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Efficient synthesis of ether phosphonates using trichloroacetimidate and acetate coupling methods

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A series of ether phosphonates have been prepared by trichloroacetimidate and acetate coupling methods. Trichloroacetimidates or acetates were treated with primary and secondary alcohols as *O*-nucleophiles in the presence of catalytic TMSOTf to afford 21 examples of diethyl alkyloxy(substitutedphenyl)methyl phosphonates *via* C–O bond formation in 55–90% yields and short reaction time.

Introduction

Phosphonates are an important class of organic compounds showing remarkable applications as isosteric analogs of natural phosphate esters.[1,2] Phosphonates are key intermediates in a variety of synthetically important reactions. The reaction of stabilized phosphonate carbanions (ylides) with aldehydes or ketones to afford E-selective alkenes is known as Horner–Wadsworth–Emmons reaction (a modified Wittig reaction).[3–5] A number of methods have been reported for the preparation of phosphonates. The Michaelis–Arbuzov reaction[6,7] is an abundant method for the preparation of phosphonates *via* P–C bond formation. It involves the reaction of an aryl/alkyl halide with trialkyl phosphite to give alkyl phosphonate. Hirao method[8,9] shows the palladium-catalyzed cross-coupling of dialkylphosphite with aromatic electrophiles for the synthesis of arylphosphonates *via* aryl C–P bond formation. Recently, α-functional phosphonates, α-aminophosphonates,[10] α-acetoxyphosphonates[11] and α-hydroxyphosphonates[12–15] showed interesting medicinal applications as antiviral agents and attracted the attention of many research groups. Abramov and Pudovik method[16,17] described the reaction of aldehydes with di and trialkyl phosphite in the presence of a base to afford α-hydroxyphosphonates. An efficient use of α-hydroxy phosphonates enables a mild process for the preparation of α-substituted methyl phosphonates with promising biological activities.

The use of trichloroacetimidate and acetate methods are well recognized in organic and carbohydrate synthesis *via* C–O or C–C bond formations.[18–21] Earlier we described the reaction of *O*-phthalimidomethyl trichloroacetimidate and *O*-diphenylmethyl trichloroacetimidate with C-nucleophiles in the presence of TMSOTf to afford a series of *N*-substituted phthalimides,[20] and benzhydryl derivatives.[21] Also, we showed the preparation of a number of N-protected non proteinogenic α-amino acid esters using trichloroacetimidate or acetate coupling methods *via* C–C bond formation from the corresponding methyl 2-benzamido-2-hydroxyacetate and benzyl(-methoxycarbonyl)(hydroxy)methylcarbamate substrates and C-nucleophiles.[22]

The strategies of both trichloroacetimidate and acetate methods involve the transformation of the substrate hydroxyl group into an excellent leaving group, such as trichloroacetimidate or acetate by the reaction with trichloroacetonitrile or acetic anhydride, respectively. The successive addition of poor nucleophiles (alcohols) to these active intermediates in the presence of Lewis acid give interesting products *via* C–O bond formations, Fig. 1.

These findings motivated the development of a series of diethyl alkyloxy(substitutedphenyl)methyl phosphonate **6–8(a–f)**, **10** and **12** using trichloroacetimidate and acetate coupling methods *via* C–O bond formation.

Results and discussion

Nucleophilic addition of diethyl phosphite to benzaldehydes **1a–d** in 1 : 1 molar ratio using triethylamine as a base gave the diethyl(hydroxy)arylmethyl phosphonates **2a–d** in good yields (Scheme 1). The base-catalyzed addition reaction of trichloroacetonitrile to α-hydroxyphosphonates **2a–d** hydroxyl group in the presence of DBU gave the desired diethyl 2-(2,2,2-trichloro-1-iminoethoxy)(3,4-dimethoxyphenyl)methylphosphonates **3a–d**, in 80–94% yield, Scheme 1. The reactions of α-hydroxyphosphonates **2b–d** with acetic anhydride in the presence of DMAP (*N*,*N*-dimethyl aminopyridine) at room temperature afforded diethylmethylcarbonyloxy-(4-methoxyphenyl)methylphosphonates **4b–d**, Scheme 1.

The structure assignment of α-hydroxyphosphonates **2a–d**, active intermediates trichloroacetimidate derivatives **3a–d** and acetate derivatives **4b–d** were based on ^{1}H, ^{13}C and ^{31}P NMR spectroscopic and elemental analysis are shown in the experimental part.

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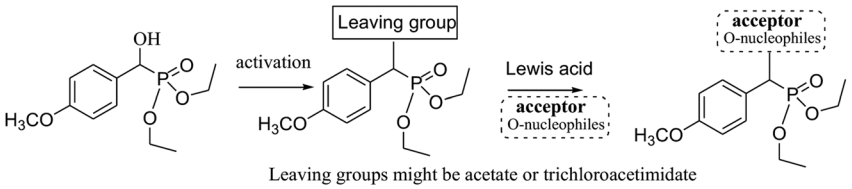
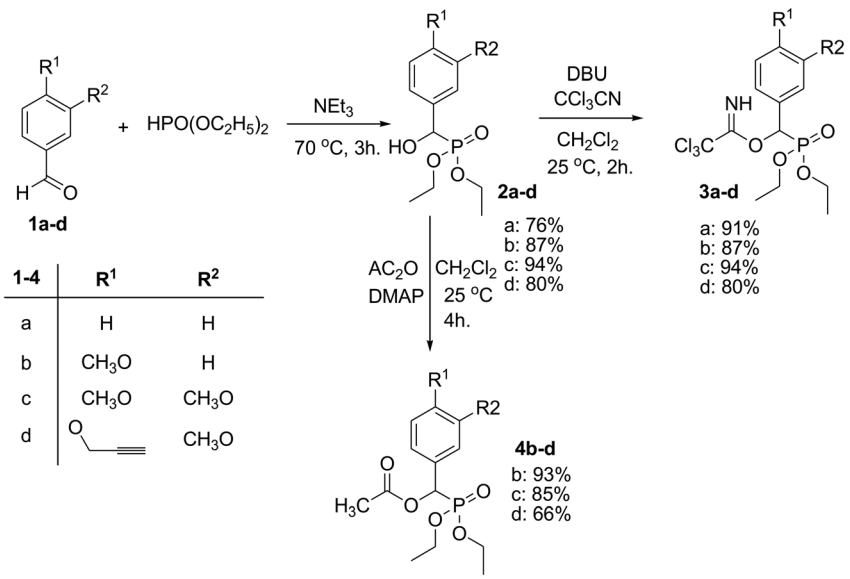


Fig. 1 The trichloroacetimidate and acetate coupling methods from functionalized alcohol substrates.

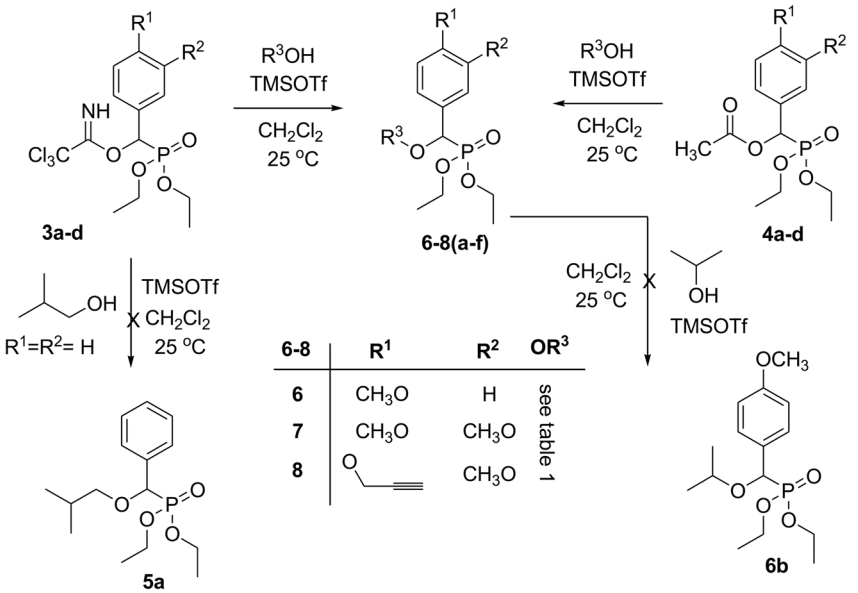
Both active intermediates trichloroacetimidates **3a–d** and acetates **4b–d** are excellent precursors for the structure modification of the diethyl phosphonate residue *via* trichloroacetimidate and acetate coupling methods. However, our early results concerning this synthetic method applying diethyl 2-(2,2,2-trichloro-1-iminoethoxy)(phenyl)methyl phosphonate (**3a**) failed to give us the desired products. Thus the reaction of trichloroacetimidate **3a** with isobutyl alcohol in the presence of a catalytic amount of TMSOTf at room temperature did not give diethyl 2-methylpropyloxy(phenyl) methyl phosphonate (**5a**) and instead decomposition was observed and a complex mixture was obtained, Scheme 2. On the other hand, trichloroacetimidates **3b–d** reacted with a variety of *O*-nucleophile acceptors (alcohols) in the presence of catalytic amount of TMSOTf at room temperature and readily gave a series of functionalized ether phosphonates **6–8(a–f)**, Scheme 2, Table 1. Similarly, the acetate derivatives **4b–d** reacted with a variety of *O*-nucleophile acceptors (alcohols) in the presence of a catalytic amount of TMSOTf at room temperature in dichloromethane and readily gave a series of functionalized ether phosphonates **6–8(a–f)**, Scheme 2, Table 1. A comparative study of both trichloroacetimidate and acetate methodologies was carried out to examine the efficiency of reaction time and % of yield in both methods. The results showed that, although all compounds were prepared in good yields, there was a slight improvement in the % of yield and in the reaction time (monitored by TLC) using the trichloroacetimidate method, see Experimental section.

According to the presumed mechanism, the TMSOTf is used to eliminate the trichloroacetimidate and acetate leaving groups with the subsequent formation of carbocation. This carbocation could be stabilized by an efficient electron donor and a phenyl group but it is insufficient. In contrast there was good stabilization in the case of a phenyl residue bearing an electron-donating –OR group at the 4-position. The final step is the nucleophilic attack of the weak alcohol nucleophiles at the stabilized carbocation to form the desired products **6–8(a–f)** *via* an overall S_N1 mechanism. The attempted reaction of diethyl 2-methylpropyloxy(4-methoxyphenyl)methyl phosphonate (**6a**) with isopropyl alcohol under the same reaction conditions, in the presence of a catalytic amount of TMSOTf at room temperature in dichloromethane, failed to give the corresponding isopropyl ether phosphonate derivative **6b** *via* transetherification, Scheme 2.

Structure assignment of ether derivatives **6–8(a–f)** were based on ^{1}H, ^{13}C and ^{31}P-NMR spectral and physicochemical analysis. The ^{1}H-NMR spectrum of **6a** shows an interesting doublet signal at $\delta = 4.52$ ppm with coupling constant 15.0 Hz typically associated with CHP. This chemical shift is common for all isolated phosphonate derivatives **6–8(a–f)** with chemical shifts ranging from 4.37–4.93 ppm and with coupling constant ranging from 12–18 Hz. The ^{1}H-NMR spectrum exhibit signals at δ 0.90, 0.93, 1.84–1.97 and 3.16–3.28 ppm due to two CH_3, CH and CH_2 groups, respectively of the isobutyl-residue and signals at δ 1.24–1.28 and 4.02–4.12 ppm



Scheme 1 Synthetic pathway of phosphonates trichloroacetimidates and acetates **3a–d** and **4b–d**.



Scheme 2 Synthetic pathway of phosphonates 6–8(a–f) *via* C–O bond formation.

due to two OCH_2CH_3 residue. The ^{13}C NMR spectrum of **6a** shows interesting doublet signals at δ 16.3, 16.4, 62.7, 63.0, 76.9 and 77.5 ppm having coupling constants J_{CP} 6.0, 6.0, 6.8, 6.8, 32.4 and 169.6 Hz corresponding to CH_3, CH_3, OCH_2P, OCH_2P, CH_2OCHP and CHP groups, respectively. These signals are common for all isolated products, which confirm the C–O bond formation. The previously mentioned signals are good evidences for either the C–P coupling, the diastereotopic nature or both for these individual groups. The ^{31}P-NMR spectrum of **6a** showed a single signal at δ = 19.5 ppm corresponding to phosphonate phosphorus and was used as an indicator for the purity of the products.

The trichloroacetimidate method proved to be an excellent method for the structure modification of diethyl hydroxy(substituted phenyl)methylphosphonate **2a–d**. Next, the use of an interesting derivatized alcohols was explored: (5-methyl-2-phenyl-1,3-dioxan-5-yl)methanol **9** and 2-(*N*-methyl-*N*-phenylamino) ethanol **11**. The dioxane derivative **9** was prepared by heating 1,1,1-tris(hydroxymethyl)ethane with benzaldehyde in the presence of toluene-*p*-sulfonic acid in benzene and this compound is known to possess potential medicinal chemistry relevance.[23] Thus the reaction of trichloroacetimidate **3a–b** with dioxane derivative **9** in the presence of a catalytic amount of TMSOTf at room temperature in dichloromethane and gave diethyl((5-methyl-2-phenyl-1,3-dioxan-5-yl)methoxy)(substitutedphenyl)methyl phosphonate **10a–b** in 62–70% yields, Scheme 3. Also trichloroacetimidate **3a** reacted with 2-(*N*-methyl-*N*-phenylamino)ethanol (**11**) in the presence of a catalytic amount of TMSOTf at room temperature in dichloromethane and gave diethyl 2-(*N*-methyl-*N*-phenylamino)ethyloxy(4-methoxyphenyl)methyl phosphonate **12** in 29% yield, Scheme 3.

Conclusion

In conclusion, an efficient and very simple method for the synthesis of various ether phosphonates by trichloroacetimidate and acetate coupling methods is described. Trichloroacetimidates **3a–d** or acetates **4b–d** were treated with Lewis acid followed by reaction with *O*-nucleophiles to afford the desired products *via* C–O bond formation. Both methods gave good yields of desired products in short reaction times, and generally slightly better results were obtained using the trichloroacetimidate method. Applications of this methodology to synthesize various phosphonate analogues of alcohols containing primary and secondary hydroxy groups as *O*-nucleophiles are under progress in our laboratory.

Experimental

Solvents were purified and dried in the usual way. The boiling range of the petroleum ether used was 40–60 °C. Thin-layer chromatography (TLC) utilized silica gel 60 F254 plastic plates (E. Merck, layer thickness 0.2 mm). Detection was by UV absorption. Melting points were determined on a Buchi 510 melting point apparatus. The ^1H, ^{13}C and ^{31}P NMR spectra were recorded at 300 MHz, 75.5 and 194.4 MHz, respectively (Bruker AC 300) in $CDCl_3$ with tetramethylsilane as an internal standard. The NMR analysis were performed at Organic Chemistry Department Masaryk University, Brno, Czech Republic. Elemental analyses were performed on a Flash EA-1112 instrument at the Microanalytical Laboratory, Faculty of Science, Suez Canal University, Ismailia, Egypt. 3,4-Dimethoxybenzaldehyde **1c** and 3-methoxy-4-(prop-2-ynyloxy)benzaldehyde **1d** was prepared by alkylation of vaniline as described in the literature.[24]

Diethyl hydroxy(substitutedphenyl)methyl phosphonate 2a–d[25]

To a mixture of (20.7 g, 0.15 mol) of diethyl phosphonate and 1.09 g (0.011 mol) of triethylamine was added (0.15 mol) of aldehydes **1a–d** portion wise during a period of 1 h at 50–70 °C. The reaction mixture was subsequently stirred at 70 °C for 2 h. After cooling it was left over night to give white crystals, filter

Table 1 Synthesis of ether phosphonate derivatives **6–8(a–f)** and the comparative results between trichloroacetimidate and acetate coupling methods[a]

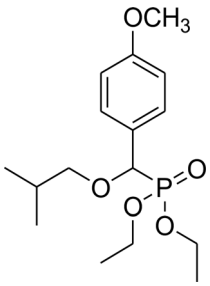
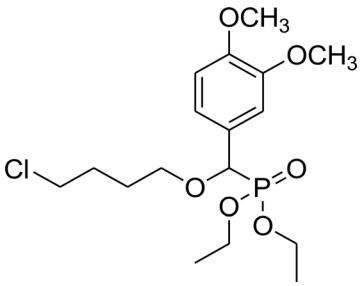
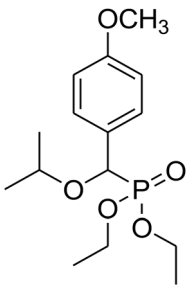
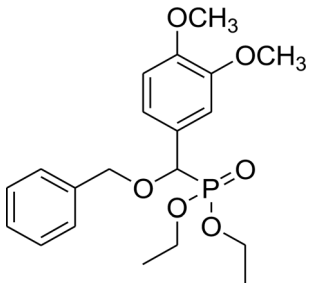
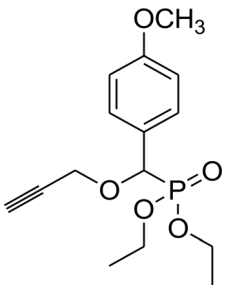
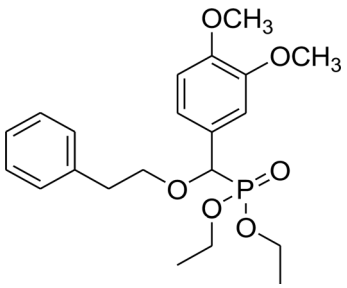
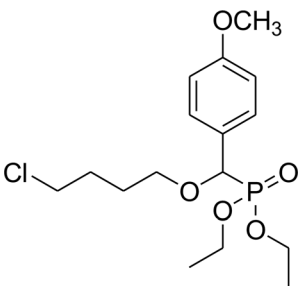
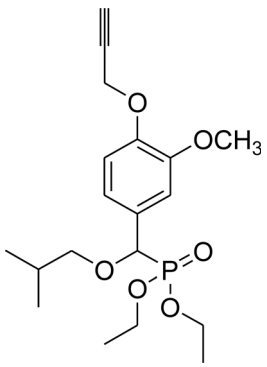
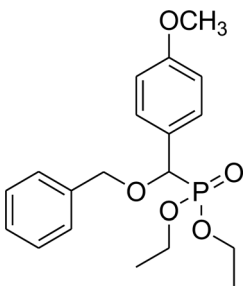
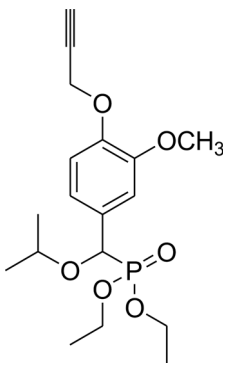
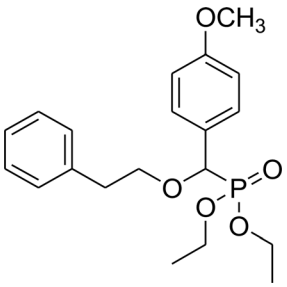
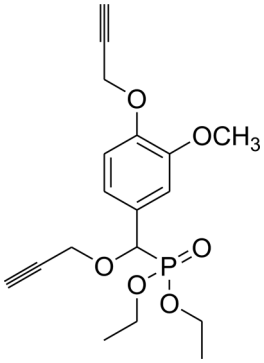
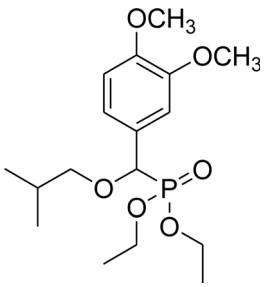
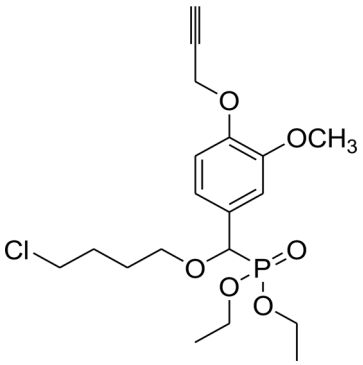
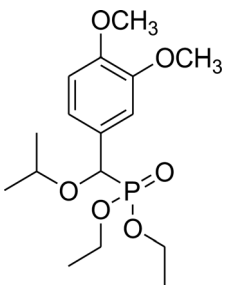
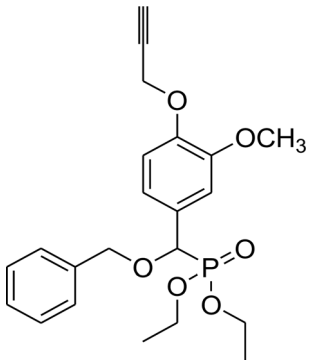
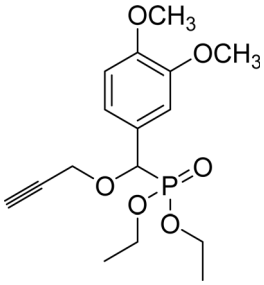
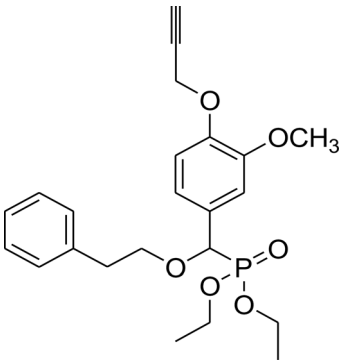
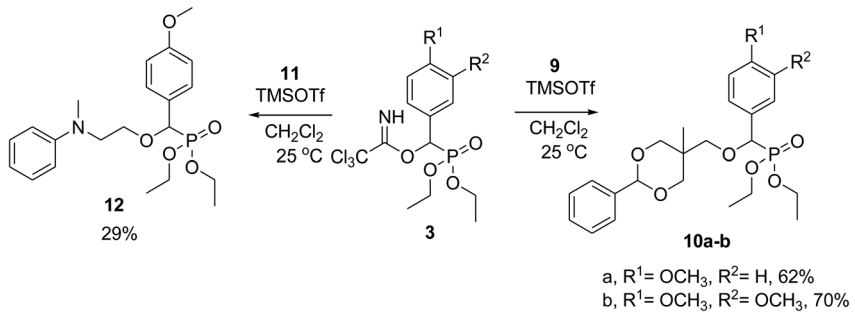
No.	Structure	TCI and Ac yield (time)	No.	Structure	TCI and Ac yield (time)
6a		81% (2 h), 76% (4 h)	**7d**		78% (3 h), 59% (4 h)
6b		72% (2 h), 64% (5 h)	**7e**		79% (1 h), 73% (5 h)
6c		75% (3 h), 71% (5 h)	**7f**		86% (2 h), 79% (4 h)
6d		82% (2 h), 76% (5 h)	**8a**		79% (2 h), 75% (2 h)
6e		67% (2 h), 71% (3 h)	**8b**		74% (1 h), 66% (3 h)

Table 1 (*Contd.*)

No.	Structure	TCI and Ac yield (time)	No.	Structure	TCI and Ac yield (time)
6f		71% (3 h), 56% (4 h)	**8c**		80% (2 h), 78% (4 h)
7a		86% (1 h), 77% (4 h)	**8d**		81% (3 h), 72% (3 h)
7b		78% (1 h), 68% (4 h)	**8e**		71% (2 h), 63% (3 h)
7c		86% (2 h), 74% (4 h)	**8f**		79% (2 h), 69% (4 h)

[a] Abbrev. TCI: trichloroacetimidate method, Ac: acetate method.



Scheme 3 Synthesis of phosphonates **10a–b** and **12** *via* C–O bond formation.

and wash with cold toluene and then recrystallized from toluene to give pure crystals.

Diethyl hydroxy(phenyl)methyl phosphonate (2a)

27.5 g, yield 76% white crystals. Mp 80–81 °C. ^{1}H NMR spectrum, (300 MHz, $CDCl_3$), δ, ppm (J, Hz): 1.19–1.34 (m, 6H, $2CH_3$), 3.82 (s, 3H, OCH_3), 3.91–4.10 (m, 4H, $2CH_2$), 3.54 (bs, 1H, OH), 5.00 (d, J_{HP} = 8.0 Hz, 1H, CHP), 7.24–7.46 (m, 5H, H-Ar). ^{13}C-NMR (75.0 MHz, $CDCl_3$), δ, ppm: 16.3 (d, J_{CP} = 4.0, CH_3), 16.4 (d, J_{CP} = 4.0, CH_3), 55.3 (OCH_3), 62.7 (d, J_{CP} = 7.6, CH_2OP), 63.4 (d, J_{CP} = 7.6, CH_2OP), 70.2 (d, J_{CP} = 158.4, CHP), 127.1, 127.2, 128.1, 128.3, 136.8 (C-Ar). ^{31}P-NMR (194.4 MHz, $CDCl_3$), δ, ppm: 21.6 (P). Found, %: C, 53.89; H, 6.94. For $C_{11}H_{17}O_4P$ (244.1). Calculated, %: C, 54.10; H, 7.02.

Diethyl hydroxy(4-methoxyphenyl)methyl phosphonate (2b)

34.4 g, yield 84% white crystals. Mp 90–91 °C. ^{1}H-NMR spectrum, (300 MHz, $CDCl_3$), δ, ppm (J, Hz): 1.19–1.29 (m, 6H, $2CH_3$), 3.80 (s, 3H, OCH_3), 3.89–4.10 (m, 4H, $2CH_2$), 4.33 (bs, 1H, OH), 4.95 (d, J_{HP} = 9.0 Hz, 1H, CHP), 6.87 (d, J = 9.0 Hz, 2H, H-Ar), 7.39–7.43 (m, 2H, H-Ar). ^{13}C-NMR (75.0 MHz, $CDCl_3$), δ, ppm: 16.3 (d, J_{CP} = 4.0, CH_3), 16.4 (d, J_{CP} = 4.0, CH_3), 55.2 (OCH_3), 62.9 (d, J_{CP} = 7.6, CH_2OP), 63.2 (d, J_{CP} = 7.6, CH_2OP), 70.3 (d, J_{CP} = 161.6, CHP), 113.0, 113.7, 128.4, 128.5, 128.8, 159.5 (C-Ar). ^{31}P-NMR (194.4 MHz, $CDCl_3$), δ, ppm: 21.7 (P). Found, %: C, 52.39; H, 6.81. For $C_{12}H_{19}O_5P$ (274.1). Calculated, %: C, 52.55; H, 6.98.

Diethyl hydroxy(3,4-dimethoxyphenyl)methyl phosphonate (2c)

40.6 g, yield 89% white crystals. Mp 101–103 °C. ^{1}H-NMR spectrum, (300 MHz, $CDCl_3$), δ, ppm (J, Hz): 1.16–1.26 (m, 6H, $2CH_3$), 3.83 (s, 3H, OCH_3), 3.88 (s, 3H, OCH_3), 3.92–4.07 (m, 4H, $2CH_2$), 4.62 (bs, 1H, OH), 4.89 (d, J_{HP} = 9.0 Hz, 1H, CHP), 6.81 (d, J = 9.0 Hz, 1H, H-Ar), 6.95–7.07 (m, 1H, H-Ar), 7.08 (s, 1H, H-Ar). ^{13}C-NMR (75.0 MHz, $CDCl_3$), δ, ppm: 16.3 (d, J_{CP} = 4.0, CH_3), 16.4 (d, J_{CP} = 4.0, CH_3), 55.8 (OCH_3), 55.9 (OCH_3), 62.9 (d, J_{CP} = 7.6, CH_2OP), 63.2 (d, J_{CP} = 7.6, CH_2OP), 70.4 (d, J_{CP} = 161.6, CHP), 110.5, 110.8, 110.9, 129.3, 148.7, 148.8 (C-Ar). ^{31}P-NMR (194.4 MHz, $CDCl_3$), δ, ppm: 21.7 (P). Found, %: C, 51.12; H, 6.89. For $C_{13}H_{21}O_6P$ (304.1). Calculated, %: C, 51.31; H, 6.96.

Diethyl hydroxy(3-methoxy-4-(prop-2-yn-1-yloxy)phenyl) methyl phosphonate (2d)

36.9 g, yield 75% white crystals. Mp 87–88 °C. ^{1}H-NMR spectrum, (300 MHz, $CDCl_3$), δ, ppm (J, Hz): 1.19–1.37 (m, 6H, $2CH_3$), 2.50 (t, J = 3.0 Hz, 1H, CH), 3.86 (s, 3H, OCH_3), 3.92–4.17 (m, 4H, $2CH_2$), 4.39 (bs, 1H, OH), 4.74 (d, J = 3.0 Hz, 2H, OCH_2), 4.93 (d, J_{HP} = 9.0 Hz, 1H, CHP), 6.99–7.12 (m, 3H, H-Ar). ^{13}C-NMR (75.0 MHz, $CDCl_3$), δ, ppm: 16.3 (d, J_{CP} = 4.0, CH_3), 16.4 (d, J_{CP} = 4.0, CH_3), 55.9 (OCH_3), 56.8 (OCH_2), 63.0 (d, J_{CP} = 7.6, CH_2OP), 63.2 (d, J_{CP} = 7.6, CH_2OP), 70.5 (d, J_{CP} = 160.8, CHP), 75.8 (C≡CH), 78.5 (C≡CH), 110.9, 114.0, 119.5, 130.7, 146.6, 149.6 (C-Ar). ^{31}P-NMR (194.4 MHz, $CDCl_3$), δ, ppm: 21.5 (P). Found, %: C, 54.68; H, 6.43. For $C_{15}H_{21}O_6P$ (328.1). Calculated, %: C, 54.88; H, 6.45.

Preparation of diethyl 2-(2,2,2-trichloro-1-iminoethoxy)(substitutedphenyl) methyl phosphonate 3a–d

A stirred solution of diethyl hydroxy(substitutedphenyl)methylphosphonate **2a–d** (10.0 mmol) in dry dichloromethane (30 mL) was treated with trichloroacetonitrile (2.9 mL, 20 mmol) and DBU (0.8 mL, 5.0 mmol). The reaction mixture was stirred at room temperature for 2 h. The solvent was evaporated under reduced pressure and the product was purified by column chromatography 5% triethylamine in dichloromethane, to give **3a–d** as whitish oil.

Diethyl 2-(2,2,2-trichloro-1-iminoethoxy)(phenyl)methyl phosphonate (3a)

1.92 g, yield 91% brownish oil. ^{1}H NMR spectrum, (300 MHz, $CDCl_3$), δ, ppm (J, Hz): 1.16–1.29 (m, 6H, $2CH_3$), 3.78 (s, 3H, OCH_3), 3.94–4.17 (m, 4H, $2CH_2$), 6.22 (d, J_{HP} = 15.0 Hz, 1H, CHP), 6.95–7.53 (m, 5H, H-Ar), 8.55 (brs, 1H, NH). ^{31}P-NMR (194.4 MHz, $CDCl_3$), δ, ppm: 16.4 (P). Found, %: C, 40.04; H, 4.32; N, 3.48. For $C_{13}H_{17}Cl_3NO_4P$ (387.1). Calculated, %: C, 40.18; H, 4.41; N, 3.60.

Diethyl(2,2,2-trichloro-1-iminoethoxy)(4-methoxyphenyl) methyl phosphonate (3b)

3.6 g, yield 87% brownish oil. ^{1}H-NMR spectrum, (300 MHz, $CDCl_3$), δ, ppm (J, Hz): 1.20–1.27 (m, 6H, $2CH_3$), 3.76 (s, 3H, OCH_3), 3.97–4.16 (m, 4H, $2CH_2$), 6.20 (d, J_{HP} = 15.0 Hz, 1H, CHP), 6.86 (d, J = 9.0 Hz, 2H, H-Ar), 7.44 (d, J = 6.0 Hz, 2H, H-

Ar), 8.51 (brs, 1H, NH). ^{13}C-NMR (75.0 MHz, CDCl3), δ, ppm: 16.3 (d, J_{CP} = 6.0, CH_3), 16.4 (d, J_{CP} = 6.0, CH_3), 55.2 (OCH_3), 63.3 (d, J_{CP} = 6.0, CH_2OP), 63.5 (d, J_{CP} = 6.0, CH_2OP), 74.8 (d, J_{CP} = 172.1, CHP), 90.9 (CCl_3), 113.8, 113.9, 124.7, 124.7, 129.2, 129.3 (C-Ar), 161.1 (C=N). ^{31}P-NMR (194.4 MHz, $CDCl_3$), δ, ppm: 16.5 (P). Found, %: C, 39.96; H, 4.42; N, 3.29. For $C_{14}H_{19}Cl_3NO_5P$ (417.0). Calculated, %: C, 40.17; H, 4.57; N, 3.35.

Diethyl(2,2,2-trichloro-1-iminoethoxy)(3,4-dimethoxyphenyl) methyl phosphonate (3c)

4.2 g, yield 94% brownish oil. ^{1}H-NMR spectrum, (300 MHz, $CDCl_3$), δ, ppm (J, Hz): 1.25–1.32 (m, 6H, $2CH_3$), 3.89 (s, 6H, 2 OCH_3), 4.02–4.23 (m, 4H, $2CH_2$), 6.23 (d, J_{HP} = 12.0 Hz, 1H, CHP), 6.86 (d, J = 9.0 Hz, 1H, H-Ar), 7.09 (d, J = 9.0 Hz, 2H, H-Ar), 8.53 (brs, 1H, NH). ^{13}C-NMR (75.0 MHz, $CDCl_3$), δ, ppm: 16.4 (d, J_{CP} = 6.0, CH_3), 16.5 (d, J_{CP} = 6.0, CH_3), 55.8 (OCH_3), 63.3 (d, J_{CP} = 6.0, CH_2OP), 63.7 (d, J_{CP} = 6.0, CH_2OP), 74.9 (d, J_{CP} = 172.1, CHP), 91.0 (CCl_3), 110.8, 120.6, 120.7, 125.2, 148.9, 149.5 (C-Ar), 161.2 (C=N). ^{31}P-NMR (194.4 MHz, $CDCl_3$), δ, ppm: 16.5 (P). Found, %: 40.02; H, 4.67; N, 3.05. For $C_{15}H_{21}Cl_3NO_6P$ (447.0). Calculated, %: C, 40.15; H, 4.72; N, 3.12.

Diethyl(2,2,2-trichloro-1-iminoethoxy)(3-methoxy-4-(prop-2-yn-1-yloxy)phenyl)methyl phosphonate (3d)

3.8 g, yield 80% brownish oil. ^{1}H-NMR spectrum, (300 MHz, $CDCl_3$), δ, ppm (J, Hz): 1.22 (m, 6H, $2CH_3$), 2.50 (s, 1H, CH), 3.85 (s, 3H, OCH_3), 3.99–4.16 (m, 4H, CH, $2CH_2$), 4.73 (d, J = 3.0 Hz, 2H, OCH_2), 6.20 (d, J_{HP} = 12.0 Hz, 1H, CHP), 6.99–7.28 (m, 3H, H-Ar), 8.53 (brs, 1H, NH). ^{13}C-NMR (75.0 MHz, $CDCl_3$), δ, ppm: 16.4 (d, J_{CP} = 6.0, CH_3), 16.5 (d, J_{CP} = 6.0, CH_3), 55.9 (OCH_3), 56.7 (OCH_2), 63.3 (d, J_{CP} = 6.8, CH_2OP), 63.6 (d, J_{CP} = 6.8, CH_2OP), 74.1 (d, J_{CP} = 171.4, CHP), 75.9 (C≡CH), 78.4 (C≡CH), 90.9 (CCl_3), 111.2, 113.9, 120.3, 126.6, 147.3, 149.6 (C-Ar), 161.1 (C=N). ^{31}P-NMR (194.4 MHz, $CDCl_3$), δ, ppm: 16.3 (P). Found, %: C, 43.11; H, 4.36; N, 2.82. For $C_{17}H_{21}Cl_3NO_6P$ (471.0). Calculated, %: C, 43.20; H, 4.48; N, 2.96.

Preparation of diethyl methylcarbonyloxy(substitutedphenyl) methyl phosphonate 4b–d

A solution of diethyl hydroxy(substitutedphenyl)methylphosphonate **2a–c** (10.0 mmol) in acetic anhydride (1.2 mL, 12.0 mmol) and DMAP (0.61 g, 5.0 mmol) and NEt_3 (1.1 mL, 12.0 mmol) was stirred at room temperature for 4 h. The reaction mixture was evaporated under reduced pressure. The residue was purified by column chromatography 4 : 1 pet. ether/ethyl-acetate, to give **4a–c** as white oil.

Diethyl methylcarbonyloxy(4-methoxyphenyl)methyl phosphonate (4b)

2.94 g, yield 93% whitish oil. ^{1}H NMR spectrum, (300 MHz, $CDCl_3$), δ, ppm (J, Hz): 1.19 (t, J = 6.0 Hz, 3H, CH_3), 1.28 (t, J = 6.0 Hz, 3H, CH_3), 2.13 (s, 3H, CH_3), 3.79 (s, 3H, OCH_3), 3.87–4.13 (m, 4H, $2CH_2$), 6.07 (d, J_{HP} = 12.0 Hz, 1H, CHP), 6.87 (d, J = 6.0 Hz, 2H, H-Ar), 7.40–7.44 (m, 2H, H-Ar). ^{13}C-NMR (75.0 MHz, $CDCl_3$), δ, ppm: 16.2 (d, J_{CP} = 6.0, CH_3), 16.4 (d, J_{CP} = 6.0, CH_3), 20.9 (CH_3), 55.2 (OCH_3), 63.1 (d, J_{CP} = 6.8, CH_2OP), 63.6 (d, J_{CP} = 6.8, CH_2OP), 70.1 (d, J_{CP} = 172.9, CHP), 113.9, 125.5, 129.5, 129.6, 159.9 (C-Ar), 169.3 (CO). ^{31}P-NMR (194.4 MHz, $CDCl_3$), δ, ppm: 18.0 (P). Found, %: C, 53.13; H, 6.57. For $C_{14}H_{21}O_6P$ (316.1). Calculated, %: C, 53.16; H, 6.69.

Diethyl methylcarbonyloxy(3,4-dimethoxyphenyl)methyl phosphonate (4c)

2.94 g, yield 85% whitish oil. ^{1}H NMR spectrum, (300 MHz, $CDCl_3$), δ, ppm (J, Hz): 1.15 (t, J = 6 Hz, 3H, CH_3), 1.24 (t, J = 6.0 Hz, 3H, CH_3), 2.10 (s, 3H, CH_3), 3.82 (s, 3H, OCH_3), 3.88 (s, 3H, OCH_3), 3.91–4.11 (m, 4H, $2CH_2$), 6.02 (d, J_{HP} = 12.0 Hz, 1H, CHP), 6.79 (d, J = 6.0 Hz, 1H, H-Ar), 6.98–7.02 (m, 2H, H-Ar). ^{13}C-NMR (75.0 MHz, $CDCl_3$), δ, ppm: 16.3 (d, J_{CP} = 6.0, CH_3), 16.4 (d, J_{CP} = 6.0, CH_3), 20.8 (CH_3), 55.8 (CH_3), 55.9 (CH_3), 63.1 (d, J_{CP} = 6.8, CH_2OP), 63.7 (d, J_{CP} = 6.8, CH_2OP), 70.3 (d, J_{CP} = 172.9, CHP), 110.9, 120.9, 121.0, 125.7, 148.9, 149.4 (C-Ar), 169.2 (CO). ^{31}P-NMR (194.4 MHz, $CDCl_3$), δ, ppm: 17.9 (P). Found, %: C, 51.85; H, 6.54. For $C_{15}H_{23}O_7P$ (346.1). Calculated, %: C, 52.02; H, 6.69.

Diethyl methylcarbonyloxy(3-methoxy-4-propargyloxyphenyl) methyl phosphonate (4d)

2.44 g, yield 66% whitish oil. ^{1}H NMR spectrum, (300 MHz, $CDCl_3$), δ, ppm (J, Hz): 1.13 (t, J = 6.0 Hz, 3H, CH_3), 1.31 (t, J = 6.0 Hz, 3H, CH_3), 2.21 (s, 3H, $COCH_3$), 2.51 (s, 1H, CH), 3.87 (s, 3H, OCH_3), 3.92–4.13 (m, 4H, CH, $2CH_2$), 4.74 (d, J = 3.0 Hz, 2H, CH_2), 6.07 (d, J_{HP} = 12.0 Hz, 1H, CHP), 6.98–7.08 (m, 3H, H-Ar). ^{13}C-NMR (75.0 MHz, $CDCl_3$), δ, ppm: 16.3 (d, J_{CP} = 6.0, CH_3), 16.4 (d, J_{CP} = 6.0, CH_3), 20.9 (CH_3), 56.0 (OCH_3), 56.7 (OCH_2), 63.2 (d, J_{CP} = 6.0, CH_2OP), 63.3 (d, J_{CP} = 6.0, CH_2OP), 70.1 (d, J_{CP} = 172.9, CHP), 75.9 (C≡CH), 78.4 (C≡CH), 111.9, 114.0, 120.7, 127.2, 147.3, 149.6 (C-Ar), 169.2 (CO). ^{31}P-NMR (194.4 MHz, $CDCl_3$), δ, ppm: 17.9 (P). Found, %: C, 55.04; H, 6.19. For $C_{17}H_{23}O_7P$ (370.1). Calculated, %: C, 55.13; H, 6.26.

General procedure for the preparation of diethyl alkyloxy(substitutedphenyl)methyl phosphonate 6–8(a–f), 10 and 12

A solution of trichloroacetimidate **3a–d** or acetate **4b–d** (1.0 mmol) in dichloromethane (40 mL) was added *O*-nucleophiles (alcohols) (1.0 mmol) and TMSOTf (0.1 mmol). The reaction mixture was stirred at room temperature till completion of the reaction (TLC monitored and the time was recorded). The reaction mixture was neutralized with solid sodium bicarbonate, filtered and concentrated *in vacuo*. The residue was purified by flash chromatography 1 : 2 pet. ether/ethyl-acetate to give the pure alkyloxy phosphonates **6–8(a–f)**, **10** and **12** as colorless oil.

Diethyl 2-methylpropyloxy(4-methoxyphenyl)methyl phosphonate (6a)

0.26 g, yield 78% colorless oil. ^{1}H NMR spectrum, (300 MHz, $CDCl_3$), δ, ppm (J, Hz): 0.90 (d, J = 3.0 Hz, 3H, CH_3), 0.93 (d, J = 3.0 Hz, 3H, CH_3), 1.24–1.28 (m, 6H, $2CH_3$), 1.84–1.97 (m, 1H,

CH), 3.16–3.28 (m, 2H, CH_2), 3.82 (s, 3H, OCH_3), 4.02–4.12 (m, 4H, $2CH_2$), 4.52 (d, J_{HP} = 15.0 Hz, 1H, CHP), 6.90 (d, J = 6.0 Hz, 2H, H-Ar), 7.28–7.39 (m, 2H, H-Ar). ^{13}C-NMR (75.0 MHz, $CDCl_3$), δ, ppm: 16.3 (d, J_{CP} = 6.0, CH_3), 16.4 (d, J_{CP} = 6.0, CH_3), 19.2 (CH_3), 19.3 (CH_3), 28.4 (CH), 55.2 (OCH_3), 62.7 (d, J_{CP} = 6.8, CH_2OP), 63.0 (d, J_{CP} = 6.8, CH_2OP), 76.9 (d, J_{CP} = 32.4, CH_2-OCHP), 77.5 (d, J_{CP} = 169.6, CHP), 113.7, 113.8, 127.0, 129.2, 129.3, 159.7 (C-Ar). ^{31}P-NMR (194.4 MHz, $CDCl_3$), δ, ppm: 19.5 (P). Found, %: C, 58.04; H, 8.16. For $C_{16}H_{27}O_5P$ (330.2). Calculated, %: C, 58.17; H, 8.24.

Diethyl 1-methylethyloxy(4-methoxyphenyl)methyl phosphonate (6b)

0.26 g, yield 83% colorless oil. ^{1}H NMR spectrum, (300 MHz, $CDCl_3$), δ, ppm (J, Hz): 1.08 (d, J = 6.0 Hz, 3H, CH_3), 1.14 (d, J = 6.0 Hz, 3H, CH_3), 1.19–1.25 (m, 6H, $2CH_3$), 3.57–3.76 (m, 1H, CH), 3.87 (s, 3H, OCH_3), 3.92–4.09 (m, 4H, $2CH_2$), 4.64 (d, J_{HP} = 18.0 Hz, 1H, CHP), 6.84 (d, J = 9.0 Hz, 2H, H-Ar), 7.33–7.36 (m, 2H, H-Ar). ^{13}C-NMR (75.0 MHz, $CDCl_3$), δ, ppm: 16.3 (d, J_{CP} = 6.0, CH_3), 16.4 (d, J_{CP} = 6.0, CH_3), 20.9 (CH_3), 23.0 (CH_3), 55.1 (OCH_3), 62.7 (d, J_{CP} = 8.0, CH_2OP), 63.1 (d, J_{CP} = 8.0, CH_2OP), 71.3 (d, J_{CP} = 13.6, CHOCHP), 75.5 (d, J_{CP} = 171.4, CHP), 113.6, 113.7, 117.6, 129.3, 159.5, 159.6 (C-Ar). ^{31}P-NMR (194.4 MHz, $CDCl_3$), δ, ppm: 20.0 (P). Found, %: C, 56.78; H, 7.83. For $C_{15}H_{25}O_5P$ (316.1). Calculated, %: C, 56.95; H, 7.97.

Diethyl propargyloxy(4-methoxyphenyl)methyl phosphonate (6c)

0.19 g, yield 62% colorless oil. ^{1}H NMR spectrum, (300 MHz, $CDCl_3$), δ, ppm (J, Hz): 1.21 (t, J = 6.0 Hz, 3H, CH_3), 1.30 (t, J = 6.0 Hz, 3H, CH_3), 2.46 (s, 1H, CH), 3.81 (s, 3H, OCH_3), 3.89–3.95 (m, 2H, CH_2), 4.01–4.08 (m, 4H, $2CH_2$), 4.93 (d, J_{HP} = 15.0 Hz, 1H, CHP), 6.70–6.91 (m, 4H, H-Ar). ^{13}C-NMR (75.0 MHz, $CDCl_3$), δ, ppm: 16.3 (d, J_{CP} = 6.0, CH_3), 16.4 (d, J_{CP} = 6.0, CH_3), 55.2 (OCH_3), 56.4 (d, J_{CP} = 15.9, CH_2OCHP), 62.8 (d, J_{CP} = 7.6, CH_2OP), 63.1 (d, J_{CP} = 7.6, CH_2OP), 75.5 (C≡CH), 75.6 (d, J_{CP} = 172.1, CHP), 78.6 (C≡CH), 113.9, 114.0, 125.2, 129.8, 129.9, 160.0 (C-Ar). ^{31}P-NMR (194.4 MHz, $CDCl_3$), δ, ppm: 19.2 (P). Found, %: C, 57.57; H, 6.63. For $C_{15}H_{21}O_5P$ (312.1). Calculated, %: C, 57.69; H, 6.78.

Diethyl 4-chlorobutyloxy(4-methoxyphenyl) methyl phosphonate (6d)

0.17 g, yield 46% colorless oil. ^{1}H NMR spectrum, (300 MHz, $CDCl_3$), δ, ppm (J, Hz): 1.17 (t, J = 6.0 Hz, 3H, CH_3), 1.28 (t, J = 6.0 Hz, 3H, CH_3), 1.56–1.92 (m, 4H, $2CH_2$), 3.38–3.64 (m, 4H, $2CH_2$), 3.83 (s, 3H, OCH_3), 3.98–4.08 (m, 4H, $2CH_2$), 4.56 (d, J_{HP} = 12.0 Hz, 1H, CHP), 6.84 (d, J = 9.0 Hz, 2H, H-Ar), 7.33–7.23 (m, 2H, H-Ar). ^{13}C-NMR (75.0 MHz, $CDCl_3$), δ, ppm: 16.3 (d, J_{CP} = 6.0, CH_3), 16.4 (d, J_{CP} = 6.0, CH_3), 26.7 (CH_2), 29.3 (CH_2), 44.9 ($ClCH_2$), 55.6 (OCH_3), 62.6 (d, J_{CP} = 8.0, CH_2OP), 63.1 (d, J_{CP} = 8.0, CH_2OP), 71.6 (d, J_{CP} = 13.6, CH_2OCHP), 77.5 (d, J_{CP} = 172.1, CHP), 113.6, 114.0, 125.1, 129.7, 129.9, 159.8 (C-Ar). ^{31}P-NMR (194.4 MHz, $CDCl_3$), δ, ppm: 19.1 (P). Found, %: C, 52.56; H, 7.03. For $C_{16}H_{26}ClO_5P$ (364.1). Calculated, %: C, 52.68; H, 7.18.

Diethyl benzyloxy(4-methoxyphenyl)methylphosphonate (6e)

0.33 g, yield 90% colorless oil. ^{1}H NMR spectrum, (300 MHz, $CDCl_3$), δ, ppm (J, Hz): 1.20 (t, J = 6.0 Hz, 3H, CH_3), 1.27 (t, J = 6.0 Hz, 3H, CH_3), 3.82 (s, 3H, OCH_3), 3.92–4.13 (m, 4H, $2CH_2$), 4.37 (d, J_{HP} = 12.0 Hz, 1H, CHP), 4.60–4.71 (m, 2H, CH_2), 6.92 (d, J = 6.0 Hz, 2H, H-Ar), 7.31–40 (m, 7H, H-Ar). ^{13}C-NMR (75.0 MHz, $CDCl_3$), δ, ppm: 16.3 (d, J_{CP} = 6.0, CH_3), 16.4 (d, J_{CP} = 6.0, CH_3), 55.3 (OCH_3), 62.9 (d, J_{CP} = 6.0, CH_2OP), 63.2 (d, J_{CP} = 6.0, CH_2OP), 71.4 (d, J_{CP} = 15.1, CH_2OCHP), 76.4 (d, J_{CP} = 172.9, CHP), 113.9, 114.0, 126.2, 128.0, 128.2, 128.4, 129.6, 129.7, 137.1, 159.9 (C-Ar). ^{31}P-NMR (194.4 MHz, $CDCl_3$), δ, ppm: 19.6 (P). Found, %: C, 62.48; H, 6.76. For $C_{19}H_{25}O_5P$ (364.1). Calculated, %: C, 62.63; H, 6.92.

Diethyl 2-phenylethyloxy(4-methoxyphenyl)methyl phosphonate (6f)

0.15 g, yield 39% colorless oil. ^{1}H NMR spectrum, (300 MHz, $CDCl_3$), δ, ppm (J, Hz): 1.13–1.21 (m, 6H, $2CH_3$), 2.84–2.89 (m, 2H, CH_2), 3.59–3.69 (m, 2H, CH_2), 3.73 (s, 3H, OCH_3), 3.89–4.01 (m, 4H, $2CH_2$), 4.56 (d, J_{HP} = 15.0 Hz, 1H, CHP), 6.83 (d, J = 9.0 Hz, 2H, H-Ar), 7.14–7.28 (m, 7H, H-Ar). ^{13}C-NMR (75.0 MHz, $CDCl_3$), δ, ppm: 16.3 (d, J_{CP} = 6.0, CH_3), 16.4 (d, J_{CP} = 6.0, CH_3), 36.2 (CH_2), 55.7 (OCH_3), 62.8 (d, J_{CP} = 8.0, CH_2OP), 63.2 (d, J_{CP} = 8.0, CH_2OP), 71.3 (CH_2) (d, J_{CP} = 13.6, CH_2OCHP), 78.4 (d, J_{CP} = 170.6, CHP), 113.7, 113.8, 126.2, 126.5, 128.2, 128.9, 129.3, 129.4, 138.6, 159.7, 159.8, 163.6 (C-Ar). ^{31}P-NMR (194.4 MHz, $CDCl_3$), δ, ppm: 19.1 (P). Found, %: C, 63.26; H, 7.13. For $C_{20}H_{27}O_5P$ (378.2). Calculated, %: C, 63.48; H, 7.19.

Diethyl 2-methylpropyloxy(3,4-dimethoxyphenyl)methyl phosphonate (7a)

0.23 g, yield 65% colorless oil. ^{1}H NMR spectrum, (300 MHz, $CDCl_3$), δ, ppm (J, Hz): 0.86 (d, J = 3.0 Hz, 3H, CH_3), 0.89 (d, J = 3.0 Hz, 3H, CH_3), 1.19–1.23 (m, 6H, $2CH_3$), 1.80–1.91 (m, 1H, CH), 3.12–3.24 (m, 2H, CH_2), 3.83 (s, 3H, OCH_3), 3.85 (s, 3H, OCH_3), 4.01–4.07 (m, 4H, $2CH_2$), 4.48 (d, J_{HP} = 18.0 Hz, 1H, CHP), 6.79–6.92 (m, 2H, H-Ar), 7.00 (s, 1H, H-Ar). ^{13}C-NMR (75.0 MHz, $CDCl_3$), δ, ppm: 16.3 (d, J_{CP} = 5.3, CH_3), 16.4 (d, J_{CP} = 5.3, CH_3), 19.1 (CH_3), 19.2 (CH_3), 28.4 (CH), 55.8 (2 OCH_3), 62.7 (d, J_{CP} = 6.8, CH_2OP), 63.0 (d, J_{CP} = 6.8, CH_2OP), 78.7 (d, J_{CP} = 160.0, CHP), 76.9 (d, J_{CP} = 32.5, CH_2OCHP), 110.7, 110.8, 111.0, 120.6, 127.4, 149.0 (C-Ar). ^{31}P-NMR (194.4 MHz, $CDCl_3$), δ, ppm: 19.4 (P). Found, %: C, 56.64; H, 8.07. For $C_{17}H_{29}O_6P$ (360.2). Calculated, %: C, 56.66; H, 8.11.

Diethyl 1-methylethyloxy(3,4-dimethoxyphenyl)methyl phosphonate (7b)

0.26 g, yield 74% colorless oil. ^{1}H NMR spectrum, (300 MHz, $CDCl_3$), δ, ppm (J, Hz): 1.08 (d, J = 6.0 Hz, 6H, $2CH_3$), 1.11–1.22 (m, 6H, $2CH_3$), 3.54–3.62 (m, 1H, CH), 3.80 (s, 3H, OCH_3), 3.88 (s, 3H, OCH_3), 3.92–4.06 (m, 4H, $2CH_2$), 4.59 (d, J_{HP} = 18.0 Hz, 1H, CHP), 6.76–6.91 (m, 2H, H-Ar), 6.99 (s, 1H, H-Ar). ^{13}C-NMR (75.0 MHz, $CDCl_3$), δ, ppm: 16.3 (d, J_{CP} = 5.3, CH_3), 16.4 (d, J_{CP} = 5.3, CH_3), 21.0 (CH_3), 23.0 (CH_3), 55.7 (OCH_3), 55.8 (OCH_3), 62.8 (d, J_{CP} = 6.8, CH_2OP), 63.1 (d, J_{CP} = 6.8, CH_2OP), 71.5 (OCH) (d,

J_{CP} = 13.6, CHOCHP), 75.6 (d, J_{CP} = 167.6, CHP), 110.7, 110.8, 111.0, 120.4, 128.1, 148.8 (C-Ar). ^{31}P-NMR (194.4 MHz, $CDCl_3$), δ, ppm: 19.8 (P). Found, %: C, 55.39; H, 7.67. For $C_{16}H_{27}O_6P$ (346.2). Calculated, %: C, 55.48; H, 7.86.

Diethyl propargyloxy(3,4-dimethoxyphenyl)methyl phosphonate (7c)

0.19 g, yield 56% colorless oil. ^{1}H NMR spectrum, (300 MHz, $CDCl_3$), δ, ppm (J, Hz): 1.05 (t, J = 6.0 Hz, 3H, CH_3), 1.15 (t, J = 6.0 Hz, 3H, CH_3), 2.39 (s, 1H, CH), 3.72 (s, 3H, OCH_3), 3.82 (s, 3H, OCH_3), 3.87–3.94 (m, 2H, CH_2), 3.99–4.17 (m, 4H, $2CH_2$), 4.75 (d, J_{HP} = 15.0 Hz, 1H, CHP), 6.70–6.91 (m, 3H, H-Ar). ^{13}C-NMR (75.0 MHz, $CDCl_3$), δ, ppm: 16.2 (d, J_{CP} = 6.0, CH_3), 16.3 (d, J_{CP} = 6.0, CH_3), 55.7 (OCH_3), 55.8 (OCH_3), 56.3 (d, J_{CP} = 15.9, CH_2OCHP), 62.8 (d, J_{CP} = 6.8, CH_2OP), 63.2 (d, J_{CP} = 6.8, CH_2OP), 75.6 (C≡CH), 75.7 (d, J_{CP} = 172.1, CHP), 78.4 (C≡CH), 110.8, 111.2, 121.3, 125.6, 148.9, 149.4 (C-Ar). ^{31}P-NMR (194.4 MHz, $CDCl_3$), δ, ppm: 19.0 (P). Found, %: C, 55.95; H, 6.60. For $C_{16}H_{23}O_6P$ (342.1). Calculated, %: C, 56.14; H, 6.77.

Diethyl 4-chlorobutyloxy(3,4-dimethoxyphenyl)methyl phosphonate (7d)

0.27 g, yield 69% colorless oil. ^{1}H NMR spectrum, (300 MHz, $CDCl_3$), δ, ppm (J, Hz): 1.19 (t, J = 6.0 Hz, 3H, CH_3), 1.34 (t, J = 6.0 Hz, 3H, CH_3), 1.50–1.72 (m, 4H, $2CH_2$), 3.51–3.70 (m, 2H, CH_2), 3.88 (s, 3H, OCH_3), 3.90 (s, 3H, OCH_3), 4.02–4.10 (m, 2H, CH_2), 4.53 (d, J_{HP} = 15.0 Hz, 1H, CHP), 6.71–6.87 (m, 2H, H-Ar), 7.63 (s, 1H, H-Ar). ^{13}C-NMR (75.0 MHz, $CDCl_3$), δ, ppm: 16.3 (d, J_{CP} = 6.0, CH_3), 16.4 (d, J_{CP} = 6.0, CH_3), 27.3 (CH_2), 29.3 (CH_2), 44.7 ($ClCH_2$), 55.4 (OCH_3), 56.9 (OCH_3), 62.6 (d, J_{CP} = 6.8, CH_2OP), 63.5 (d, J_{CP} = 6.8, CH_2OP), 71.4 (d, J_{CP} = 13.6, CH_2-OCHP), 78.1 (d, J_{CP} = 170.6, CHP), 110.5, 112.0, 121.8, 126.4, 149.0, 149.7 (C-Ar). ^{31}P-NMR (194.4 MHz, $CDCl_3$), δ, ppm: 19.2 (P). Found, %: C, 51.56; H, 7.01. For $C_{17}H_{28}ClO_6P$ (394.1). Calculated, %: C, 51.71; H, 7.15.

Diethyl benzyloxy(3,4-dimethoxyphenyl)methyl phosphonate (7e)

0.32 g, yield 81% colorless oil. ^{1}H NMR spectrum, (300 MHz, $CDCl_3$), δ, ppm (J, Hz): 1.17 (t, J = 6.0 Hz, 3H, CH_3), 1.25 (t, J = 6.0 Hz, 3H, CH_3), 3.86 (s, 3H, OCH_3), 3.99 (s, 3H, OCH_3), 4.02–4.12 (m, 4H, $2CH_2$), 4.37 (d, J_{HP} = 12.0 Hz, 1H, CHP), 4.61 (dd, J = 9.0, 12.0 Hz, 2H, CH_2), 6.83 (d, J = 9.0 Hz, 1H, H-Ar), 6.94–6.96 (m, 1H, H-Ar), 7.05 (s, 1H, H-Ar), 7.29 (s, 5H, H-Ar). ^{13}C-NMR (75.0 MHz, $CDCl_3$), δ, ppm: 16.3 (d, J_{CP} = 6.0, CH_3), 16.4 (d, J_{CP} = 6.0, CH_3), 55.8 (OCH_3), 55.9 (OCH_3), 62.7 (d, J_{CP} = 6.8, CH_2OP), 63.2 (d, J_{CP} = 6.8, CH_2OP), 71.4 (d, J_{CP} = 14.3, CH_2-OCHP), 76.6 (d, J_{CP} = 171.4, CHP), 110.8, 110.9, 111.2, 111.3, 121.1, 121.2, 126.7, 127.9, 128.2, 128.3, 137.1, 149.1 (C-Ar). ^{31}P-NMR (194.4 MHz, $CDCl_3$), δ, ppm: 19.5 (P). Found, %: C, 60.87; H, 6.74. For $C_{20}H_{27}O_6P$ (394.2). Calculated, %: C, 60.91; H, 6.90.

Diethyl 2-phenylethyloxy(3,4-dimethoxyphenyl)methyl phosphonate (7f)

0.28 g, yield 69% colorless oil. ^{1}H NMR spectrum, (300 MHz, $CDCl_3$), δ, ppm (J, Hz): 1.21 (t, J = 6.0 Hz, 3H, CH_3), 1.26 (t, J = 6.0 Hz, 3H, CH_3), 2.90 (t, J = 9.0, 6.0 Hz, 2H, CH_2), 3.63–3.79 (m, 2H, CH_2), 3.85 (s, 3H, OCH_3), 3.90 (s, 3H, OCH_3), 3.97–4.04 (s, 4H, $2CH_2$), 4.55 (d, J_{HP} = 15.0 Hz, 1H, CHP), 6.79–6.93 (m, 3H, H-Ar), 7.14–7.28 (m, 5H, H-Ar). ^{13}C-NMR (75.0 MHz, $CDCl_3$) δ, ppm: 16.3 (d, J_{CP} = 6.0, CH_3), 16.4 (d, J_{CP} = 6.0, CH_3), 36.2 (CH_2), 55.8 (OCH_3), 55.9 (OCH_3), 62.8 (d, J_{CP} = 6.8, CH_2OP), 63.2 (d, J_{CP} = 6.8, CH_2OP), 71.3 (d, J_{CP} = 14.3, CH_2OCHP), 78.6 (d, J_{CP} = 169.9, CHP), 110.7, 110.8, 110.9, 120.7, 120.8, 126.2, 127.1, 128.2, 128.9, 138.7, 149.0, 149.2 (C-Ar). ^{31}P-NMR (194.4 MHz, $CDCl_3$) δ, ppm: 19.1 (P). Found, %: C, 61.52; H, 7.08. For $C_{21}H_{29}O_6P$ (408.2). Calculated, %: C, 61.76; H, 7.16.

Diethyl 2-methylpropyloxy(3-methoxy-4-propargyloxyphenyl) methyl phosphonate (8a)

0.25 g, yield 66% colorless oil. ^{1}H NMR spectrum, (300 MHz, $CDCl_3$), δ, ppm (J, Hz): 0.90 (t, J = 3.0 Hz, 6H, $2CH_3$), 1.21–1.27 (m, 6H, $2CH_3$), 1.82–1.95 (m, 1H, CH), 2.50 (d, J = 3.0 Hz, 1H, CH), 3.15–3.27 (m, 2H, CH_2), 3.86 (s, 3H, OCH_3), 3.98–4.09 (m, 4H, $2CH_2$), 4.51 (d, J_{HP} = 15.0 Hz, 1H, CHP), 4.73 (d, J = 3.0 Hz, 2H, CH_2), 6.90–7.04 (m, 3H, H-Ar). ^{13}C-NMR (75.0 MHz, $CDCl_3$), δ, ppm: 16.3 (d, J_{CP} = 5.3, CH_3), 16.4 (d, J_{CP} = 5.3, CH_3), 19.2 (CH_3), 19.3 (CH_3), 28.4 (CH), 55.8 (OCH_3), 56.8 (OCH_2), 62.8 (d, J_{CP} = 6.8, CH_2OP), 63.1 (d, J_{CP} = 6.8, CH_2OP), 75.8 (C≡CH), 76.9 (d, J_{CP} = 31.7, CH_2OCHP), 77.7 (C≡CH), 78.6 (d, J_{CP} = 160.6, CHP), 111.3, 113.9, 120.5, 128.9, 146.8, 149.6 (C-Ar). ^{31}P-NMR (194.4 MHz, $CDCl_3$), δ, ppm: 19.3 (P). Found, %: C, 59.23; H, 7.46. For $C_{19}H_{29}O_6P$ (384.2). Calculated, %: C, 59.37; H, 7.60.

Diethyl 1-methylethyloxy(3-methoxy-4-propargyloxyphenyl) methyl phosphonate (8b)

0.34 g, yield 89% colorless oil. ^{1}H NMR spectrum, (300 MHz, $CDCl_3$), δ, ppm (J, Hz): 1.17–1.25 (m, 12H, $4CH_3$), 2.49 (d, J = 3.0 Hz, 1H, CH), 3.58–3.66 (m, 1H, CH), 3.84 (s, 3H, OCH_3), 3.93–4.09 (m, 4H, $2CH_2$), 4.63 (d, J_{HP} = 18.0 Hz, 1H, CHP), 4.70 (d, J = 3.0 Hz, 2H, CH_2), 6.89–7.04 (m, 3H, H-Ar). ^{13}C-NMR (75.0 MHz, $CDCl_3$), δ, ppm: 16.3 (d, J_{CP} = 6.0, CH_3), 16.4 (d, J_{CP} = 6.0, CH_3), 21.0 (CH_3), 23.1 (CH_3), 55.9 (OCH_3), 56.8 (OCH_2), 62.8 (d, J_{CP} = 7.8, CH_2OP), 63.3 (d, J_{CP} = 7.8, CH_2OP), 71.6 (d, J_{CP} = 13.6, CHOCHP), 75.8 (C≡CH), 75.6 (d, J_{CP} = 171.4, CHP), 78.5 (C≡CH), 111.3, 111.5, 113.9, 120.4, 129.6, 146.8 (C-Ar). ^{31}P-NMR (194.4 MHz, $CDCl_3$), δ, ppm: 19.8 (P). Found, %: C, 59.22; H, 7.46. For $C_{19}H_{29}O_6P$ (384.2). Calculated, %: C, 59.37; H, 7.60.

Diethyl propargyloxy(3-methoxy-4-propargyloxyphenyl)methyl phosphonate (8c)

0.27 g, yield 74% colorless oil. ^{1}H NMR spectrum, (300 MHz, $CDCl_3$), δ, ppm (J, Hz): 1.11 (t, J = 6.0 Hz, 3H, CH_3), 1.20 (t, J = 6.0 Hz, 3H, CH_3), 2.42 (t, J = 3.0 Hz, 1H, CH), 2.47 (t, J = 3.0 Hz, 1H, CH), 3.78 (s, 3H, OCH_3), 3.82–3.94 (m, 2H, CH_2), 3.98–4.08 (m, 4H, $2CH_2$), 4.65 (d, J = 3.0 Hz, 2H, OCH_2), 4.81 (d, J_{HP} = 15.0 Hz, 1H, CHP), 6.86–6.98 (m, 3H, H-Ar). ^{13}C-NMR (75.0

MHz, $CDCl_3$), δ, ppm: 16.2 (d, J_{CP} = 6.0, CH_3), 16.4 (d, J_{CP} = 6.0, CH_3), 55.9 (OCH_3), 56.5 (d, J_{CP} = 15.9, CH_2OCHP), 56.9 (OCH_2), 62.9 (d, J_{CP} = 6.8, CH_2OP), 63.2 (d, J_{CP} = 6.8, CH_2OP), 75.7 (d, J_{CP} = 169.1, CHP), 75.7 (C≡CH), 76.0 (C≡CH), 78.3 (C≡CH), 78.5 (C≡CH), 111.6, 113.9, 121.1, 127.1, 147.2, 149.7 (C-Ar). ^{31}P-NMR (194.4 MHz, $CDCl_3$), δ, ppm: 18.9 (P). Found, %: C, 58.92; H, 6.29. For $C_{18}H_{23}O_6P$ (366.1). Calculated, %: C, 59.01; H, 6.33.

Diethyl 4-chlorobutyloxy(3-methoxy-4-propargyloxyphenyl) methyl phosphonate (8d)

0.26 g, yield 62% colorless oil. ^{1}H NMR spectrum, (300 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.15–1.48 (m, 6H, $2CH_3$), 1.58–1.89 (m, 4H, $2CH_2$), 2.51 (t, *J* = 3.0 Hz, 1H, CH), 3.41–3.61 (m, 4H, $2CH_2$), 3.84 (s, 3H, OCH_3), 3.99–4.06 (m, 4H, $2CH_2$), 4.48 (d, J_{HP} = 12.0 Hz, 1H, CHP), 4.71 (d, *J* = 3.0 Hz, 2H, OCH_2), 6.89–7.13 (m, 3H, H-Ar). ^{13}C-NMR (75.0 MHz, $CDCl_3$), δ, ppm: 16.3 (d, J_{CP} = 6.0, CH_3), 16.4 (d, J_{CP} = 6.0, CH_3), 26.9 (CH_2), 29.3 (CH_2), 44.7 (CH_2), 55.9 (OCH_3), 56.0 (OCH_3), 56.7 (OCH_2), 62.9 (d, J_{CP} = 6.8, CH_2OP), 63.1 (d, J_{CP} = 6.8, CH_2OP), 69.9 (d, J_{CP} = 13.6, CH_2-OCHP), 75.9 (C≡CH), 78.4 (d, J_{CP} = 170.6, CHP), 78.6 (C≡CH), 110.8, 112.0, 121.8, 126.4, 149.0, 149.7 (C-Ar). ^{31}P-NMR (194.4 MHz, $CDCl_3$), δ, ppm: 19.2 (P). ^{31}P-NMR (194.4 MHz, $CDCl_3$), δ, ppm: 19.2 (P). Found, %: C, 54.34; H, 6.65. For $C_{19}H_{28}ClO_6P$ (418.1). Calculated, %: C, 54.48; H, 6.74.

Diethyl benzyloxy(3-methoxy-4-propargyloxyphenyl)methyl phosphonate (8e)

0.36 g, yield 87% colorless oil. ^{1}H NMR spectrum, (300 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.19 (d, *J* = 6.0 Hz, 3H, CH_3), 1.24 (d, *J* = 6.0 Hz, 3H, CH_3), 2.52 (d, *J* = 3.0 Hz, 1H, CH), 3.87 (s, 3H, OCH_3), 3.90–4.13 (m, 4H, $2CH_2$), 4.38 (d, *J* = 12.0 Hz, 1H, CH), 4.40 (d, J_{HP} = 12.0 Hz, 1H, CHP), 4.67 (d, *J* = 12.0 Hz, 1H, CH), 4.77 (d, *J* = 3.0 Hz, 2H, CH_2), 6.94–6.98 (m, 3H, H-Ar), 7.06–7.32 (m, 5H, H-Ar). ^{13}C-NMR (75.0 MHz, $CDCl_3$), δ, ppm: 16.3 (d, J_{CP} = 6.0, CH_3), 16.5 (d, J_{CP} = 6.0, CH_3), 55.9 (OCH_3), 56.8 (OCH_2), 62.8 (d, J_{CP} = 6.8, CH_2OP), 63.1 (d, J_{CP} = 6.8, CH_2OP), 71.5 (d, J_{CP} = 14.3, CH_2OCHP), 75.9 (C≡CH), 76.6 (d, J_{CP} = 170.6, CHP), 78.5 (C≡CH), 111.6, 111.7, 113.9, 120.8, 120.9, 127.9, 128.2, 128.4, 137.1, 147.1, 149.8 (C-Ar), ^{31}P-NMR (194.4 MHz, $CDCl_3$), δ, ppm: 19.4 (P). Found, %: C, 63.03; H, 6.48. For $C_{22}H_{27}O_6P$ (418.2). Calculated, %: C, 63.15; H, 6.50.

Diethyl 2-phenylethyloxy(3-methoxy-4-propargyloxyphenyl) methyl phosphonate (8f)

0.35 g, yield 82% colorless oil. ^{1}H NMR spectrum, (300 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.16–1.24 (m, 6H, $2CH_3$), 2.51 (s, 1H, CH), 2.88–2.93 (m, 2H, CH_2), 3.67–3.71 (m, 2H, CH_2), 3.79 (s, 3H, OCH_3), 3.92–4.04 (m, 4H, $2CH_2$), 4.56 (d, J_{HP} = 15.0 Hz, 1H, CHP), 4.73 (d, *J* = 3.0 Hz, 2H, CH_2), 6.86–6.98 (m, 3H, H-Ar), 7.17–7.38 (m, 5H, H-Ar). ^{13}C-NMR (75.0 MHz, $CDCl_3$), δ, ppm: 16.3 (d, J_{CP} = 6.0, CH_3), 16.4 (d, J_{CP} = 6.0, CH_3), 36.2 (CH_2), 55.8 (OCH_3), 56.8 (OCH_2), 62.9 (d, J_{CP} = 6.8, CH_2OP), 63.2 (d, J_{CP} = 6.8, CH_2OP), 71.5 (d, J_{CP} = 13.6, CH_2OCHP), 75.8 (C≡CH), 78.5 (C≡CH), 78.6 (d, J_{CP} = 169.9, CHP), 111.2, 111.3, 113.9, 120.5, 120.6, 126.2, 128.3, 128.6, 129.0, 138.7, 146.9, 149.7 (C-Ar); ^{31}P-NMR (194.4 MHz, $CDCl_3$), δ, ppm: 18.9 (P). Found, %: C, 63.69; H, 6.72. For $C_{23}H_{29}O_6P$ (432.2). Calculated, %: C, 63.88; H, 6.76.

Diethyl((5-methyl-2-phenyl-1,3-dioxan-5-yl)methoxy)(4-methoxyphenyl)methyl phosphonate (10a)

0.29 g, yield 62% colorless oil. ^{1}H NMR spectrum, (300 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 0.87 (s, 3H, CH_3), 1.20–1.33 (m, 6H, $2CH_3$), 3.59–3.73 (m, 4H, $2CH_2$), 3.81 (s, 3H, OCH_3), 3.88–4.16 (m, 6H, $3CH_2$), 4.65 (d, J_{HP} = 15.0 Hz, 1H, CHP), 5.39 (s, IH, CH), 6.90 (d, *J* = 9.0 Hz, 2H, H-Ar), 7.32–7.43 (m, 7H, H-Ar). ^{13}C-NMR (75.0 MHz, $CDCl_3$), δ, ppm: 16.4 (d, J_{CP} = 5.3, CH_3), 16.5 (d, J_{CP} = 5.3, CH_3), 19.2 (CH_3), 34.6 (C), 55.7 (OCH_3), 62.6 (d, J_{CP} = 7.8, CH_2OP), 63.1 (d, J_{CP} = 7.8, CH_2OP), 72.8 (OCH_2), 73.0 (d, J_{CP} = 14.3, CH_2OCHP), 73.7 (OCH_2), 79.0 (d, J_{CP} = 170.6, CHP), 101.7 (OCH), 113.9, 114.0, 126.1, 126.2, 128.2, 128.9, 129.5, 129.6, 138.3, 159.8 (C-Ar). ^{31}P-NMR (194.4 MHz, $CDCl_3$), δ, ppm: 19.2 (P). Found, %: C, 61.95; H, 7.14. For $C_{24}H_{33}O_7P$ (464.2). Calculated, %: C, 62.06; H, 7.16.

Diethyl((5-methyl-2-phenyl-1,3-dioxan-5-yl)methoxy)(3,4-dimethoxyphenyl)-methyl phosphonate (10b)

0.35 g, yield 70% colorless oil. ^{1}H NMR spectrum, (300 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 0.87 (s, 3H, CH_3), 1.19 (t, *J* = 6.0 Hz, 3H, CH_3), 1.26 (t, *J* = 6.0 Hz, 3H, CH_3), 3.63–3.75 (m, 4H, $2CH_2$), 3.59–3.79 (m, 2H, CH_2), 3.88 (s, 3H, OCH_3), 3.96 (s, 3H, OCH_3), 4.01–4.15 (m, 4H, $2CH_2$), 4.63 (d, J_{HP} = 15.0 Hz, 1H, CHP), 5.38 (s, IH, CH), 6.84–7.00 (m, 2H, H-Ar), 7.05 (s, 1H, H-Ar), 7.28–7.37 (m, 5H, H-Ar). ^{13}C-NMR (75.0 MHz, $CDCl_3$), δ, ppm: 16.4 (d, J_{CP} = 6.0, CH_3), 16.5 (d, J_{CP} = 6.0, CH_3), 19.1 (CH_3), 35.0 (C), 55.8 (OCH_3), 55.9 (OCH_3), 62.8 (d, J_{CP} = 7.8, CH_2OP), 63.1 (d, J_{CP} = 7.8 CH_2OP), 72.9 (d, J_{CP} = 14.3, CH_2OCHP), 73.2 (OCH_2), 73.3 (OCH_2), 79.0 (d, J_{CP} = 170.6, CHP), 101.8 (OCH), 110.8, 111.1, 111.2, 120.8, 120.9, 126.1, 128.2, 128.3, 128.9, 138.3, 149.0, 149.3 (C-Ar). ^{31}P-NMR (194.4 MHz, $CDCl_3$), δ, ppm: 19.2 (P). Found, %: C, 60.62; H, 6.85. For $C_{25}H_{35}O_8P$ (494.2). Calculated, %: C, 60.72; H, 7.13.

Diethyl 2-(*N*-methyl-*N*-phenylamino)ethyloxy(4-methoxyphenyl)methyl phosphonate (12)

0.12 g, yield 29% colorless oil. ^{1}H NMR spectrum, (300 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.21 (t, *J* = 6.0 Hz, 3H, CH_3), 1.26 (t, *J* = 6.0 Hz, 3H, CH_3), 2.98 (s, 3H, CH_3), 3.57–3.68 (m, 4H, $2CH_2$), 3.82 (s, 3H, OCH_3), 3.93–4.11 (m, 4H, $2CH_2$), 4.58 (d, J_{HP} = 15.0 Hz, 1H, CHP), 6.68 (d, *J* = 9.0 Hz, 2H, H-Ar), 6.87 (d, *J* = 9.0 Hz, 2H, H-Ar), 7.18–7.35 (m, 5H, H-Ar). ^{13}C-NMR (75.0 MHz, $CDCl_3$), δ, ppm: 16.3 (d, J_{CP} = 6.0, CH_3), 16.4 (d, J_{CP} = 6.0, CH_3), 36.2 (CH_3), 55.7 (OCH_3), 55.8 (NCH_2), 62.8 (d, J_{CP} = 7.8, CH_2OP), 63.6 (d, J_{CP} = 7.8, CH_2OP), 71.4 (d, J_{CP} = 14.3, CH_2OCHP), 78.7 (d, J_{CP} = 163.1, CHP), 110.7, 110.8, 110.9, 120.7, 120.8, 126.1, 127.1, 128.2, 128.9, 138.7, 149.0 (C-Ar). ^{31}P-NMR (194.4 MHz, $CDCl_3$) δ, ppm: 19.1 (P). Found, %: C, 61.87; H, 7.38; N, 3.44. For $C_{21}H_{30}NO_5P$ (407.2). Calculated, %: C, 61.90; H, 7.42; N, 3.44.

Conflicts of interest

There are no conflicts to declare.

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