH_3)_3$), 141.71 (d, J=16.5 Hz, *ipso*-$C_6H_2(OCH_3)_3$), 154.87 (s, 2×*m*-$C_6H_2(OCH_3)_3$); MS (CI) (m/z): 320 (3%, M^+), 303 (100, M^+(−OH)); MS (EI) (m/z): 320 (33%, M^+), 302 (13, M^+(−H_2O)), 287 (7, M^+(−H_2O, −CH_3)), 210 (100, M^+(−HP(O)$(OMe)_2$)); HRMS (EI) (m/z): calcd for $C_{13}H_{21}PO_7$: 320.10249, found: 320.10228.

3.3. Oxidations of 2-aryl-2-hydroxymethylphosphonates 3a, 3b, 5a, 5b, 7

To a solution of **3a** (0.2 mmol) in CH_3CH/H_2O (9:1 v/v) (5 mL), CAN (0.6 mmol, 3.0 equiv) was added in one portion at room temperature. The reaction mixture was stirred at 20 °C for 18 h. The reaction mixture was diluted with CH_2Cl_2 (10 mL). The organic layer was washed with water (3×10 mL), dried ($MgSO_4$), and then the solvent was removed in vacuo. The crude product was purified by column chromatography (petroleum ether/EtOAc).

To a solution of **3a** (0.2 mmol) in ethyl acetate (1 mL), Oxone® (0.4 mmol, 2.0 equiv) dissolved in H_2O (1 mL) was added dropwise at 20 °C. The reaction mixture was stirred at the same temperature for 2 h. The reaction mixture was diluted with ethyl acetate (5 mL). The organic layer was washed with water (3×10 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The crude product was purified by column chromatography (petroleum ether/EtOAc).

The oxidations of **3a**, **3b**, **5a**, **5b**, **7** by PCC or PDC were performed according to the literature procedure[7] under conditions indicated in Table 1 in a 1 mmol scale.

The oxidations of 2-aryl-2-hydroxymethylphosphonates performed by $KMnO_4$ on silica gel[8] or $KMnO_4/CuSO_4 \cdot 5H_2O$ or $KMnO_4/CuSO_4/Al_2O_3$ were performed according to Shaabani and Lee procedures[9] under conditions shown in Table 1.

The oxidations of 2-aryl-2-hydroxymethylphosphonates with CrO_3 supported on SiO_2 and H_2O_2 in the presence of salen as a catalyst were performed according to Kiasat et al.[10] and Mardani and Golchoubian[11] procedures, respectively.

Reactions with SIBX were performed according to the Ozanne et al. procedure.[14]

3.3.1. Dimethyl 2-(6-(benzyloxy (3,4,5-trimethoxyphenyl) methyl) benzo[d][1,3]dioxol-5-yl)-2-oxoethylphosphonate (**8a**)

A light-yellow oil; R_f=0.55 (ethyl acetate); IR (thin film) ν/cm^{-1}: 2994 (m, O–CH_2–O), 2953 (m, O–CH_2), 2851 (m, O–CH_3), 1677 (s, C═O), 1591 (s), 1505 (s), 1487 (s), 1456 (s, C(O)–CH_2), 1419 (m), 1330 (m), 1242 (vs, P═O), 1127 (s, CH–O–CH), 1036 (vs, P–O–C), 808 (m),

737 (w), 701 (w); ^{31}P NMR ($CDCl_3$): δ 23.04; ^{31}P NMR (C_6D_6): δ 22.59; ^{1}H NMR ($CDCl_3$): δ 3.383.43 (m, 1H, $CH_2P(O)$), 3.49–3.54 (m, 1H, $CH_2P(O)$), 3.75 (d, J_{PH}=11.2 Hz, 6H, $P(O)(OCH_3)_2$), 3.81 (s, 3H, *p*-$C_6H_2(OCH_3)_3$), 3.82 (s, 6H, 2×*m*-$C_6H_2(OCH_3)_3$), 4.48 (s, 2H, OCH_2Ph), 6.01–6.04 (m, 2H, OCH_2O), 6.15 (s, 1H, CHOBn), 6.71 (s, 2H, 2×*o*-$C_6H_2(OCH_3)_3$), 7.10 (s, 1H, Ar–H), 7.28 (s, 1H, Ar–H), 7.28–7.38 (m, 6H, Ar–H, Ph); ^{1}H NMR (C_6D_6) δ 3.21 (d, J_{PH}=22.3 Hz, 2H, $CH_2P(O)$), 3.34 (d, J_{PH}=11.2 Hz, 3H, $P(O)OCH_3$), 3.37 (d, J_{PH}=11.3 Hz, 3H, $P(O)OCH_3$), 3.47 (s, 6H, 2×*m*-$C_6H_2(OCH_3)_3$), 3.83 (s, 3H, *p*-$C_6H_2(OCH_3)_3$), 4.61 (s, 2H, OCH_2Ph), 5.13–5.22 (m, 2H, OCH_2O), 6.57 (s, 1H, CHOBn), 7.08 (s, 2H, 2×*o*-$C_6H_2(OCH_3)_3$), 7.09–7.21 (m, 3H, Ph), 7.25 (s, 1H, Ar), 7.46 (s, 1H, Ar); ^{13}C NMR (C_6D_6): δ 41.59 (d, J_{PC}=128.2 Hz, $CH_2P(O)$), 52.94 (d, J_{PC}=6.4 Hz, $P(O)OCH_3$), 53.16 (d, J_{PC}=6.2 Hz, $P(O)OCH_3$), 56.55 (s, 2×*m*-$C_6H_2(OCH_3)_3$), 60.99 (s, *p*-$C_6H_2(OCH_3)_3$), 71.97 (s, OCH_2Ph), 78.94 (s, CHOBn), 102.47 (s, OCH_2O), 105.76 (s, 2×*o*-$C_6H_2(OCH_3)_3$), 109.44 (s, Ar–H), 109.87 (s, Ar–H), 127.50 (s, *m*-Ph), 127.80 (s, *p*-Ph), 128.20 (s, *o*-Ph), 132.44 (s, *p*-$C_6H_2(OCH_3)_3$), 138.55 (s, C–C(O)), 139.25 (s, *ipso*-Ph), 139.68 (s, C–CHOBn), 140.78 (s, *ipso*-$C_6H_2(OCH_3)_3$), 147.53 (s, C–OCH_2O), 151.67 (s, C–OCH_2O), 154.77 (s, 2×*m*-$C_6H_2(OCH_3)_3$), 194.41 (d, J_{PC}=6.0 Hz, C=O); MS (CI) (*m*/*z*): 558 (0.2%, M^+), 541 (2, M^++H(−H_2O)), 451 (100, M^++H(−BnOH)). Anal. $C_{28}H_{31}O_{10}P$ requires: C, 60.21%; H, 5.59%. Found: C, 59.92%; H, 5.50%.

3.3.2. Diethyl 2-(6-(benzyloxy (3,4,5-trimethoxyphenyl) methyl) benzo[d][1,3]dioxol-5-yl)-2-oxoethylphosphonate (**8b**)

A light-yellow oil; R_f=0.58 (ethyl acetate); IR (thin film) ν/cm^{-1}: 2982 (m), 2936 (m, O–CH_2–O), 2838 (w, O–CH_3), 1677 (m, C=O), 1591 (m), 1506 (s), 1487 (s), 1456 (m, C(O)–CH_2), 1419 (m), 1330 (m), 1242 (vs, P=O), 1127 (vs, CH–O–CH), 1036 (vs, P–O–C), 968 (m), 791 (w), 738 (w), 701 (w); ^{31}P NMR (C_6D_6): δ 20.05; ^{1}H NMR (C_6D_6): δ 0.99 (t, J=7.1 Hz, 3H, $P(O)OCH_2CH_3$), 1.01 (t, J=7.0 Hz, 3H, $P(O)OCH_2CH_3$), 3.23 (d, J=2.3 Hz, 1H, $CH_2P(O)$), 3.35 (d, J=1.3 Hz, 1H, $CH_2P(O)$), 3.49 (s, 6H, 2×*m*-$C_6H_2(OCH_3)_3$), 3.83 (s, 3H, *p*-$C_6H_2(OCH_3)_3$), 3.83–3.97 (m, 4H, $P(O)(OCH_2CH_3)$), 4.62 (s, 2H, OCH_2Ph), 5.17 (s, 1H, OCH_2O), 5.22 (s, 1H, OCH_2O), 6.59 (s, 1H, CHOBn), 7.06–7.19 (m, 3H, *m*-, *p*-Ph), 7.09 (s, 2H, 2×*o*-$C_6H_2(OCH_3)_3$), 7.35 (s, 1H, Ar), 7.34–7.39 (m, 2H, *o*-Ph), 7.47 (s, 1H, Ar); ^{13}C NMR (C_6D_6): δ 16.99 (d, J=5.7 Hz, CH_3, $P(O)(OCH_2CH_3)_2$), 56.59 (s, CH_3, 2×*m*-$C_6H_2(OCH_3)_3$), 61.12 (s, CH_3, *p*-$C_6H_2(OCH_3)_3$), 63.13 (d, J=8.8 Hz, CH_2, $P(O)(OCH_2CH_3)_2$), 72.13 (s, OCH_2Ph), 79.13 (s, CHOBn), 102.54 (s, CH, OCH_2O), 106.05 (s, CH, 2×*o*-$C_6H_2(OCH_3)_3$), 109.57 (s, Ar–H), 110.16 (s, Ar–H), 127.49 (s, *m*-Ph), 127.81 (s, *p*-Ph), 128.18 (s, *o*-Ph), 132.71 (s, *p*-$C_6H_2(OCH_3)_3$), 138.71 (s, C–C(O)), 139.49 (s, *ipso*-Ph), 139.85 (s, C–CHOBn), 140.91 (s, *ipso*-$C_6H_2(OCH_3)_3$), 147.64 (s, C–OCH_2O), 151.74 (s, C–OCH_2O), 154.92 (s, 2×*m*-$C_6H_2(OCH_3)_3$), 194.57 (d, J=6.4 Hz, C=O); MS (CI) (*m*/*z*): 586 (0.4%, M^+), 569 (5, M^++H(−H_2O)), 479 (100, M^++H(−BnOH)). Anal. $C_{30}H_{35}O_{10}P$ requires: C, 61.43%; H, 6.01%. Found: C, 61.49%; H, 6.10%.

3.3.3. Dimethyl 2-(6-bromobenzo[d][1,3]dioxol-5-yl)-2-oxoethylphosphonate (**9a**)

A light-yellow oil; R_f=0.33 (petroleum ether/acetone 1:1 v/v); IR (KBr) ν/cm^{-1}: 3433 (br w), 2961 (w), 2902 (w, O–CH_2–O), 2855 (w, O–CH_3), 1691 (s, C=O), 1612 (m, C=C), 1510 (m, C=C), 1496 (m, C=C), 1484 (m), 1343 (m), 1263 (s, P=O), 1238 (P–O–C), 1034 (vs, P–O–C), 1022 (vs), 806 (m); ^{31}P NMR ($CDCl_3$): δ 22.34; ^{1}H NMR ($CDCl_3$): δ 3.66 (d, J=22.3 Hz, 2H, $CH_2P(O)$), 3.76 (d, J=11.2 Hz, 6H, $P(O)(OCH_3)_2$), 6.03 (s, 2H, OCH_2O), 7.02 (s, 1H, Ar–H), 7.07 (s, 1H, Ar–H); ^{13}C NMR ($CDCl_3$): δ 40.73 (d, J=129.5 Hz, $CH_2P(O)$), 53.10 (d, J=6.5 Hz, $P(O)(OCH_3)_2$), 102.54 (s, OCH_2O), 109.83 (s, 2-Ar–H), 111.99 (s, C-Br), 113.76 (s, 5-Ar–H), 133.55 (s, C–(C=O)), 147.44 (s, C–OCH_2O), 150.72 (s, C–OCH_2O), 193.25 (d, J=6.6 Hz, C=O); MS (CI) (*m*/*z*): 352 (98%, M^+ (^{81}Br)), 350 (100, M^+ (^{79}Br)), 271 (24, M^+(−Br)); HRMS (CI) (*m*/*z*): calcd for $C_{11}H_{12}PBrO_6$: 349.9555, found: 349.95506.

3.3.4. Dimethyl 2-(benzo[d][1,3]dioxol-5-yl)-2-oxoethylphosphonate (**9b**)

A white solid; mp=78–80 °C (from petroleum ether/ethyl acetate 3:1 v/v); R_f=0.20 (hexane/ethyl acetate 1:1 v/v), 0.40 (hexane/ethyl acetate 1:4 v/v); IR (KBr) ν/cm^{-1}: 3434 (br w), 3068 (w), 3031 (w), 2956 (w, O–CH_2–O), 2913 (w, O–CH_3), 2853 (w, O–CH_3), 1668 (s, C=O), 1600 (m), 1496 (m), 1447 (s, C(O)–CH_2), 1271 (vs, P=O), 1245 (s), 1061 (s), 1030 (vs, P–O–C), 1005 (s), 927 (m), 901 (m), 872 (m), 832 (m), 813 (m); ^{31}P NMR (C_6D_6): δ 22.81; ^{1}H NMR (C_6D_6): δ 3.23 (d, J=22.7 Hz, 2H, $CH_2P(O)$), 3.38 (d, J=11.0 Hz, 6H, $P(O)(OCH_3)_2$), 5.13 (s, 2H, OCH_2O), 6.46 (d, J=7.4 Hz, 1H, 6-Ar–H), 7.47 (d, J=7.4 Hz, 1H, 5-Ar–H), 7.60 (s, 1H, 2-Ar–H); ^{13}C NMR (C_6D_6): δ 38.72 (d, J=128.8 Hz, $CH_2P(O)$), 53.31 (d, J=6.0 Hz, 2×$P(O)(OCH_3)_2$), 102.57 (s, OCH_2O), 108.61 (s, 2-Ar–H), 109.56 (s, 5-Ar–H), 126.92 (s, 6-Ar–H), 132.70 (s, C–(C=O)), 149.22 (s, $COCH_2O$), 153.05 (s, $COCH_2O$), 190.11 (d, J=6.1 Hz, C=O); MS (CI) (*m*/*z*): 273 (100%, M^++H), 257 (4, M^++H(−O)); HRMS (CI) (*m*/*z*): calcd For $C_{11}H_{13}PO_6$: 272.04497, found: 272.04442.

3.3.5. Dimethyl 2-oxo-2-(3,4,5-trimethoxyphenyl) ethylphosphonate (**10**)

A light-yellow oil; R_f=0.11 (hexane/ethyl acetate 1:1 v/v), 0.29 (hexane/ethyl acetate 1:4 v/v); IR (film) ν/cm^{-1}: 2953 (m), 2844 (m, O–CH_3), 1675 (s, C=O), 1585 (s), 1506 (m, C=C), 1459 (m, C=C), 1417 (m), 1336 (vs, C(O)–CH_2), 1257 (s, P=O), 1228 (vs, P–O–C), 1032 (vs, P–O–C), 808 (m); ^{31}P NMR ($CDCl_3$): δ 22.00; ^{1}H NMR ($CDCl_3$): δ 3.61 (d, J=22.3 Hz, 2H, $CH_2P(O)$), 3.79 (d, J=11.1 Hz, 6H, $P(O)(OCH_3)_2$), 3.92 (s, 9H, $C_6H_2(OCH_3)_3$), 7.30 (s, 2H, 2×*o*-$C_6H_2(OCH_3)_3$); ^{13}C NMR ($CDCl_3$): δ 37.80 (d, J=131.1 Hz, $CH_2P(O)$), 53.22 (d, J=6.5 Hz, 2×$P(O)(OCH_3)_2$), 56.31 (s, 2×*o*-$C_6H_2(OCH_3)_3$), 60.93 (s, *p*-$C_6H_2(OCH_3)_3$), 106.62 (s, 2×*o*-$C_6H_2(OCH_3)_3$), 131.45 (s, *ipso*-$C_6H_2(OCH_3)_3$), 143.22 (s, *p*-$C_6H_2(OCH_3)_3$), 153.01 (s, 2×*m*-$C_6H_2(OCH_3)_3$), 190.35 (s, C=O); MS (CI) (*m*/*z*): 319 (100%, M^++H). HRMS (CI) (*m*/*z*): calcd for $C_{13}H_{19}PO_7$: 318.086842, found: 318.08656.

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References and notes

1. Mikołajczyk, M.; Bałczewski, P. In *Topics in Current Chemistry*; Majoral, J.-P., Ed.; Springer: Berlin, Heidelberg, 2002; Vol. 223, pp 161–214; Nicolaou, K. C.; Härter, M. W.; Gunzner, J. L.; Nadin, A. *Liebigs Ann./Recueil* **1997**, 1283–1301.
2. Jacobson, H. I.; Griffin, M. J.; Preis, S.; Jensen, E. V. *J. Am. Chem. Soc.* **1957**, *79*, 2608–2612; Cotton, F. A.; Schunn, R. A. *J. Am. Chem. Soc.* **1963**, *85*, 2394–2402.
3. Mathey, F.; Savignac, P. *Tetrahedron* **1978**, *34*, 649–654.
4. Genov, D. G.; Tebby, J. C. *J. Org. Chem.* **1996**, *61*, 2454–2459; Bałczewski, P.; Pietrzykowski, W. M. *Tetrahedron* **1996**, *52*, 13681–13694; Truel, I.; Mohamed-Hachi, A.; About-Jaudet, E.; Collignon, N. *Synth. Commun.* **1997**, *27*, 297–302.
5. (a) Obayashi, M.; Ito, E.; Matsui, K.; Kondo, K. *Tetrahedron Lett.* **1982**, *23*, 2323–2326; Piettre, S. R.; Girol, C.; Schelcher, C. G. *Tetrahedron Lett.* **1996**, *37*, 4711–4712; Faucher, A.-M.; White, P. W.; Brochu, C.; Grand-Maitre, C.; Rancourt, J.; Fazal, G. *J. Med. Chem.* **2004**, *47*, 18–21; (b) Snyder, C. D.; Bondinell, W. E.; Rapoport, H. *J. Org. Chem.* **1971**, *36*, 3951–3960; (c) Ganzhorn, A. J.; Hoflack, J.; Pelton, P. D.; Strasser, F.; Chanal, M.-Ch.; Piettre, S. R. *Bioorg. Med. Chem.* **1998**, *6*, 1865–1874; Colvin, E. W.; Hamill, B. J. *J. Chem. Soc., Perkin Trans. 1* **1977**, 869–874; Mualler, E. L.; Modro, A. M.; Modro, T. A. *Org. Prep. Proced. Int.* **1999**, *31*, 216–220.
6. (a) *Lignans: Chemical, Biological and Clinical Properties*; Ayers, D. C., Loike, J. D., Eds.; Cambridge University Press: Cambridge; New York, NY, 1990; Coleman, R. S.; Gurrala, S. R.; Mitra, S.; Raao, A. *J. Org. Chem.* **2005**, *70*, 8932–8941; (b) Robinson, R. *Proc. Univ. Durham Phil. Soc.* **1927–1928**, *8*, 14–59; Haworth, R. D. *Ann. Rep. Prog. Chem.* **1936**, *33*, 266–279.
7. Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975**, 2647–2650; Piancatelli, G.; Scettri, A.; D'Auria, M. *Synthesis* **1982**, 245–258; Vanden, E. J. J.; Mayence, A.; Maquestiau, A. *Tetrahedron* **1992**, *48*, 463–468; Cainelli, G.; Cardillo, G. *Chromium Oxidations in Organic Chemistry*; Springer: New York, NY, 1984.
8. Regen, S. L.; Koteel, Ch. *J. Am. Chem. Soc.* **1977**, *99*, 3837–3838; Shaabani, A.; Mirzaei, P.; Naderi, S.; Lee, D. G. *Tetrahedron* **2004**, *60*, 11415–11420.
9. Shaabani, A.; Lee, D. G. *Tetrahedron Lett.* **2001**, *42*, 5833–5836.
10. Kiasat, A. R.; Kazemi, F.; Nourbakhsh, K. *Synth. Commun.* **2005**, *35*, 1555–1558; Santaniello, E.; Ponti, F.; Manzocchi, A. *Synthesis* **1978**, 534; Lou, J.-D. *Synth.*

Commun. **1989**, *19*, 1841–1846; Singh, R. P.; Subbarao, H. N.; Dev, S. *Tetrahedron* **1979**, *35*, 1789–1793; Gruttadauria, M.; Liotta, L. F.; Deganello, G.; Noto, R. *Tetrahedron* **2003**, *59*, 4997–5002.
11. Mardani, H. R.; Golchoubian, H. *Tetrahedron Lett.* **2006**, *47*, 2349–2352.
12. Bovicelli, P.; Bernini, R.; Antonioletti, R.; Mincione, E. *Tetrahedron Lett.* **2002**, *43*, 5563–5567.
13. Trahanovsky, W. S.; Brown, G. L.; Young, B. L. *J. Org. Chem.* **1967**, *32*, 3865–3868; Ho, T.-L. *Synthesis* **1973**, 347–354; Ho, T.-L. *Synthesis* **1978**, 936–937.
14. Ozanne, A.; Pouysegu, L.; Depernet, D.; Francois, B.; Quideau, S. *Org. Lett.* **2003**, *5*, 2903–2906.
15. Cossy, J.; Bouzbouz, S.; Lachgar, M.; Hakiki, A.; Tabyaoui, B. *Tetrahedron Lett.* **1998**, *39*, 2561–2564.
16. Fatiadi, A. J. *Synthesis* **1976**, 65–104; Fatiadi, A. J. *Synthesis* **1976**, 133–167.
17. Bernstein, J.; Davis, R. E.; Shimoni, L.; Chang, N.-L. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1555–1573.
18. Sheldrick, G. M. *Acta Crystallogr. A* **2008**, *64*, 112–122.