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Article

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One-Pot, Three-Component Approach to Diarylmethylphosphonates: A Direct Entry to Polycyclic Aromatic Systems

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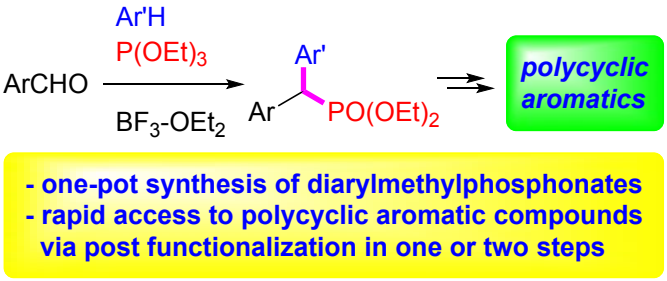
Table of Contents



Abstract: A new type of three-component reaction was developed consisting of aldehydes, electron-rich (hetero)arenes, and trialkyl phosphite, which provided facile access to a wide range of diarylmethylphosphonates under mild reaction conditions. Simple one- or two-step synthetic manipulation of the resulting compounds enabled us to reach several polycyclic (hetero)aromatic systems efficiently.

Keywords: Multicomponent reaction; Diarylmethylphosphonates; Friedel-Crafts reaction;

Alkenes; Polycyclic heteroaromatics; Tandem reaction.

Introduction

Recently, we have reported a direct access to diarylacetonitriles **3** via one-pot, three-component reaction of aldehydes **1**, electron-rich (hetero)arenes, and TMSCN under the influence of BF_3-Et_2O (Scheme 1a).[1] Mechanistically, this reaction was presumed to occur via **2**, which would be formed by initial attack of TMSCN to aldehydes **1**. Synthesis of **3** from **2** can be explained by subsequent Friedel-Crafts type displacement of OR by (hetero)arenes with the help of Lewis acid.[2] As an extension of this protocol, we reasoned that other nucleophiles instead of TMSCN could be employed to form a new type of three-component reaction. In this regard, trialkyl phosphite was chosen in this reaction as a substitute for TMSCN. Indeed, this new combination proceeded well to lead to various diarylmethylphosphonates **5** (Scheme 1b). To the best of our knowledge, no one-pot synthesis of diarylmethylphosphonates from commercially available materials has not been disclosed yet. They have been prepared by multiple steps and/or under harsh reaction conditions.[3] Due to the importance of a number of organophosphonate compounds in agricultural and medicinal sciences as well as organic chemistry (Figure 1),[4] we hoped to investigate our findings in detail. Here we wish to report our preliminary results on direct one-pot synthesis of diarylmethylphosphonates and application of this protocol to polycyclic aromatic systems.

Scheme 1. Synthetic Plans for Three-Component Reactions

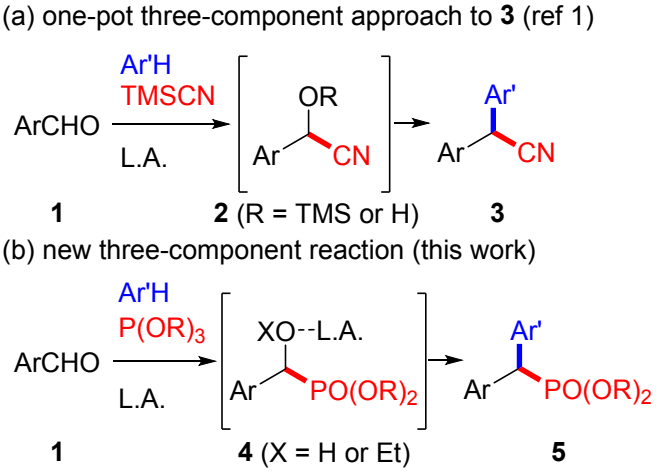
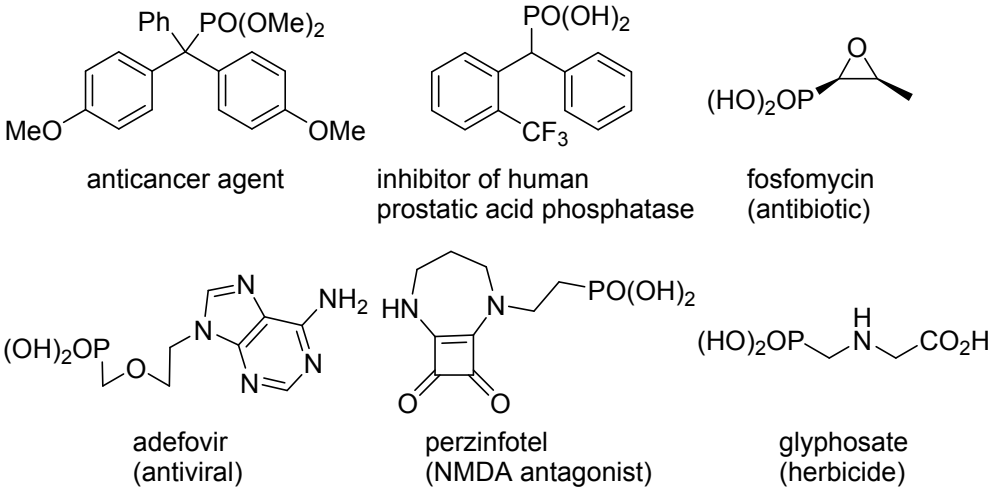


Figure 1. Some Bioactive Organophosphonates

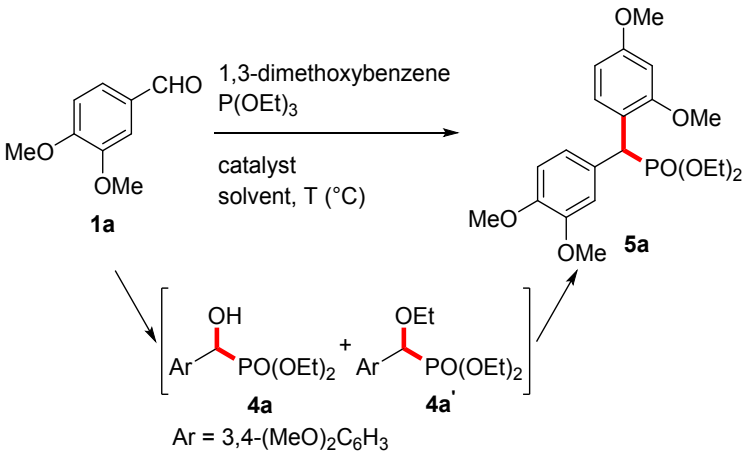


Results and discussion

After brief screening of several Lewis and Brønsted acids (Table 1), we were pleased to find that reaction of 3,4-dimethoxybenzaldehyde **(1a)** with 1,3-dimethoxybenzene and triethyl phosphite in the presence of BF_3-OEt_2 (1.0 equiv) at 80 °C gave rise to the desired product **5a** in 95% yield (entry 16).[5] However, when the reaction was carried out at room temperature, formation of intermediates **4a** (47%) and **4a'** (40%) was only observed (entry 17). Treatment of **4a** or **4a'** with 1,3-dimethoxybenzene and BF_3-OEt_2 at 80 °C produced **5a** in quantitative yield.[6] Although more catalyst loading resulted in a slight increase in chemical yield as well

as shortening of the reaction time (entries 18-19), we decided to use 1.0 equiv of BF_3-OEt_2 for subsequent reaction scope studies.

Table 1. Reaction Optimization[a]

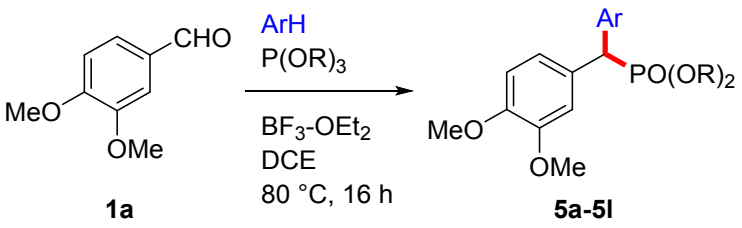


entry	catalyst (equiv)	solvent	temp (°C)	time (h)	yield (%)[b]
1	$Bi(OTf)_3$ (0.1)	DCE	rt	52	NR
2	$Bi(OTf)_3$ (0.1)	DCE	80	24	50
3	$Bi(OTf)_3$ (0.1)	DCE	80	48	52
4	$Bi(OTf)_3$ (0.1)	CH_3NO_2	80	48	54
5	$Bi(OTf)_3$ (0.1)	CH_3NO_2	90	48	54
6	$Cu(OTf)_2$ (0.1)	CH_3NO_2	80	48	20
7	$Yb(OTf)_3$ (0.1)	CH_3NO_2	80	24	38
8	$Sc(OTf)_3$	CH_3NO_2	80	48	34
9	AgOTf (0.1)	CH_3NO_2	80	24	NR
10	$Zn(OTf)_2$ (0.1)	CH_3NO_2	80	24	trace
11	$FeCl_3$ (0.1)	CH_3NO_2	80	24	trace
12	$FeCl_3$ (0.2)	CH_3NO_2	80	24	19
13	BF_3-OEt_2 (0.2)	DCE	80	52	25
14	BF_3-OEt_2 (0.5)	DCE	80	24	64
15	BF_3-OEt_2 (0.5)	CH_3NO_2	80	24	49
16	BF_3-OEt_2 (1.0)	DCE	80	16	95
17	BF_3-OEt_2 (1.0)	DCE	rt	52	-[c]
18	BF_3-OEt_2 (1.5)	DCE	80	12	96
19	BF_3-OEt_2 (2.0)	DCE	80	8	97
20	PTSA (0.2)	CH_3NO_2	80	48	NR
21	TFA (0.2)	CH_3NO_2	80	48	NR
22	CH_3SO_3H (0.2)	CH_3NO_2	80	48	15
23	TfOH (0.2)	CH_3NO_2	80	48	45
24	TfOH (0.5)	CH_3NO_2	80	48	77

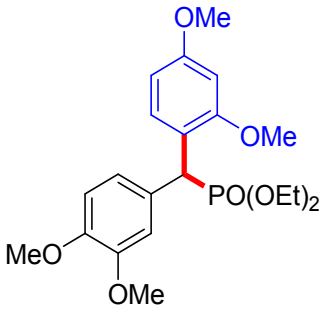
[a] A mixture of **1a** (100 mg, 0.6 mmol, 1 equiv), 1,3-dimethoxybenzene (1.2 equiv), $P(OEt)_3$ (1.1 equiv), and catalyst in solvent (1 mL) was stirred at the temperature indicated in the Table. [b] Isolated yield (%) [c] Only **4a** (47%) and **4a'** (40%) were isolated.

Other electron-rich arenes also successfully took part in these reactions to afford the corresponding products in good to excellent yields (Table 2) Triphenyl phosphite and tributyl phosphite were also employed to give **5i** and **5j** in good yields. While use of xylene and mesitylene as arenes gave rise to **5k** and **5l**, respectively, only **4a'** was isolated in 62% yield in case of toluene.

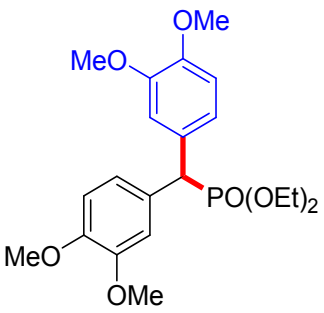
Table 2. Synthesis of 5a-5l[a,b]



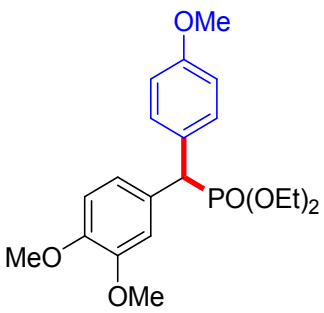
1a **5a-5l**



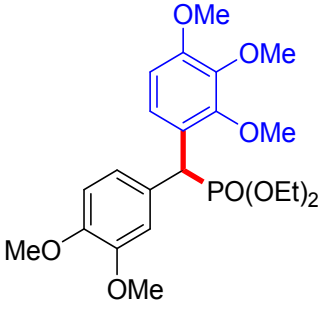
5a (95%)



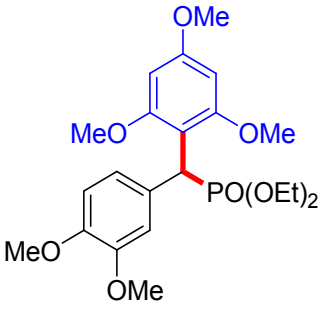
5b (91%)



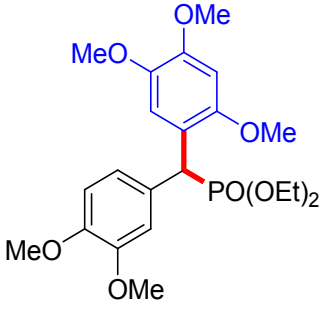
5c (93%)



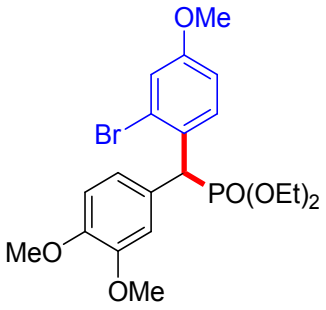
5d (92%)



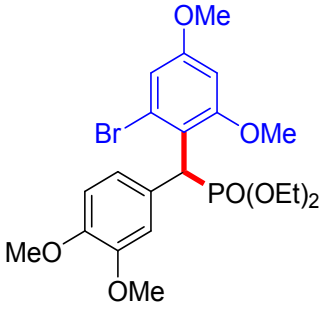
5e (88%)



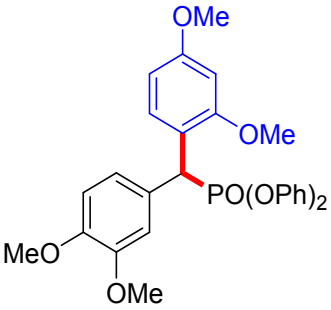
5f (90%)



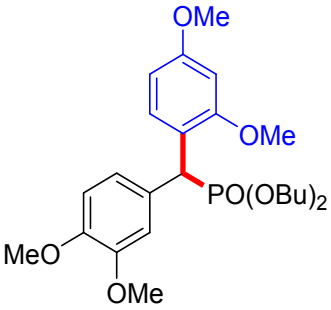
5g (78%)



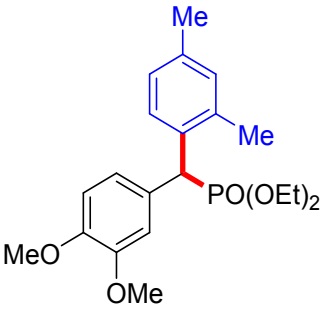
5h (74%)



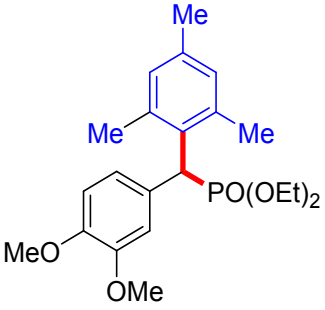
5i (62%)[c]



5j (74%)[d]



5k (54%)[e]



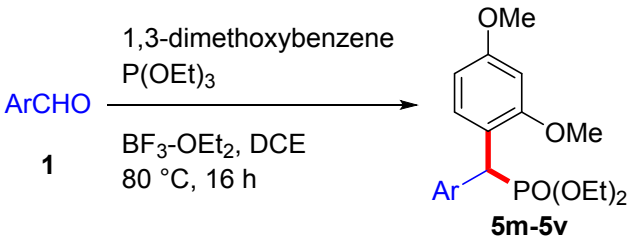
5l (68%)

[a] A mixture of **1a** (100 mg, 0.6 mmol, 1 equiv), ArH (1.2 equiv), $P(OEt)_3$ (1.1 equiv), and BF_3-OEt_2 (1.0 equiv) in dry DCE (1 mL) was stirred at 80 °C for 16 h unless otherwise indicated. [b] Isolated yield (%). [c] $P(OPh)_3$ (1.1 equiv) was used. [d] $P(OBu)_3$ (1.1 equiv) was used. [e] Xylene (3.2 equiv) was used.

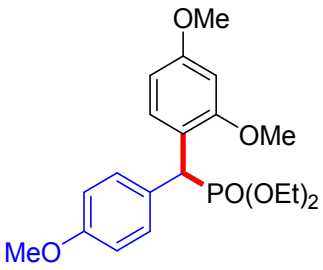
Reaction scope was further examined with different aldehydes as shown in Table 3. Various aldehydes having alkoxy, hydroxyl, or amino group(s) at the *o*- and/or *p*-position reacted well with 1,3-dimethoxybenzene and triethyl phosphite under optimized conditions to give the corresponding diarylmethylphosphonates in good yields. Intriguingly, heteroaromatic aldehydes such as 3-arylbenzofuran-2-carbaldehyde and 1-methyl-1*H*-indole-3-carbaldehyde were also good substrates for this reaction to furnish **5u** (89%) and **5v** (87%), respectively. When less reactive aldehydes such as *p*-tolualdehyde and *trans*-cinnamaldehyde were exposed to the optimized reaction conditions with 1,3-dimethoxybenzene, respectively, **4a'**-type compounds (**4a'-1** and **4a'-2**) were obtained in 62 and 74% yields instead of the corresponding diarylmethylphosphonates,[7] implying the importance of resonance stabilization effect of the reaction intermediate by alkoxy, hydroxyl, amino group(s) at the ortho- and(or) para-position(s)

of aldehydes for successful three-component coupling reactions under these conditions.

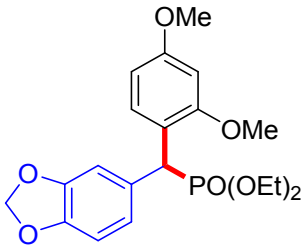
Table 3. Synthesis of 5m-5v[a,b]



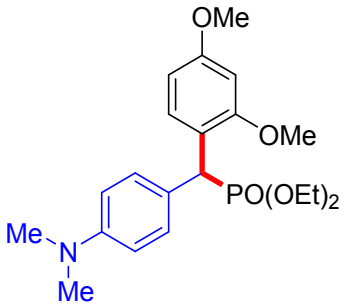
5m-5v



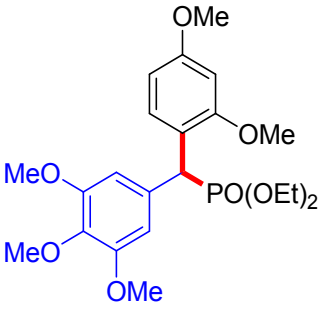
5m (94%)



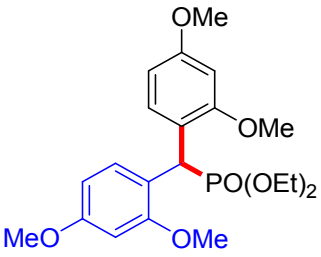
5n (90%)



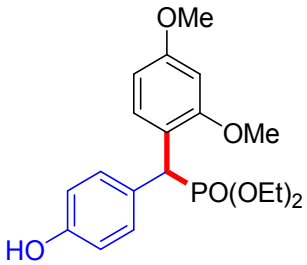
5o (87%)



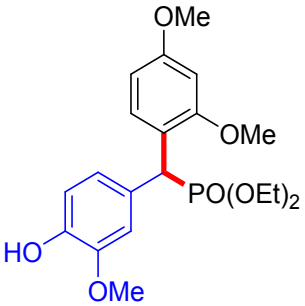
5p (91%)



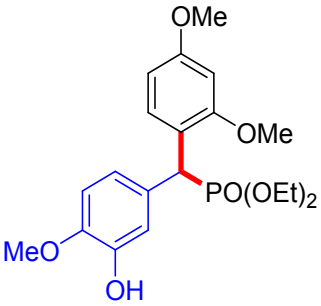
5q (88%)



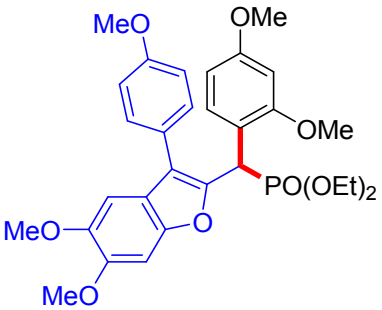
5r (66%)



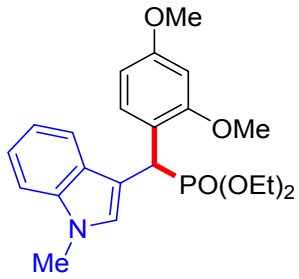
5s (71%)



5t (74%)



5u (89%)

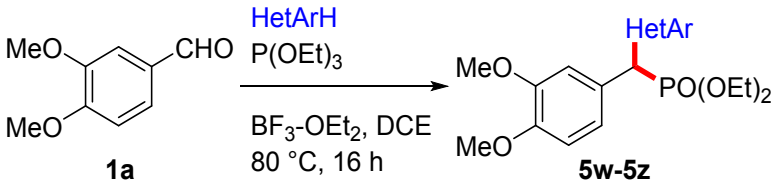


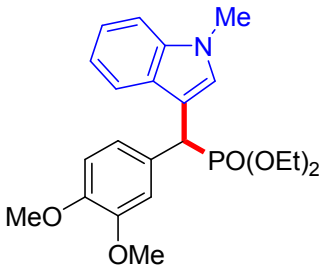
5v (87%)

[a] A mixture of **1** (100 mg, 1 equiv), 1,3-dimethoxybenzene (1.2 equiv), $P(OEt)_3$ (1.1 equiv), and BF_3-OEt_2 (1.0 equiv) in dry DCE (1 mL) was stirred at 80 °C for 16 h. [b] Isolated yield (%).

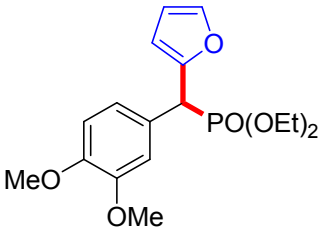
Heterocycles were successfully employed as nucleophiles in this process as well (Table 4). Thus, indole, furan, thiophene, and benzofuran-containing diarylmethylphosphonates were formed in good to excellent yields.

Table 4. Synthesis of 5w-5z[a,b]

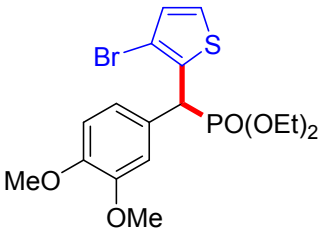




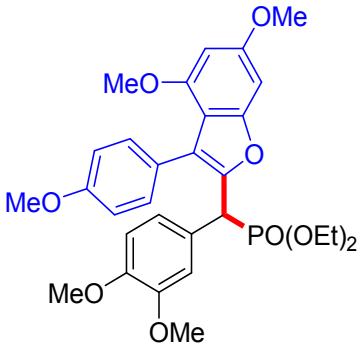
5w (93%)



5x (58%)[c]



5y (71%)

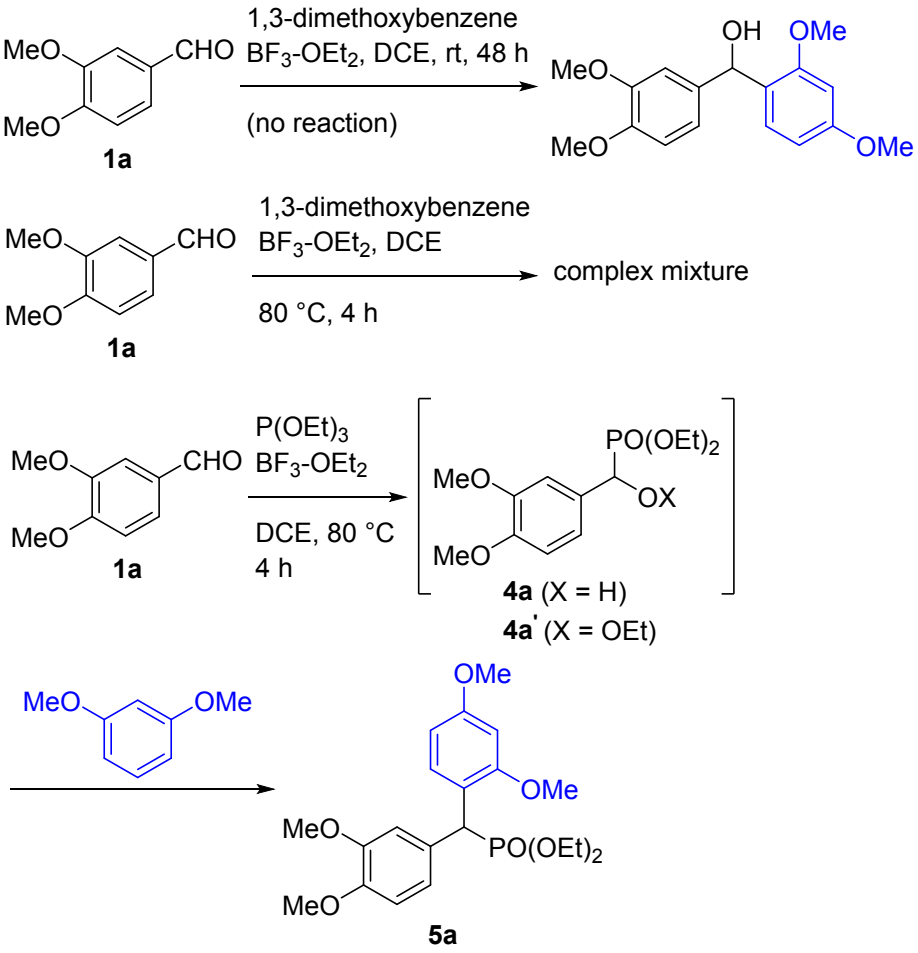


5z (87%)

[a] A mixture of **1a** (100 mg, 0.6 mmol, 1 equiv), HetArH (1.2 equiv), $P(OEt)_3$ (1.1 equiv), and BF_3-OEt_2 (1.0 equiv) in dry DCE (1 mL) was stirred at 80 °C for 16 h. [b] Isolated yield (%). [c] HetArH (2.1 equiv) was used.

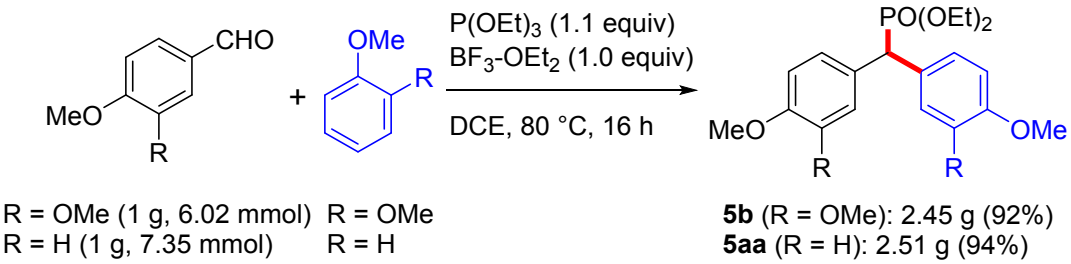
For elucidation of this reaction mechanism, a coupling reaction of 3,4-dimethoxybenzaldehyde **(1a)** with 1,3-dimethoxybenzene in the presence of BF_3-OEt_2 was conducted to get diarylcarbinol (Scheme 2). While no reaction was observed at room temperature, a complex mixture of products was obtained at 80 °C, indicating that formation of diarylcarbinol is not a first step in this reaction. On the other hand, when **1a** was sequentially treated with triethyl phosphite and 1,3-dimethoxybenzene under the influence of BF_3-OEt_2, the desired product **5a** was obtained in excellent yield. These results as well as observation of the reaction at rt led us to conclude that the reaction occurs via **4a**/**4a'** intermediates.

Scheme 2. Control Experiments



These one-pot, three-component reactions were performed in gram scales to demonstrate the feasibility of scale-up (Scheme 3). **5b** and **5aa** were synthesized in 92% and 94% yield, respectively. With these two compounds in hand, Horner-Wadsworth-Emmons (HWE) olefination reactions were carried out under mild conditions, leading to syntheses of triaryl-substituted alkenes **6a-d** as shown in Scheme 4.[8] Our two-step sequence would be useful for synthesis of diverse triarylethenes,[9] important structural motifs in medicinal and material sciences.[10]

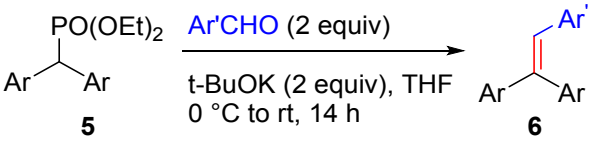
Scheme 3. Gram-scale Synthesis of Diarylmethylphosphonates



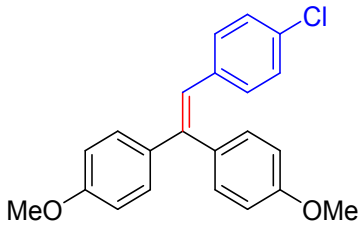
R = OMe (1 g, 6.02 mmol) R = OMe
R = H (1 g, 7.35 mmol) R = H

5b (R = OMe): 2.45 g (92%)
5aa (R = H): 2.51 g (94%)

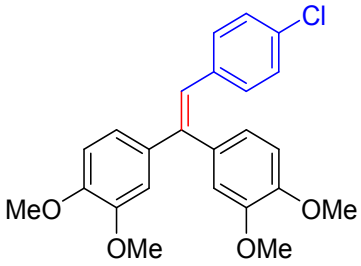
Scheme 4. HWE Reactions of Diarylmethylphosphonates



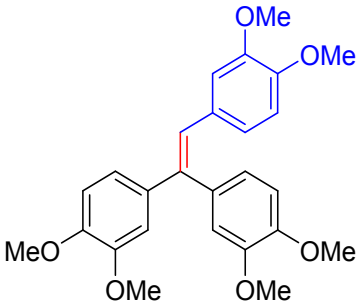
5 **6**



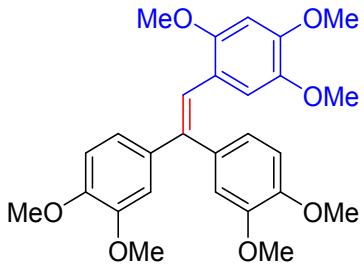
6a (78%)



6b (83%)



6c (90%)

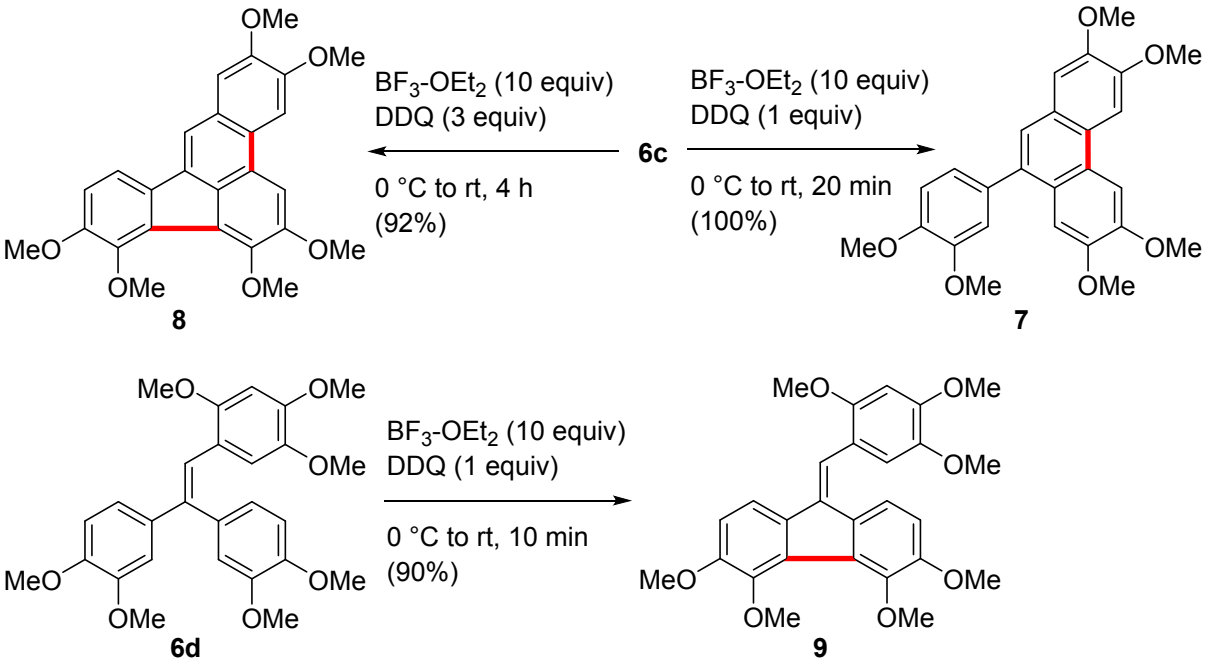


6d (85%)

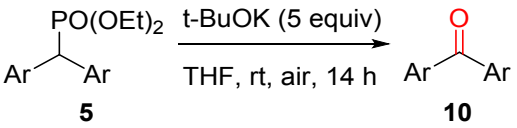
Synthetic utility of this protocol was further demonstrated in Schemes 5-7. Triarylalkene **6c** was efficiently converted to polycyclic aromatic compounds[11,12] **7** and **8** by controlling the amount of DDQ used for Scholl-type ring closure (Scheme 5).[13,14] Under similar reaction conditions, **6d** underwent Scholl cyclization to give the fluorene derivative **9** in good yield.

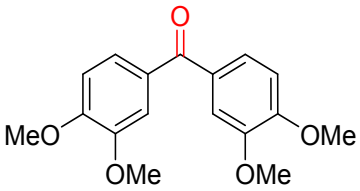
Exposure of diarylmethylphosphonates **5** with potassium *tert*-butoxide in the presence of air[15] afforded the corresponding diarylketones **10a-d** in good yields (Scheme 6). As described in Scheme 7, direct construction of phenanthrene skeletons **(11a-c)**[16] from **5g**, **5h**, and **5y** were realized respectively by allowing Suzuki-Miyaura (SM) cross-coupling and HWE olefination to occur in a one-pot manner. Notably, this type of tandem sequence for the synthesis of phenanthrenes has not been reported, to the best of our knowledge.[17]

Scheme 5. Scholl-type Cyclizations

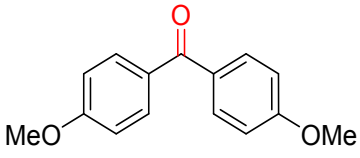


Scheme 6. Synthesis of Benzophenones

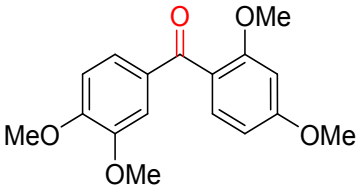




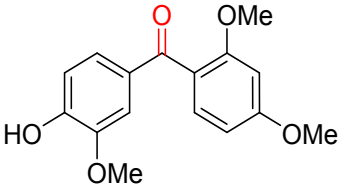
10a (92%)



10b (90%)

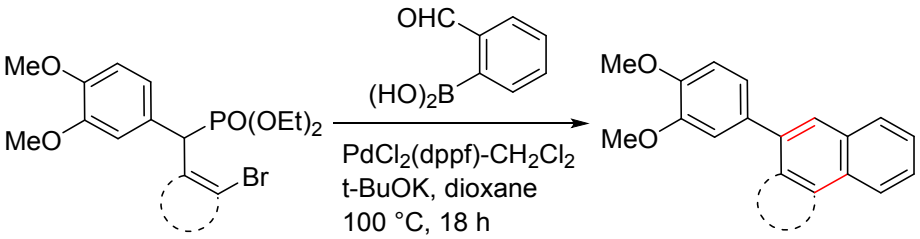


10c (88%)

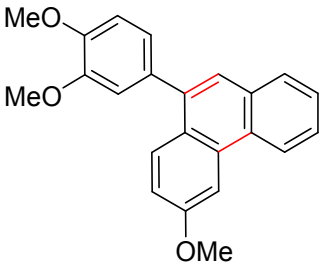
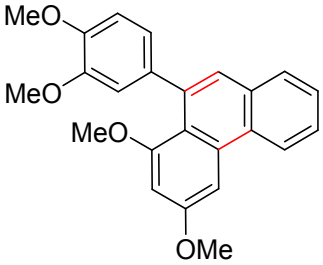


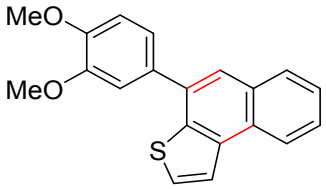
10d (75%)

Scheme 7. One-pot Synthesis of Phenanthrenes via a Tandem SM-HWE Reaction



5 **11a-c**

5	**11**		yield (%)
5g		**11a**	78
5h		**11b**	70

5y		**11c**	73

Conclusion

In conclusion, we have developed a modular one-pot approach to a wide range of diarylmethylphosphonates from aldehydes, (hetero)arenes, and $P(OEt)_3$ in the presence of BF_3-OEt_2 in good to excellent yields under mild reaction conditions. Synthetic scope of this new three-component reaction as well as mechanism study were investigated. Further elaboration of the resulting compounds in various ways including HWE olefination/Scholl annulation and tandem SM-HWE protocol permitted us to get rapid and facile access to polycyclic (hetero)aromatic systems, which are highly valuable in material sciences.

Experimental Section

General Methods

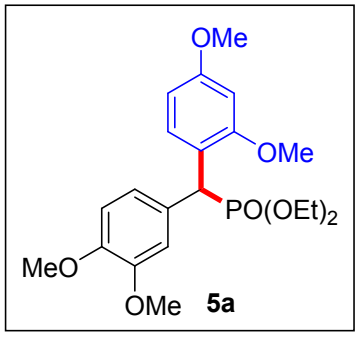
Unless specified, all reagents and starting materials were purchased from commercial sources and used as received without purification. "Concentrated" refers to the removal of volatile solvents via distillation using a rotary evaporator. "Dried" refers to pouring onto, or passing through, anhydrous magnesium sulfate followed by filtration. Flash chromatography was performed using silica gel (230−400 mesh) with hexanes, ethyl acetate, and dichloromethane as the eluents. All reactions were monitored by thin-layer chromatography on 0.25 mm silica plates (F-254) visualizing with UV light. Melting points were measured using a capillary melting point apparatus. ^{1}H and ^{13}C NMR spectra were recorded on 400 MHz NMR

spectrometer and were described as chemical shifts, multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet), coupling constant in hertz (Hz), and number of protons. HRMS was measured with electrospray ionization (ESI) and Q-TOF mass analyzer.

General Procedure for the Synthesis of Diarylmethylphosphonates (5)

To a stirred solution of 3,4-dimethoxybenzaldehyde (100 mg, 0.6 mmol), various arenes (0.72 mmol, 1.2 equiv), and triethyl phosphite (113 µL, 0.66 mmol, 1.1 equiv) in dry DCE (1 mL) was added BF_3-OEt_2 (76 µL, 0.6 mmol, 1.0 equiv) at 0 °C. After being stirred at 80 °C for 16 h, the reaction mixture was diluted with CH_2Cl_2 (20 mL), washed with aq. $NaHCO_3$ (5 mL × 2) and water (5 mL). All the organic layers were collected, dried over $MgSO_4$, and concentrated *in vacuo* to yield the crude product. Purification by flash chromatography on silica gel (hexanes:EtOAc) afforded **5**.

Diethyl ((2,4-dimethoxyphenyl)(3,4-dimethoxyphenyl)methyl)phosphonate (5a).



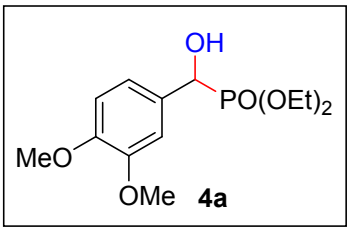
5a

Colorless viscous liquid (242 mg, 95%); R_f = 0.3 in 70% EtOAc in hexane; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.80 (dd, *J* = 8.6, 1.8 Hz, 1H), 7.09 (s, 1H), 7.03 (d, *J* = 8.3 Hz, 1H), 6.76 (d, *J* = 8.3 Hz, 1H), 6.49 (dd, *J* = 8.6, 2.3 Hz, 1H), 6.41 (s, 1H), 4.93 (d, *J* = 25.4 Hz, 1H), 4.02 – 3.91 (m, 2H), 3.87 – 3.79 (m, 8H), 3.77 (s, 3H), 3.77 (s, 3H), 1.12 (q, *J* = 7.2 Hz, 6H); **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 159.8 (d, *J* = 1.5 Hz, 1C), 157.6 (d, *J* = 10.1 Hz, 1C), 148.6 (s, 1C), 147.9 (d, *J* = 2.3 Hz, 1C), 130.6 (d, *J* = 5.1 Hz, 1C), 129.8 (d, *J* = 4.6 Hz, 1C), 121.8 (d, *J* = 8.3 Hz, 1C), 118.2 (d, *J* = 3.1 Hz, 1C), 112.9 (d, *J* = 7.5 Hz, 1C), 111.0 (s, 1C), 104.4 (s, 1C), 98.8 (s, 1C), 62.5 (d, *J* = 7.2 Hz, 1C), 62.5 (d, *J* = 6.9 Hz, 1C), 55.9 (s, 1C), 55.7 (s, 1C), 55.7 (s, 1C), 55.4 (s, 1C), 40.6 (d, *J* = 140.2

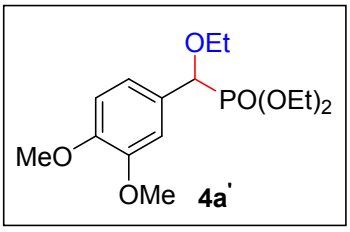
Hz, 1C), 16.4 (d, J = 2.2 Hz, 1C), 16.4 (d, J = 1.7 Hz, 1C); **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{21}H_{30}O_7P$ 425.1724, found 425.1730.

4a and **4a'** were obtained when the reaction was conducted at room temperature.

Diethyl ((3,4-dimethoxyphenyl)(hydroxy)methyl)phosphonate (4a). Colorless solid (86 mg, 47%); mp: 100-102 °C; R_f = 0.1 in 100% EtOAc; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.07 (s, 1H), 6.97 (d, J = 8.0 Hz, 1H), 6.80 (d, J = 8.2 Hz, 1H), 4.91 (dd, J = 10.1, 5.6 Hz, 1H), 4.64 (brs, 1H), 4.12 – 3.89 (m, 4H), 3.84 (s, 3H), 3.84 (s, 3H), 1.21 (dt, J = 22.4, 7.0 Hz, 6H); **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 148.8 (s, 2C), 129.2 (s, 1C), 119.7 (d, J = 7.1 Hz, 1C), 110.7 (d, J = 1.8 Hz, 1C), 110.4 (d, J = 5.1 Hz, 1C), 70.5 (d, J = 160.1 Hz, 1C), 63.3 (d, J = 7.1 Hz, 1C), 63.0 (d, J = 7.3 Hz, 1C), 55.9 (s, 2C), 16.5 (d, J = 3.4 Hz, 1C), 16.4 (d, J = 3.7 Hz, 1C); **HRMS** (ESI-QTOF) *m/z* $[M+Na]^+$ calcd for $C_{13}H_{21}NaO_6P$ 327.0968, found 327.0978.

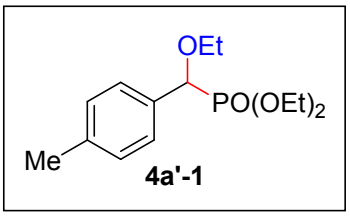


Diethyl ((3,4-dimethoxyphenyl)(ethoxy)methyl)phosphonate (4a'). Colorless liquid (80 mg, 40%); R_f = 0.2 in 100% EtOAc; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.98 (s, 1H), 6.90 (d, J = 8.1 Hz, 1H), 6.79 (d, J = 8.2 Hz, 1H), 4.49 (d, J = 15.6 Hz, 1H), 4.09 – 3.85 (m, 4H), 3.83 (s, 3H), 3.81 (s, 3H), 3.57 – 3.36 (m, 2H), 1.21 (t, J = 7.0 Hz, 3H), 1.15 (t, J = 7.0 Hz, 6H); **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 149.0 (d, J = 3.0 Hz, 1C), 148.9 (d, J = 2.4 Hz, 1C),127.4 (d, J = 1.5 Hz, 1C), 120.6 (d, J = 7.1 Hz, 1C), 110.7 (d, J = 4.8 Hz, 1C), 110.6



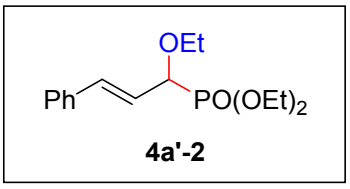
(dd, J = 2.2 Hz, 1C), 78.5 (d, J = 169.6 Hz, 1C), 66.2 (d, J = 14.3 Hz, 1C), 63.1 (d, J = 6.9 Hz, 1C), 62.7 (d, J = 6.8 Hz, 1C), 55.8 (s, 1C), 55.8 (s, 1C), 16.5 (d, J = 5.7 Hz, 1C), 16.3 (d, J = 5.9 Hz, 1C), 15.15 (s, 1C); **HRMS** (ESI-QTOF) *m/z* $[M+Na]^+$ calcd for $C_{15}H_{25}NaO_6P$ 355.1281, found 355.1293.

Diethyl (ethoxy(*p*-tolyl)methyl)phosphonate (4a'-1). Colorless liquid (148 mg, 62%); R_f = 0.4 in 70% EtOAc in hexane; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.34 (d, J = 6.8 Hz, 2H), 7.16 (d, J = 7.4 Hz, 2H), 4.59 (d, J = 15.8 Hz, 1H), 4.15 – 3.93 (m, 4H), 3.64 – 3.40 (m, 2H), 2.34 (s, 3H), 1.32 – 1.15 (m, 9H); **^{13}C{^{1}H} NMR** (100 MHz) δ 137.7 (d, J = 3.4 Hz, 1C), 131.8 (d, J = 1.9 Hz, 1C), 128.8 (d, J = 2.4 Hz, 2C), 127.7 (d, J = 6.0 Hz, 2C), 78.2 (d, J = 168.0 Hz, 1C), 66.0 (d, J = 14.2 Hz, 1C), 62.8 (d, J = 7.0 Hz, 1C), 62.6 (d, J = 7.0 Hz, 1C), 20.9 (s, 1C), 16.2 (d, J = 6.0 Hz, 1C), 16.1 (d, J = 6.0 Hz, 1C); 14.9 (s, 1C); **HRMS** (ESI-QTOF) *m/z* $[M+Na]^+$ calcd for $C_{14}H_{23}NaO_4P$ 309.1226, found 309.1213.



4a'-1

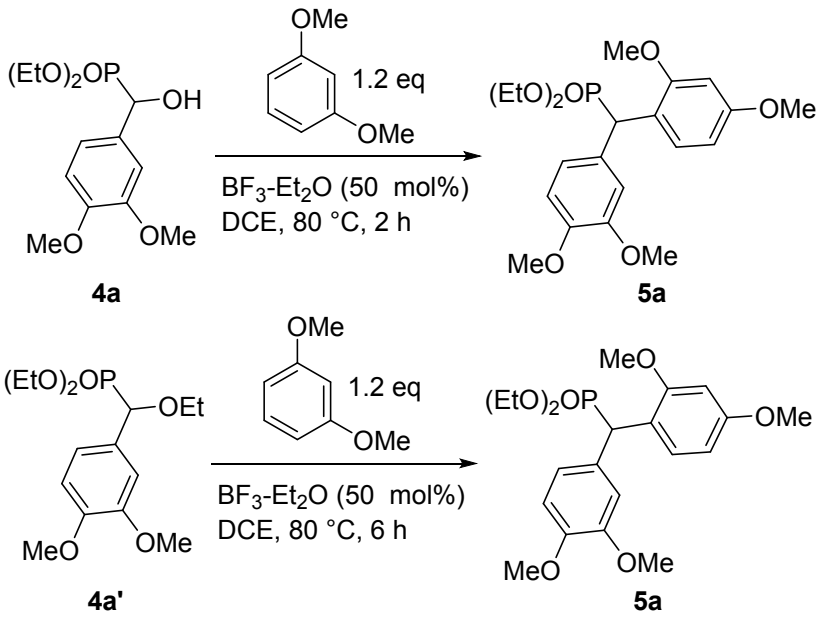
Diethyl (*E*)-(1-ethoxy-3-phenylallyl)phosphonate (4a'-2). Colorless liquid (167 mg, 74%); R_f = 0.4 in 80% EtOAc in hexane; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.42 (d, J = 7.4 Hz, 2H), 7.33 (t, J = 7.4 Hz, 2H), 7.28 (dd, J = 8.5, 5.3 Hz, 1H), 6.72 (dd, J = 15.9, 4.3 Hz, 1H), 6.25 (ddd, J = 15.9, 7.1, 5.2 Hz, 1H), 4.29 (dd, J = 16.4, 7.2 Hz, 1H), 4.26 – 4.14 (m, 4H), 3.77– 3.69 (m, 1H), 3.65 – 3.55 (m, 1H), 1.33 (t, J = 7.1 Hz, 6H), 1.26 (t, J = 7.0 Hz, 3H); **^{13}C{^{1}H} NMR** (100 MHz) δ 136.2 (d, J = 2.7 Hz, 1C), 133.9 (d, J = 13.5 Hz, 1C), 128.7 (s, 2C), 128.1 (s, 1C), 126.8 (d, J = 1.5 Hz, 2C), 123.1 (d, J = 4.1 Hz, 1C), 77.3 (d, J = 168.0 Hz, 1C), 66.6 (d, J =



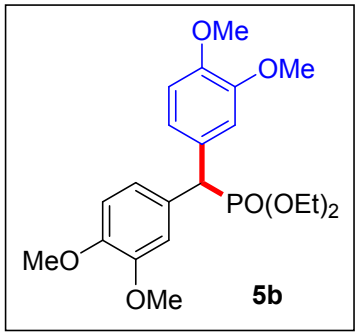
4a'-2

12.0 Hz, 1C), 63.2 (d, J = 6.9 Hz, 1C), 62.9 (d, J = 6.9 Hz, 1C), 16.6 (t, J = 4.1 Hz, , 2C), 15.3 (s, 1C); **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{15}H_{24}O_4P$ 299.1407, found 299.1406.

Subjection of **4a** or **4a'** to 1,3-dimethoxybenzene and BF_3-OEt_2 at 80 °C gave rise to **5a** in quantitative yield, respectively.

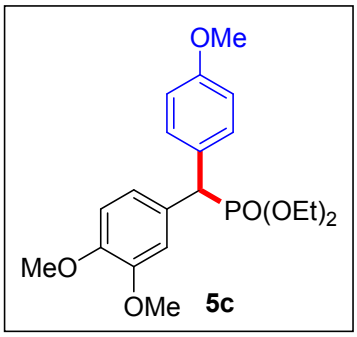


Diethyl (bis(3,4-dimethoxyphenyl)methyl)phosphonate (5b). Colorless viscous liquid (231 mg, 91%); R_f = 0.3 in 70% EtOAc in hexane; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.06 (s, 2H), 7.01 (d, J = 8.3 Hz, 2H), 6.78 (d, J = 8.3 Hz, 2H), 4.28 (d, J = 25.3 Hz, 1H), 4.02 – 3.90 (m, 2H), 3.87 – 3.73 (m, 14H), 1.11 (t, J = 7.0 Hz, 6H); **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 148.7 (s, 2C), 148.1 (d, J = 2.0 Hz, 2C), 129.4 (d, J = 5.0 Hz, 2C), 121.6 (d, J = 8.6 Hz, 2C), 112.6 (d, J = 7.7 Hz, 2C), 111.1 (s, 2C),

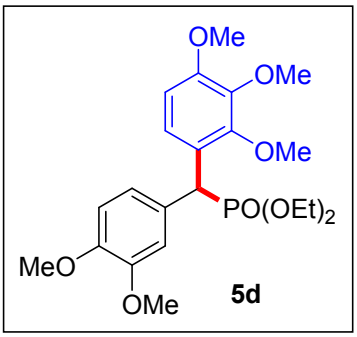


62.7 (d, J = 7.2 Hz, 2C), 55.8 (s, 2C), 55.8 (s, 2C), 50.0 (d, J = 137.9 Hz, 1C), 16.4 (d, J = 5.9 Hz, 2C); **HRMS** (ESI-QTOF) *m/z* $[M+Na]^+$ calcd for $C_{21}H_{29}NaO_7P$ 447.1543, found 447.1556.

Diethyl ((3,4-dimethoxyphenyl)(4-methoxyphenyl)methyl)phosphonate (5c). Colorless viscous liquid (219 mg, 93%); R_f = 0.3 in 60% EtOAc in hexane; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.40 (dd, J = 8.6, 1.6 Hz, 2H), 7.07 (s, 1H), 7.01 (dd, J = 8.3, 1.8 Hz, 1H), 6.86 – 6.79 (m, 2H), 6.77 (d, J = 8.3 Hz, 1H), 4.29 (d, J = 25.3 Hz, 1H), 4.02 – 3.88 (m, 2H), 3.87 – 3.75 (m, 8H), 3.73 (s, 3H), 1.20 – 1.01 (m, 6H); **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 158.6 (d, J = 2.1 Hz, 1C), 148.7 (s, 1C), 148.0 (d, J = 1.7 Hz, 1C), 130.3 (d, J = 7.8 Hz, 2C), 129.6 (d, J = 5.0 Hz, 1C), 129.1 (d, J = 5.2 Hz, 1C), 121.6 (d, J = 8.6 Hz, 1C), 113.9 (d, J = 1.0 Hz, 2C), 112.6 (d, J = 7.9 Hz, 1C), 111.1 (s, 1C), 62.6 (d, J = 7.1 Hz, 2C), 55.8 (s, 1C), 55.8 (s, 1C), 55.2 (s, 1C), 49.7 (d, J = 138.0, 1C), 16.3 (d, J = 6.3 Hz, 2C); **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{20}H_{28}O_6P$ 395.1618, found 395.1627.

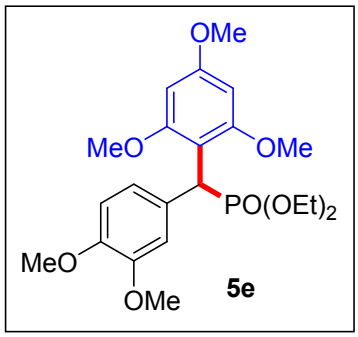


Diethyl ((3,4-dimethoxyphenyl)(2,3,4-trimethoxyphenyl)methyl)phosphonate (5d). Light yellow viscous liquid (252 mg, 92%); R_f = 0.3 in 60% EtOAc in hexane; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.61 (dd, J = 8.7, 1.8 Hz, 1H), 7.11 (s, 1H), 7.04 (d, J = 8.3 Hz, 1H), 6.77 (d, J = 8.3 Hz, 1H), 6.68 (d, J = 8.8 Hz, 1H), 4.89 (d, J = 25.1 Hz, 1H), 4.02–3.92 (m, 2H), 3.88 – 3.77 (m, 17H), 1.12 (dd, J = 15.5, 7.2 Hz, 6H); **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 152.9 (d, J = 1.5 Hz, 1C), 151.6 (d, J = 10.6 Hz, 1C), 148.7 (s, 1C), 148.1 (s, 1C), 142.2 (s, 1C), 129.8 (d, J = 5.0 Hz, 1C), 124.4 (d, J = 5.3 Hz, 1C),

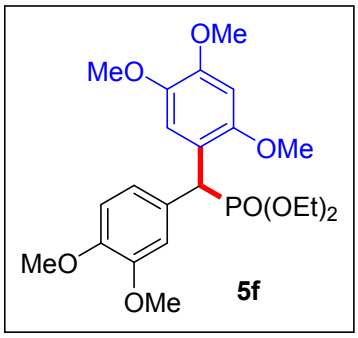


123.5 (d, J = 2.8 Hz, 1C), 121.8 (d, J = 8.3 Hz, 1C), 112.8 (d, J = 7.3 Hz, 1C), 111.1 (s, 1C), 107.4 (d, J = 2.1 Hz, 1C), 62.6 (t, J = 7.2 Hz, 2C), 61.3 (s, 1C), 60.8 (s, 1C), 55.9 (s, 1C), 55.9 (s, 1C), 55.9 (s, 1C), 41.5 (d, J = 140.5 Hz, 1C), 16.5 (d, J = 3.8 Hz, 1C), 16.4 (d, J = 3.7 Hz, 1C); **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{22}H_{32}O_8P$ 455.1829, found 455.1849.

Diethyl ((3,4-dimethoxyphenyl)(2,4,6-trimethoxyphenyl)methyl)phosphonate (5e). White solid (241 mg, 88%); mp: 110-112 °C; R_f = 0.3 in 70% EtOAc in hexane; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.19 (s, 1H), 6.94 (d, J = 8.3 Hz, 1H), 6.70 (d, J = 8.3 Hz, 1H), 6.11 (s, 2H), 5.12 (d, J = 28.3 Hz, 1H), 4.01 – 3.85 (m, 4H), 3.82 (s, 3H), 3.78 (s, 3H), 3.77 (s, 6H), 3.76 (s, 3H), 1.14 (dt, J = 17.8, 7.1 Hz, 6H); **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 160.4 (d, J = 2.0 Hz, 1C), 158.8 (s, 1C), 148.1 (d, J = 1.2 Hz, 2C), 147.5 (d, J = 2.0 Hz, 1C), 129.8 (d, J = 3.9 Hz, 1C), 121.8 (d, J = 8.6 Hz, 1C), 113.2 (d, J = 6.7 Hz, 1C), 110.6 (s, 1C), 107.5 (d, J = 4.0 Hz, 1C), 91.0 (s, 1C), 61.9 (d, J = 6.9 Hz, 1C), 61.8 (d, J = 7.1 Hz, 1C), 55.7 (s, 3C), 55.7 (s, 1C), 55.3 (s, 1C), 55.4 (s, 1C), 39.4 (d, J = 143.3 Hz, 1C), 16.4 (d, J = 6.0 Hz, 1C), 16.3 (d, J = 6.1 Hz, 1C); **HRMS** (ESI-QTOF) *m/z* $[M+Na]^+$ calcd for $C_{22}H_{31}NaO_8P$ 477.1649, found 477.1666.

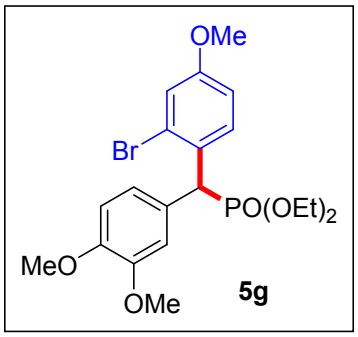


Diethyl ((3,4-dimethoxyphenyl)(2,4,5-trimethoxyphenyl)methyl)phosphonate (5f). Colorless viscous liquid (246 mg, 90%); R_f = 0.4 in 100% EtOAc; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.52 (d, J = 1.1 Hz, 1H), 7.07 (s, 1H), 7.02 (d, J = 8.3 Hz, 1H), 6.74 (d, J = 8.3 Hz, 1H), 6.47 (s, 1H), 4.92 (d, J = 25.2 Hz, 1H), 4.00 – 3.89 (m, 2H), 3.88 – 3.80 (m, 11H), 3.79 (s, 3H), 3.75 (s,

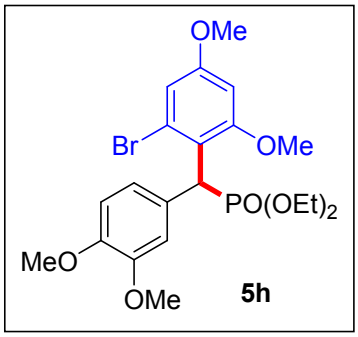


3H), 1.10 (q, J = 7.1 Hz, 6H); **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 151.0 (d, J = 11.0 Hz, 1C), 148.5 (s, 2C), 147.9 (d, J = 2.2 Hz, 1C), 142.9 (d, J = 1.5 Hz, 1C), 129.6 (d, J = 4.7 Hz, 1C), 121.6 (d, J = 8.3 Hz, 1C), 117.1 (d, J = 3.4 Hz, 1C), 113.7 (d, J = 4.8 Hz, 1C), 112.7 (d, J = 7.6 Hz, 1C), 111.0 (d, J = 1.1 Hz, 1C), 97.8 (s, 1C), 62.5 (d, J = 6.9 Hz, 2C), 56.9 (s, 1C), 56.5 (s, 1C), 56.0 (s, 1C), 55.8 (s, 1C), 55.8 (s, 1C), 40.7 (d, J = 140.3, 1C), 16.4 (d, J = 3.1 Hz, 1C), 16.3 (d, J = 3.1 Hz, 1C); **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{22}H_{32}O_8P$ 455.1829, found 455.1836.

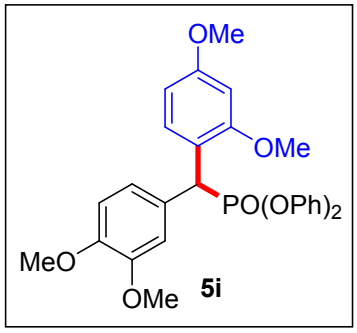
Diethyl ((2-bromo-4-methoxyphenyl)(3,4-dimethoxyphenyl)methyl)phosphonate (5g). Light yellow viscous liquid (221 mg, 78%); R_f = 0.3 in 70% EtOAc in hexane; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.96 (dd, J = 8.8, 1.7 Hz, 1H), 7.12 – 7.08 (m, 2H), 7.05 (d, J = 8.3 Hz, 1H), 6.88 (dd, J = 8.8, 2.6 Hz, 1H), 6.78 (d, J = 8.2 Hz, 1H), 4.95 (d, J = 25.7 Hz, 1H), 4.05 – 3.85 (m, 7H), 3.83 (s, 3H), 3.76 (s, 3H), 1.14 (td, J = 7.0, 3.8 Hz, 6H); **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 159.0 (d, J = 1.4 Hz, 1C), 148.8 (s, 1C), 148.2 (d, J = 2.2 Hz, 1C), 131.2 (d, J = 4.8 Hz, 1C), 128.8 (dd, J = 9.1, 2.3 Hz, 1C), 125.6 (d, J = 13.6 Hz, 1C), 121.9 (d, J = 8.3 Hz, 1C), 118.4 (s, 2C), 113.8 (d, J = 1.8 Hz, 1C), 112.8 (d, J = 7.6 Hz, 1C), 111.1 (s, 1C), 62.8 (d, J = 7.3 Hz, 1C), 62.7 (d, J = 7.4 Hz, 1C), 55.9 (s, 1C), 55.9 (s, 1C), 55.6 (s, 1C), 47.7 (d, J = 140.2 Hz, 1C), 16.4 (d, J = 2.7 Hz, 1C), 16.3 (d, J = 2.8 Hz, 1C); **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{20}H_{27}{}^{81}BrO_6P$ 475.0703, found 475.0701.



Diethyl ((2-bromo-4,6-dimethoxyphenyl)(3,4-dimethoxyphenyl)methyl)phosphonate (5h).



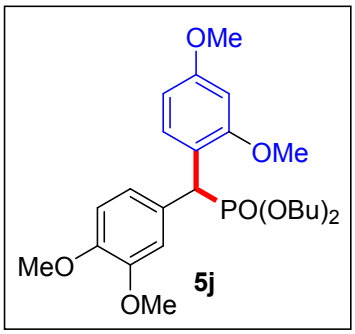
Light yellow viscous liquid (224 mg, 74%); R_f = 0.2 in 100% EtOAc; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.19 (s, 1H), 6.99 (d, *J* = 8.3 Hz, 1H), 6.73 (d, *J* = 8.3 Hz, 2H), 6.42 (d, *J* = 2.0 Hz, 1H), 5.14 (d, *J* = 28.2 Hz, 1H), 4.03 – 3.88 (m, 4H), 3.83 (s, 3H), 3.81 (s, 3H), 3.79 (s, 3H), 3.75 (s, 3H), 1.19 (t, *J* = 7.1 Hz, 3H), 1.14 (t, *J* = 7.1 Hz, 3H); **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 159.9 (d, *J* = 1.1 Hz, 1C), 159.5 (d, *J* = 4.2 Hz, 1C), 148.3 (s, 1C), 147.8 (s, 1C), 128.6 (d, *J* = 4.3 Hz, 1C), 126.8 (d, *J* = 12.4 Hz, 1C), 121.9 (d, *J* = 8.6 Hz, 1C), 119.5 (d, *J* = 3.3 Hz, 1C), 113.1 (d, *J* = 6.9 Hz, 1C), 110.7 (s, 1C), 109.7 (s, 1C), 99.2 (s, 1C), 62.2 (d, *J* = 6.7 Hz, 1C), 62.1 (d, *J* = 6.9 Hz, 1C), 55.8 (s, 2C), 55.7 (s, 1C), 55.6 (s, 1C), 47.8 (d, *J* = 143.5 Hz, 1C), 16.5 (d, *J* = 6.0 Hz, 1C), 16.40 (d, *J* = 6.0 Hz, 1C); **HRMS** (ESI-QTOF) *m/z* $[M+Na]^+$ calcd for $C_{21}H_{28}BrNaO_7P$ 525.0648, found 525.0668.



Diphenyl ((2,4-dimethoxyphenyl)(3,4-dimethoxyphenyl)methyl)phosphonate (5i). Colorless viscous liquid (191 mg, 61%); R_f = 0.4 in 70% EtOAc in hexane; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.89 (dd, *J* = 8.5, 1.7 Hz, 1H), 7.20 (t, *J* = 7.4 Hz, 4H), 7.17 – 7.11 (m, 2H), 7.08 (t, *J* = 7.4 Hz, 2H), 6.88 (d, *J* = 8.1 Hz, 4H), 6.79 (d, *J* = 8.3 Hz, 1H), 6.52 (dd, *J* = 8.5, 2.2 Hz, 1H), 6.43 (s, 1H), 5.33 (d, *J* = 26.0 Hz, 1H), 3.84 (s, 3H), 3.81 (s, 3H), 3.79 (s, 3H), 3.75 (s, 3H); **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 160.3 (d, *J* = 1.6 Hz, 1C), 157.7 (d, *J* = 11.0 Hz, 1C), 150.8 (d, *J* = 3.0 Hz, 1C), 150.7 (d, *J* = 3.0 Hz, 1C), 148.9 (s, 1C), 148.3 (d, *J* = 2.6 Hz, 1C), 130.8 (d, *J* = 5.4 Hz, 1C), 129.5 (d, *J* = 3.3 Hz, 4C), 128.6 (d, *J* = 4.6 Hz, 1C), 124.9 (s, 2C), 122.2 (d, *J* = 9.1

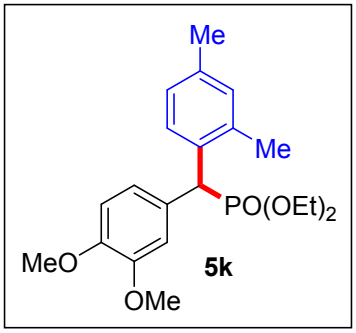
Hz, 1C), 120.7 (dd, J = 4.3, 2.3 Hz, 4C), 117.1 (d, J = 2.9 Hz, 1C), 113.1 (d, J = 7.8 Hz, 1C), 111.3 (s, 1C), 104.6 (s, 1C), 98.9 (s, 1C), 55.9 (s, 2C), 55.7 (s, 1C), 55.5 (s, 1C), 41.0 (d, J = 141.0, 1C); **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{25}H_{38}O_7P$ 481.2350, found 481.2350.

Dibutyl ((2,4-dimethoxyphenyl)(3,4-dimethoxyphenyl)methyl)phosphonate (5j).



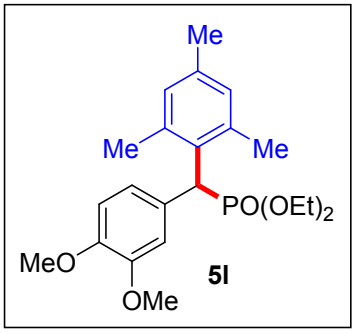
Colorless liquid (242 mg, 84%); R_f = 0.4 in 50% EtOAc in hexane; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.82 (dd, J = 8.5, 1.6 Hz, 1H), 7.11 (s, 1H), 7.04 (d, J = 8.3 Hz, 1H), 6.77 (d, J = 8.3 Hz, 1H), 6.50 (dd, J = 8.5, 2.3 Hz, 1H), 6.42 (s, 1H), 4.94 (d, J = 25.4 Hz, 1H), 3.96 – 3.88 (m, 2H), 3.87 (s, 3H), 3.83 (s, 3H), 3.78 (s, 6H), 3.78 – 3.70 (m, 2H), 1.43 (dt, J = 15.3, 7.8 Hz, 4H), 1.23 (dp, J = 14.1, 7.2 Hz, 4H), 0.82 (td, J = 7.4, 3.6 Hz, 6H); **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 159.9 (d, J = 1.8 Hz, 1C), 157.7 (d, J = 10.2 Hz, 1C), 148.7 (s, 1C), 148.0 (d, J = 1.5 Hz, 1C), 130.7 (d, J = 5.3 Hz, 1C), 130.1 (d, J = 4.5 Hz, 1C), 121.9 (d, J = 8.4 Hz, 1C), 118.4 (d, J = 3.1 Hz, 1C), 113.1 (d, J = 7.5 Hz, 1C), 111.2 (s, 1C), 104.5 (s, 1C), 98.8 (s, 1C), 66.3 (d, J = 7.1 Hz, 1C), 66.2 (d, J = 7.3 Hz, 1C), 55.9 (s, 2C), 55.8 (s, 1C), 55.5 (s, 1C), 40.3 (d, J = 140.4 Hz, 1C), 32.6 (d, J = 3.3 Hz, 1C), 32.6 (d, J = 3.3 Hz, 1C), 18.8 (s, 1C), 18.7 (s, 1C), 13.7 (s, 2C); **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{25}H_{37}O_7P$ 481.2350, found 481.2350.

Diethyl ((3,4-dimethoxyphenyl)(2,4-dimethylphenyl)methyl)phosphonate (5k). Colorless liquid (127 mg, 54%); R_f = 0.3 in 50% EtOAc in hexane; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.79 (d, J = 7.9 Hz, 1H), 7.05 (s, 1H), 7.02 (d, J = 8.3 Hz, 1H), 6.96 (d, J = 7.4 Hz, 2H), 6.76 (d,

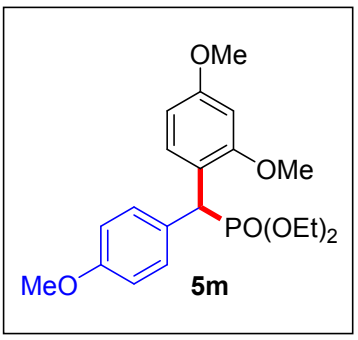


J = 8.3 Hz, 1H), 4.56 (d, J = 26.1 Hz, 1H), 4.01 – 3.92 (m, 2H), 3.84 (s, 3H), 3.83 – 3.75 (m, 5H), 2.29 (s, 3H), 2.27 (s, 3H), 1.16 (t, J = 7.1 Hz, 3H), 1.11 (t, J = 7.3 Hz, 3H); **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 148.8 (d, J = 1.3 Hz, 1C), 148.1 (d, J = 2.5 Hz, 1C), 136.7 (d, J = 1.3 Hz, 1C), 136.2 (s, 1C), 136.1 (s, 1C), 132.5 (d, J = 3.7 Hz, 1C), 131.5 (s, 1C), 129.2 (d, J = 5.4 Hz, 1C), 126.9 (d, J = 1.4 Hz, 1C), 122.1 (d, J = 8.4 Hz, 1C), 113.1 (d, J = 7.2 Hz, 1C), 111.1 (s, 1C), 62.7 (d, J = 7.2 Hz, 1C), 62.5 (d, J = 7.2 Hz, 1C), 55.9 (s, 1C), 55.9 (s, 1C), 45.8 (d, J = 139.1 Hz, 1C), 21.0 (s, 1C), 20.0 (s, 1C), 16.4 (d, J = 7.0 Hz, 1C), 16.3 (d, J = 6.1 Hz, 1C); **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{21}H_{30}O_5P$ 393.1825, found 393.1802.

Diethyl ((3,4-dimethoxyphenyl)(mesityl)methyl)phosphonate (5l). Colorless liquid (127 mg, 68%); R_f = 0.3 in 50% EtOAc in hexane; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.03 (s, 1H), 6.92 (d, J = 8.3 Hz, 1H), 6.88 (s, 1H), 6.75 (d, J = 8.2 Hz, 2H), 5.02 (d, J = 30.9 Hz, 1H), 4.27 – 4.05 (m, 2H), 3.89 – 3.81 (m, 4H), 3.79 (s, 3H), 3.49 – 3.32 (m, 1H), 2.45 (s, 3H), 2.24 (s, 3H), 2.08 (s, 3H), 1.34 (t, J = 7.1 Hz, 3H), 1.00 (t, J = 7.0 Hz, 3H); **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 148.6 (s, 1C), 147.4 (s, 1C), 139.5 (d, J = 4.4 Hz, 1C), 137.8 (d, J = 7.7 Hz, 1C), 136.6 (d, J = 3.2 Hz, 1C), 131.1 (d, J = 1 3.0 Hz, 1C), 131.0 (d, J = 6.3 Hz , 1C), 129.9 (d, J = 1.1 Hz, 1C), 129.0 (d, J = 1.7 Hz, 1C), 121.4 (d, J = 11.2 Hz, 1C), 112.6 (d, J = 10.7 Hz, 1C), 111.04 (s, 1C), 62.9 (d, J = 6.8 Hz, 1C), 61.5 (d, J = 7.5 Hz, 1C), 55.9 (s, 1C), 55.9 (s, 1C), 44.3 (d, J = 141.0 Hz, 1C), 21.8 (s, 1C), 21.6 (s, 1C), 20.9 (s, 1C), 16.6 (d, J = 6.0 Hz, 1C), 16.3 (d, J = 5.7 Hz, 1C); **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{22}H_{32}O_5P$ 407.1982, found 407.1980.

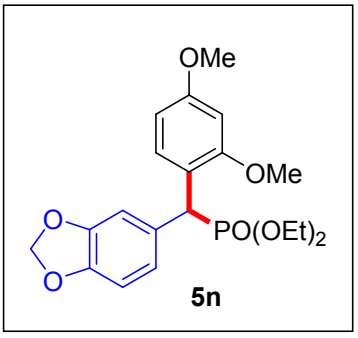


Diethyl ((2,4-dimethoxyphenyl)(4-methoxyphenyl)methyl)phosphonate (5m). Colorless



viscous liquid (223 mg, 94%); R_f = 0.3 in 50% EtOAc in hexane; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.82 (dd, *J* = 8.5, 1.3 Hz, 1H), 7.42 (d, *J* = 7.2 Hz, 2H), 6.81 (d, *J* = 8.5 Hz, 2H), 6.50 (dd, *J* = 8.5, 2.1 Hz, 1H), 6.41 (s, 1H), 4.94 (d, *J* = 25.4 Hz, 1H), 4.03 – 3.80 (m, 4H), 3.78 (s, 3H), 3.77 (s, 3H), 3.75 (s, 3H), 1.12 (td, *J* = 7.0, 3.5 Hz, 6H); **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 159.8 (s, 1C), 158.5 (d, *J* = 2.2 Hz, 1C), 157.6 (d, *J* = 10.5 Hz, 1C), 130.7 (s, 1C), 130.6 (s, 1C), 130.6 (s, 2C), 129.4 (d, *J* = 4.9 Hz, 1C), 118.4 (d, *J* = 2.9 Hz, 1C), 113.8 (s, 1C), 104.3 (s, 1C), 98.8 (s, 1C), 62.5 (d, *J* = 7.1 Hz, 1C), 62.4 (d, *J* = 7.0 Hz, 1C), 55.7 (s, 1C), 55.4 (s, 1C), 55.3 (s, 1C), 40.0 (d, *J* = 140.5, 1C), 16.4 (s, 1C), 16.3 (s, 1C); **HRMS** (ESI-QTOF) *m/z* $[M+K]^+$ calcd for $C_{20}H_{27}KO_6P$ 433.1177, found 433.1169.

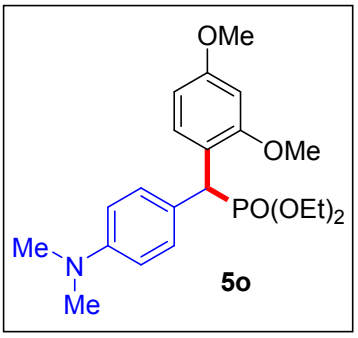
Diethyl (benzo[*d*][1,3]dioxol-5-yl(2,4-dimethoxyphenyl)methyl)phosphonate (5n).



Colorless viscous liquid (245 mg, 90%); R_f = 0.4 in 50% EtOAc in hexane; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.80 (dd, *J* = 8.5, 1.7 Hz, 1H), 7.01 (s, 1H), 6.96 (d, *J* = 8.0 Hz, 1H), 6.70 (d, *J* = 8.0 Hz, 1H), 6.50 (dd, *J* = 8.5, 2.3 Hz, 1H), 6.41 (s, 1H), 5.89 (s, 2H), 4.90 (d, *J* = 25.4 Hz, 1H), 4.05 – 3.81 (m, 4H), 3.78 (s, 3H), 3.77 (s, 3H), 1.14 (dt, *J* = 17.0, 7.1 Hz, 6H); **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 159.9 (d, *J* = 1.4 Hz, 1C), 157.7 (d, *J* = 10.3 Hz, 1C), 147.6 (s, 1C), 146.5 (d, *J* = 2.3 Hz, 1C), 131.1 (d, *J* = 4.8 Hz, 1C), 130.6 (d, *J* = 5.3 Hz, 1C), 122.9 (d, *J* = 8.4 Hz, 1C), 118.2 (d, *J* = 2.9 Hz, 1C), 110.2 (d, *J* = 7.5 Hz, 1C), 108.2 (d, *J* = 1.4 Hz, 1C), 104.4 (d, *J* = 1.4 Hz, 1C), 101.0 (s, 1C),

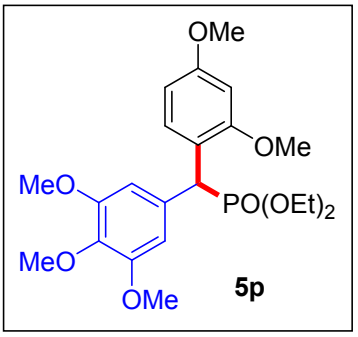
98.8 (s, 1C), 62.7 (d, J = 7.1 Hz, 1C), 62.5 (d, J = 7.1 Hz, 1C), 55.80 (s, 1C), 55.42 (s, 1C), 40.8 (d, J = 140.9, 1C), 16.4 (d, J = 3.0 Hz, 1C), 16.4 (d, J = 3.0 Hz, 1C); **HRMS** (ESI-QTOF) *m/z* $[M+Na]^+$ calcd for $C_{20}H_{25}NaO_7P$ 431.1230, found 431.1236.

Diethyl ((2,4-dimethoxyphenyl)(4-(dimethylamino)phenyl)methyl)phosphonate (5o).



Light yellow viscous liquid (237 mg, 87%); R_f = 0.4 in 50% EtOAc in hexane; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.81 (d, J = 8.4 Hz, 1H), 7.36 (d, J = 8.2 Hz, 2H), 6.65 (d, J = 8.4 Hz, 2H), 6.49 (dd, J = 8.5, 1.9 Hz, 1H), 6.40 (s, 1H), 4.91 (d, J = 25.4 Hz, 1H), 4.03 – 3.90 (m, 2H), 3.85 (dt, J = 15.9, 7.9 Hz, 2H), 3.77 (s, 6H), 2.89 (s, 6H), 1.13 (q, J = 7.0 Hz, 6H); **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 159.7 (d, J = 1.5 Hz, 1C), 157.7 (d, J = 10.4 Hz, 1C), 149.6 (s, 1C), 130.7 (d, J = 5.2 Hz, 1C), 130.3 (d, J = 7.7 Hz, 2C), 125.1 (d, J = 5.3 Hz, 1C), 118.8 (d, J = 2.8 Hz, 1C), 112.7 (d, J = 1.0 Hz, 2C), 104.3 (s, 1C), 98.8 (s, 1C), 62.5 (s, 1C), 62.4 (s, 1C), 55.8 (s, 1C), 55.4 (s, 1C), 40.8 (d, J = 140.0, 1C), 40.7 (s, 2C), 16.5 (d, J = 2.7 Hz, 1C), 16.4 (d, J = 2.7 Hz, 1C); **HRMS** (ESI-QTOF) *m/z* $[M+Na]^+$ calcd for $C_{21}H_{30}NNaO_5P$ 430.1754, found 430.1748.

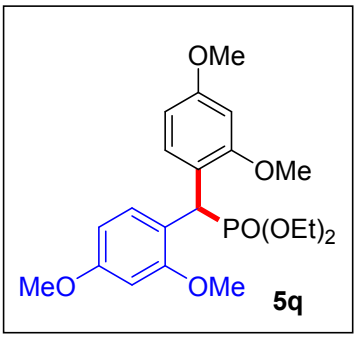
Diethyl ((2,4-dimethoxyphenyl)(3,4,5-trimethoxyphenyl)methyl)phosphonate (5p).



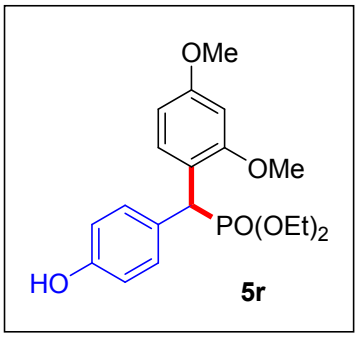
Colorless viscous liquid (210 mg, 91%); R_f = 0.3 in 50% EtOAc in hexane; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.78 (dd, J = 8.5, 1.8 Hz, 1H), 6.77 (s, 2H), 6.50 (dd, J = 8.6, 2.2 Hz, 1H), 6.43 (s, 1H), 4.92 (d, J = 25.4 Hz, 1H), 4.03 – 3.84 (m, 4H), 3.82 (s, 6H), 3.79 (s, 3H), 3.78 (s, 6H), 1.13 (dt, J = 17.4, 7.1 Hz, 6H); **^{13}C{^{1}H}**

NMR (100 MHz, $CDCl_3$) δ 159.9 (d, *J* = 1.5 Hz, 1C), 157.7 (s, 1C), 157.6 (s, 1C), 152.9 (d, *J* = 1.3 Hz, 2C), 136.9 (d, *J* = 2.5 Hz, 1C), 132.9 (d, *J* = 4.4 Hz, 1C), 130.6 (d, *J* = 5.1 Hz, 1C), 117.8 (d, *J* = 3.4 Hz, 1C), 106.8 (d, *J* = 8.2 Hz, 1C), 104.4 (d, *J* = 1.6 Hz, 1C), 98.8 (s, 1C), 62.7 (s, 1C), 62.6 (s, 1C), 60.8 (d, *J* = 2.0 Hz, 1C), 56.1 (s, 2C), 55.8 (s, 1C), 55.4 (s, 1C), 41.1 (d, *J* = 140.2, 1C), 16.4 (d, *J* = 2.0 Hz, 1C), 16.4 (d, *J* = 1.8 Hz, 1C); **HRMS** (ESI-QTOF) *m/z* $[M+Na]^+$ calcd for $C_{22}H_{31}NaO_8P$ 477.1649, found 477.1652.

Diethyl (bis(2,4-dimethoxyphenyl)methyl)phosphonate (5q). Colorless viscous liquid (225 mg, 88%); R_f = 0.3 in 70% EtOAc in hexane; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.67 (dd, *J* = 8.5, 1.7 Hz, 2H), 6.42 (dd, *J* = 8.5, 2.0 Hz, 2H), 6.37 (s, 2H), 5.48 (d, *J* = 25.1 Hz, 1H), 3.93 (tt, *J* = 16.9, 7.0 Hz, 2H), 3.86 – 3.79 (m, 2H), 3.74 (s, 6H), 3.70 (s, 6H), 1.09 (t, *J* = 7.1 Hz, 6H); **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 159.6 (d, *J* = 1.6 Hz, 2C), 157.9 (d, *J* = 9.7 Hz, 2C), 130.9 (d, *J* = 5.2 Hz, 2C), 118.5 (d, *J* = 3.4 Hz, 2C), 104.2 (d, *J* = 1.4 Hz, 2C), 98.7 (s, 2C), 62.2 (s, 1C), 62.1 (s, 1C), 55.8 (s, 2C), 55.2 (s, 2C), 32.2 (d, *J* = 142.2, 1C), 16.3 (s, 1C), 16.2 (s, 1C); **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{21}H_{30}O_7P$ 425.1724, found 425.1735.

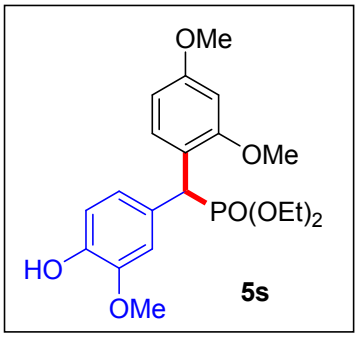


Diethyl ((2,4-dimethoxyphenyl)(4-hydroxyphenyl)methyl)phosphonate (5r). Brown solid (205 mg, 66%); mp: 90-92°C; R_f = 0.3 in 100% EtOAc; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.5 Hz, 1H), 7.27 – 7.19 (m, 2H), 6.65 (d, *J* = 8.0 Hz, 2H), 6.50 (d, *J* = 8.4 Hz, 1H), 6.41 (s, 1H), 4.94 (d, *J* = 25.6 Hz, 1H), 3.94 (ddd, *J* = 23.0, 12.8, 5.5

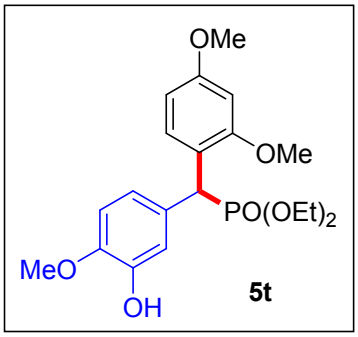


Hz, 4H), 3.78 (s, 3H), 3.75 (s, 3H), 1.13 (t, J = 6.0 Hz, 6H); **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 159.9 (d, J = 1.3 Hz, 1C), 157.7 (d, J = 10.7 Hz, 1C), 156.1 (d, J = 2.7 Hz, 1C), 130.6 (s, 1C), 130.6 (s, 1C), 130.5 (s, 2C), 127.1 (d, J = 5.4 Hz, 1C), 117.9 (d, J = 2.9 Hz, 1C), 115.8 (d, J = 1.3 Hz, 1C), 104.3 (s, 1C), 98.8 (s, 1C), 63.0 (d, J = 7.3 Hz, 1C), 60.8 (d, J = 7.0 Hz, 1C), 55.7 (s, 1C), 55.4 (s, 1C), 40.0 (d, J = 140.8, 1C), 16.4 (s, 1C), 16.3 (s, 1C); **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{19}H_{26}O_6P$ 381.1462, found 381.1469.

Diethyl ((2,4-dimethoxyphenyl)(4-hydroxy-3-methoxyphenyl)methyl)phosphonate (5s).



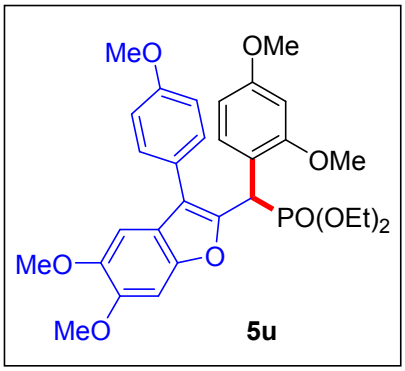
Ivory liquid (191 mg, 71%); R_f = 0.3 in 100% EtOAc; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.80 (dd, J = 8.5, 1.8 Hz, 1H), 7.08 (s, 1H), 6.94 (d, J = 8.2 Hz, 1H), 6.78 (d, J = 8.2 Hz, 1H), 6.49 (dd, J = 8.5, 2.4 Hz, 1H), 6.41 (s, 1H), 6.17 (s, 1H), 4.92 (d, J = 25.5 Hz, 1H), 4.01 – 3.92 (m, 2H), 3.87 – 3.80 (m, 5H), 3.77 (s, 6H), 1.12 (dd, J = 15.8, 7.1 Hz, 6H); **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 159.8 (d, J = 1.5 Hz, 1C), 157.6 (d, J = 10.1 Hz, 1C), 146.5 (d, J = 1.3 Hz, 1C), 144.8 (d, J = 2.3 Hz, 1C), 130.5 (d, J = 5.3 Hz, 1C), 128.8 (d, J = 4.8 Hz, 1C), 122.5 (d, J = 8.5 Hz, 1C), 118.2 (d, J = 3.1 Hz, 1C), 114.4 (s, 1C), 112.4 (d, J = 7.4 Hz, 1C), 104.4 (d, J = 1.1 Hz, 1C), 98.8 (s, 1C), 62.6 (d, J = 7.0 Hz, 1C), 62.5 (d, J = 7.0 Hz, 1C), 55.9 (s, 1C), 55.7 (s, 1C), 55.3 (s, 1C), 40.6 (d, J = 140.4 Hz, 1C), 16.4 (d, J = 1.1 Hz, 1C),16.3 (s, 1C); **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{20}H_{28}O_7P$ 411.1567, found 411.1583.



Diethyl ((2,4-dimethoxyphenyl)(3-hydroxy-4-

methoxyphenyl)methyl)phosphonate (5t). White solid (199 mg, 74%); mp: 147-149 °C; R_f = 0.3 in 100% EtOAc; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.3 Hz, 1H), 7.12 (s, 1H), 7.01 (d, *J* = 8.0 Hz, 1H), 6.74 (d, *J* = 8.3 Hz, 1H), 6.47 (d, *J* = 8.1 Hz, 1H), 6.41 (s, 1H), 6.15 – 5.89 (m, 1H), 4.91 (d, *J* = 25.4 Hz, 1H), 4.04 – 3.92 (m, 2H), 3.91 – 3.83 (m, 2H), 3.81 (s, 3H), 3.76 (s, 6H), 1.13 (dt, *J* = 13.8, 7.0 Hz, 6H); **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 159.8 (s, 1C), 157.6 (d, *J* = 10.5 Hz, 1C), 145.8 (d, *J* = 2.3 Hz, 1C), 145.5 (d, *J* = 4.2 Hz, 1C), 130.7 (d, *J* = 5.2 Hz, 1C), 130.5 (d, *J* = 4.4 Hz, 1C), 121.1 (d, *J* = 7.9 Hz, 1C), 118.3 (d, *J* = 3.3 Hz, 1C), 116.2 (d, *J* = 7.8 Hz, 1C), 110.7 (s, 1C), 104.4 (d, *J* = 1.2 Hz, 1C), 98.8 (s, 1C), 62.7 (s, 1C), 62.5 (d, *J* = 7.2 Hz, 1C), 55.9 (s, 1C), 55.8 (s, 1C), 55.4 (s, 1C), 40.5 (d, *J* = 140.7 Hz, 1C), 16.4 (d, *J* = 2.2 Hz, 1C), 16.3 (d, *J* = 2.1 Hz, 1C); **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{20}H_{28}O_7P$ 411.1567, found 411.1586.

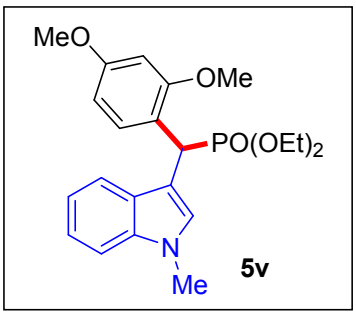
Diethyl ((5,6-dimethoxy-3-(4-methoxyphenyl)benzofuran-2-yl)(2,4-dimethoxyphenyl)methyl)phosphonate (5u). Colorless liquid (178 mg, 89%); R_f = 0.4 in 100% EtOAc; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.06 (dd, *J* = 8.6, 2.1 Hz, 1H), 7.43 (d, *J* = 8.6 Hz, 2H), 7.15 (s, 1H), 7.03 (d, *J* = 8.6 Hz, 2H), 6.90 (s, 1H), 6.55 (dd, *J* = 8.6, 2.2 Hz, 1H), 6.42 (s, 1H), 5.42 (d, *J* = 26.3 Hz, 1H), 4.03 – 3.86 (m, 10H), 3.85 (s, 3H), 3.79 (s, 3H), 3.70 (s, 3H), 1.11 (t, *J* = 7.1 Hz, 6H); **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 160.3 (d, *J* = 2.2 Hz, 1C), 158.9 (s, 1C), 157.4 (d, *J* = 7.8 Hz, 1C), 149.2 (s, 1C), 147.8 (s, 1C), 147.4 (d, *J* = 12.5 Hz, 1C), 146.6 (s, 1C), 132.1 (d, *J* = 4.4 Hz, 1C), 130.5 (s, 2C), 124.8 (d, *J* = 2.0 Hz, 1C), 120.5 (d, *J* = 1.4 Hz, 1C), 118.8 (d, *J* = 10.2 Hz, 1C), 115.1 (d, *J* = 3.9 Hz, 1C), 114.2 (s, 2C), 104.7 (d, *J* = 2.1 Hz, 1C), 101.2



5u

(s, 1C), 98.7 (s, 1C), 95.8 (s, 1C), 62.9 (d, J = 6.8 Hz, 1C), 62.6 (d, J = 7.0 Hz, 1C), 56.5 (s, 1C), 56.4 (s, 1C), 55.7 (s, 1C), 55.5 (s, 1C), 55.4 (s, 1C), 33.9 (d, J = 141.2 Hz, 1C), 16.4 (d, J = 2.2 Hz, 1C), 16.3 (d, J = 2.1 Hz, 1C); **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{30}H_{36}O_9P$ 571.2091, found 571.2089.

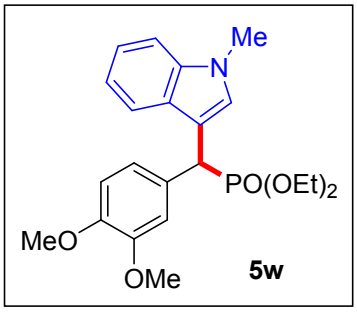
Diethyl ((2,4-dimethoxyphenyl)(1-methyl-1*H*-indol-3-yl)methyl)phosphonate (5v).



5v

Colorless liquid (228 mg, 87%); R_f = 0.3 in 100% EtOAc; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.56 – 7.50 (m, 3H), 7.24 (d, J = 8.1 Hz, 1H), 7.17 (d, J = 7.2 Hz, 1H), 7.04 (d, J = 7.4 Hz, 1H), 6.45 (s, 1H), 6.42 (d, J = 8.6 Hz, 1H), 5.35 (d, J = 25.2 Hz, 1H), 4.07 – 3.91 (m, 3H), 3.90 (s, 3H), 3.80 – 3.69 (m, 7H), 1.12 (dt, J = 22.3, 7.0 Hz, 6H); **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 159.7 (d, J = 2.5 Hz, 1C), 157.4 (d, J = 7.9 Hz, 1C), 136.6 (s, 1C), 131.2 (d, J = 4.8 Hz, 1C), 128.4 (d, J = 5.1 Hz, 1C), 127.8 (d, J = 12.8 Hz, 1C), 121.6 (s, 1C), 118.9 (d, J = 13.3 Hz, 1C), 118.3 (d, J = 4.8 Hz, 1C), 110.6 (d, J = 4.5 Hz, 1C), 109.1 (s, 1C), 104.6 (d, J = 2.4 Hz, 1C), 98.4 (s, 1C), 62.7 (d, J = 7.0 Hz, 1C), 62.4 (d, J = 7.2 Hz, 1C), 55.9 (s, 1C), 55.4 (s, 1C), 32.9 (s, 1C), 32.0 (s, 1C), 30.6 (s, 1C), 16.4 (t, J = 5.3 Hz, 2C); **HRMS** (ESI-QTOF) *m/z* $[M+Na]^+$ calcd for $C_{22}H_{28}NNaO_5P$ 440.1597, found 440.1593.

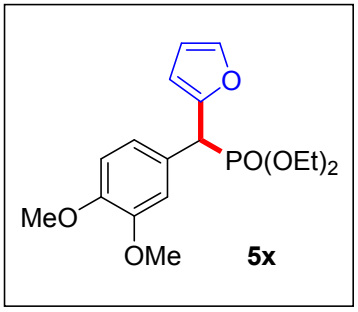
Diethyl ((3,4-dimethoxyphenyl)(1-methyl-1*H*-indol-3-yl)methyl)phosphonate (5w).



5w

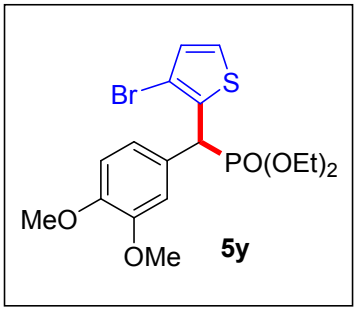
Colorless liquid (232 mg, 93%); R_f = 0.3 in 100% EtOAc; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.49 (d, J = 8.1 Hz, 2H), 7.27 (d, J = 8.3 Hz, 1H), 7.19 (dd, J = 11.2, 4.0 Hz, 1H), 7.10 (s, 1H), 7.08

– 7.01 (m, 2H), 6.78 (d, J = 8.3 Hz, 1H), 4.66 (d, J = 25.2 Hz, 1H), 4.07 – 3.87 (m, 3H), 3.86 (s, 3H), 3.82 (s, 3H), 3.77 (s, 3H), 3.76 – 3.67 (m, 1H), 1.13 (q, J = 7.2 Hz, 6H); **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 148.7 (d, J = 2.1 Hz, 1C), 148.0 (d, J = 2.8 Hz, 1C), 136.7 (s, 1C), 129.6 (d, J = 5.5 Hz, 1C), 128.3 (d, J = 5.4 Hz, 1C), 127.5 (d, J = 12.1 Hz, 1C), 121.7 (s, 1C), 121.6 (d, J = 7.6 Hz, 1C), 119.1 (s, 1C), 118.8 (s, 1C), 112.7 (d, J = 6.5 Hz, 1C), 111.0 (d, J = 2.1 Hz, 1C), 109.6 (d, J = 5.2 Hz, 1C), 109.3 (s, 1C), 62.8 (d, J = 7.2 Hz, 1C), 62.5 (d, J = 7.1 Hz, 1C), 55.9 (s, 1C), 55.8 (s, 1C), 41.3 (d, J = 139.1 Hz, 1C), 32.9 (s, 1C), 16.4 (s, 1C), 16.3 (s, 1C); **HRMS** (ESI-QTOF) *m/z* $[M+Na]^+$ calcd for $C_{22}H_{28}NNaO_5P$ 440.1597, found 440.1593.



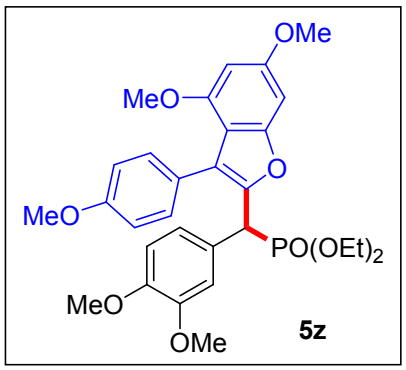
Diethyl ((3,4-dimethoxyphenyl)(furan-2-yl)methyl)phosphonate (5x). Light yellow liquid (123 mg, 58%); R_f = 0.4 in 50% EtOAc in hexane; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.32 (s, 1H), 6.99 (d, J = 1.3 Hz, 1H), 6.92 (dt, J = 7.9, 1.9 Hz, 1H), 6.77 (d, J = 8.3 Hz, 1H), 6.43 (s, 1H), 6.30 (d, J = 1.7 Hz, 1H), 4.44 (d, J = 25.9 Hz, 1H), 4.04 – 3.91 (m, 3H), 3.82 (s, 3H), 3.80 (s, 3H), 3.79 – 3.70 (m, 1H), 1.17 (t, J = 7.1 Hz, 3H), 1.09 (t, J = 7.1 Hz, 3H); **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 149.9 (d, J = 2.3 Hz, 1C), 148.7 (d, J = 2.2 Hz, 1C), 148.4 (d, J = 2.9 Hz, 1C), 142.0 (d, J = 2.0 Hz, 1C), 126.7 (d, J = 6.7 Hz, 1C), 121.6 (d, J = 7.4 Hz, 1C), 112.5 (d, J = 5.7 Hz, 1C), 111.0 (d, J = 2.2 Hz, 1C), 110.6 (d, J = 2.0 Hz, 1C), 108.5 (d, J = 5.2 Hz, 1C), 62.9 (d, J = 6.9 Hz, 1C), 62.8 (d, J = 7.0 Hz, 1C), 55.8 (s, 1C), 55.8 (s, 1C), 44.6 (d, J = 140.2 Hz, 1C), 16.3 (d, J = 6.0 Hz, 1C),16.2 (s, 1C); **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{17}H_{24}O_6P$ 355.1305, found 355.1311.

Diethyl ((3-bromothiophen-2-yl)(3,4-dimethoxyphenyl)methyl)phosphonate (5y).



Colorless liquid (192 mg, 71%); R_f = 0.4 in 100% EtOAc; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.23 (d, *J* = 5.4 Hz, 1H), 7.15 (s, 1H), 7.06 (d, *J* = 1.9 Hz, 1H), 6.90 (d, *J* = 5.4 Hz, 1H), 6.78 (d, *J* = 8.3 Hz, 1H), 4.88 (d, *J* = 25.2 Hz, 1H), 4.05 – 3.92 (m, 4H), 3.87 (s, 3H), 3.82 (s, 3H), 1.17 (t, *J* = 7.1 Hz, 3H), 1.09 (d, *J* = 6.9 Hz, 3H); **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 148.9 (d, *J* = 1.1 Hz, 1C), 148.5 (d, *J* = 2.3 Hz, 1C), 134.4 (d, *J* = 6.9 Hz, 1C), 129.3 (d, *J* = 1.5 Hz, 1C), 127.9 (d, *J* = 5.0 Hz, 1C), 125.7 (d, *J* = 2.1 Hz, 1C), 121.8 (d, *J* = 8.1 Hz, 1C), 112.6 (d, *J* = 6.5 Hz, 1C), 111.2 (s, 1C), 111.2 (s, 1C), 63.3 (d, *J* = 7.0 Hz, 1C), 63.1 (d, *J* = 7.1 Hz, 1C), 55.9 (s, 1C), 55.9 (s, 1C), 45.3 (d, *J* = 142.6 Hz, 1C), 16.4 (d, *J* = 3.2 Hz, 1C), 16.3 (d, *J* = 3.2 Hz, 1C); **HRMS** (ESI-QTOF) *m/z* $[M+Na]^+$ calcd for $C_{17}H_{22}BrNaO_5PS$ 471.0001, found 471.0018.

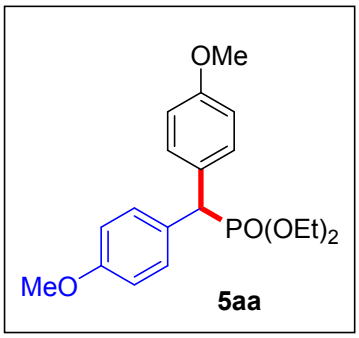
Diethyl ((4,6-dimethoxy-3-(4-methoxyphenyl)benzofuran-2-yl)(3,4-dimethoxyphenyl)methyl)phosphonate (5z).



Colorless liquid (297 mg, 87%); R_f = 0.4 in 50% EtOAc in hexane; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.33 (d, *J* = 8.3 Hz, 2H), 7.20 (s, 1H), 7.04 (d, *J* = 8.2 Hz, 1H), 6.93 (d, *J* = 8.5 Hz, 2H), 6.80 (d, *J* = 8.3 Hz, 1H), 6.76 (s, 1H), 6.29 (s, 1H), 4.58 (d, *J* = 26.2 Hz, 1H), 4.07 – 3.92 (m, 4H), 3.89 (s, 3H), 3.86 (s, 3H), 3.85 (s, 6H), 3.68 (s, 3H), 1.15 (q, *J* = 6.8 Hz, 6H); **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 158.9 (d, *J* = 3.3 Hz, 1C), 156.4 (s, 1C), 154.5 (s, 1C), 148.8 (d, *J* = 2.0 Hz, 1C), 148.4 (d, *J* = 2.4 Hz, 1C), 146.4 (s, 1C), 146.2 (s, 1C), 131.5 (d, *J* = 1.0 Hz, 2C), 127.3 (d, *J* = 4.9 Hz, 1C), 124.9

(d, J = 1.8 Hz, 1C), 121.8 (d, J = 7.0 Hz, 1C), 118.8 (d, J = 10.4 Hz, 1C), 113.3 (s, 2C), 112.9 (d, J = 5.4 Hz, 1C), 111.3 (d, J = 1.2 Hz, 1C), 111.2 (d, J = 1.6 Hz, 1C), 94.6 (s, 1C), 88.5 (s, 1C), 62.9 (d, J = 5.4 Hz, 1C), 62.8 (d, J = 5.4 Hz, 1C), 56.0 (s, 1C), 55.9 (s, 1C), 55.8 (s, 1C), 55.5 (s, 1C), 55.3 (s, 1C), 42.7 (d, J = 138.4 Hz, 1C), 16.5 (d, J = 5.6 Hz, 1C), 16.4 (d, J = 5.8 Hz, 1C); **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{30}H_{36}O_9P$ 571.2091, found 571.2109.

Diethyl (bis(4-methoxyphenyl)methyl)phosphonate (5aa). White solid (2.51 g, 94%); mp: 59-61 °C; R_f = 0.3 in 70% EtOAc in hexane; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.41 (d, J = 8.1 Hz, 4H), 6.82 (d, J = 8.3 Hz, 4H), 4.32 (d, J = 25.3 Hz, 1H), 4.00 – 3.89 (m, 2H), 3.87 – 3.77 (m, 2H), 3.74 (s, 6H), 1.11 (t, J = 7.0 Hz, 6H); **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 158.6 (d, J = 2.0 Hz, 2C), 130.4 (d, J = 8.0 Hz, 4C), 129.2 (d, J = 5.1 Hz, 2C), 113.9 (s, 4C), , 62.55 (d, J = 7.0 Hz, 2C), 55.2 (s, 2C), 49.4 (d, J = 137.9 Hz, 1C), 16.31 (d, J = 5.8 Hz, 2C); **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{19}H_{26}O_5P$ 365.1512, found 365.1512.

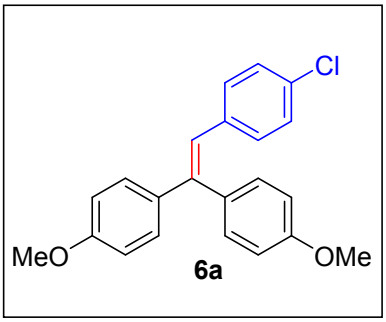


General Procedure for the Synthesis of 6

To a stirred solution of **5** (100 mg, 1 equiv) in dry THF (4 mL) under nitrogen atmosphere at 0 °C, *t*-BuOK (2 equiv) was added at 0 °C. After being stirred for 4−5 min, aldehyde (2 equiv) was cautiously added to the solution at 0 °C. The reaction was allowed to stir for 14 h at 25 °C and completion of the reaction was monitored by TLC. The resulting reaction mixture was quenched with water, washed with brine, extracted with ethyl acetate (10 mL × 3), dried over

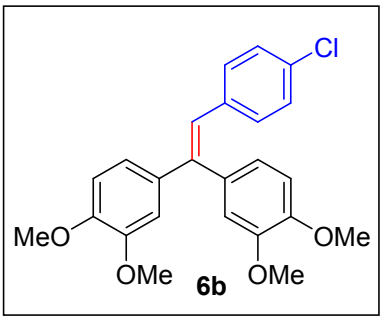
$MgSO_4$, and concentrated under reduced pressure. The crude product was purified by column chromatography using ethyl acetate and hexane (5% ethyl acetate in hexane).

4,4'-(2-(4-Chlorophenyl)ethene-1,1-diyl)bis(methoxybenzene) (6a). White solid (75 mg, 78%); mp: 96-98 °C; R_f = 0.5 in 20% EtOAc in hexane; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.24 (d, *J* = 7.4 Hz, 2H), 7.08 (d, *J* = 7.7 Hz, 4H), 6.94 (d, *J* = 8.2 Hz, 2H), 6.85 (dd, *J* = 10.4, 3.7 Hz, 4H), 6.75 (s, 1H), 3.83 (s, 3H), 3.81 (s, 3H); **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 159.5, 159.2, 142.6, 136.5, 136.2, 132.4, 131.9, 131.7, 131.7, 130.7, 130.7, 129.0, 129.0, 128.2, 128.2, 124.9, 114.2, 114.2, 113.7, 113.7, 55.4, 55.3; **HRMS** (ESI-QTOF) *m/z* $[M+Na]^+$ calcd for $C_{22}H_{19}ClNaO_2$ 373.0966, found 373.0996.



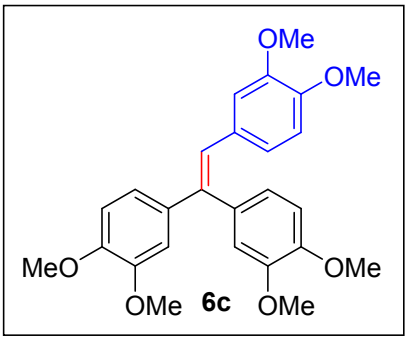
6a

4,4'-(2-(4-Chlorophenyl)ethene-1,1-diyl)bis(1,2-dimethoxybenzene) (6b). White solid (80 mg, 83%); mp: 148-150°C; R_f = 0.5 in 20% EtOAc in hexane; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.09 (d, *J* = 8.5 Hz, 2H), 6.95 (d, *J* = 8.5 Hz, 2H), 6.89 (d, *J* = 1.6 Hz, 1H), 6.86 (dd, *J* = 8.5, 1.8 Hz, 1H), 6.81 (t, *J* = 7.7 Hz, 2H), 6.78 (s, 1H), 6.73 (dd, *J* = 8.2, 1.7 Hz, 1H), 6.68 (d, *J* = 1.6 Hz, 1H), 3.90 (s, 3H), 3.88 (s, 3H), 3.83 (s, 3H), 3.70 (s, 3H); **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 149.0, 149.0, 148.7, 148.6, 142.9, 136.3, 136.2, 132.4, 132.0, 130.7, 130.7, 128.2, 128.2, 125.1, 123.0, 120.7, 113.5, 111.2, 110.8, 110.8, 56.0, 55.9, 55.9, 55.8; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{24}H_{24}ClO_4$ 411.1358, found 411.1358.

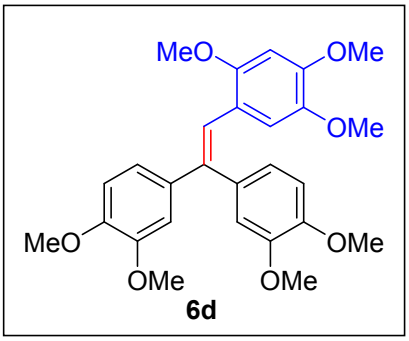


6b

4,4',4''-(Ethene-1,1,2-triyl)tris(1,2-dimethoxybenzene) (6c). White solid (92 mg, 90%); mp: 100-102 °C; R_f = 0.4 in 50% EtOAc in hexane; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.92 (d, *J* = 1.6 Hz, 1H), 6.86 (d, *J* = 8.2 Hz, 2H), 6.83 – 6.77 (m, 3H), 6.75 (d, *J* = 1.3 Hz, 1H), 6.73 – 6.66 (m, 2H), 6.53 (s, 1H), 3.90 (s, 3H), 3.88 (s, 3H), 3.84 (s, 3H), 3.83 (s, 3H), 3.73 (s, 3H), 3.53 (s, 3H); **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 149.2, 148.7, 148.7, 148.4, 148.1, 147.85, 140.36, 136.53, 133.2, 130.6, 126.2, 123.1, 122.8, 120.4, 113.6, 111.9, 111.4, 110.8, 110.7, 110.6, 56.0, 56.0, 56.0, 55.9, 55.8, 55.4; **HRMS** (ESI-QTOF) *m/z* $[M+Na]^+$ calcd for $C_{26}H_{28}NaO_6$ 459.1778, found 459.1765.



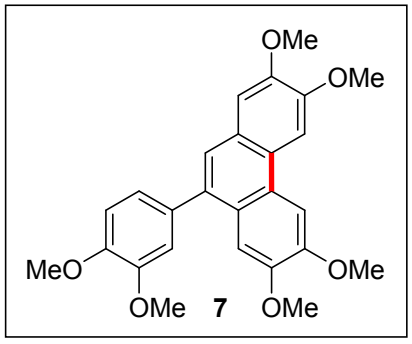
4,4'-(2-(2,4,5-Trimethoxyphenyl)ethene-1,1-diyl)bis(1,2-dimethoxybenzene) (6d). White solid (93 mg, 85%); mp: 106-108 °C; R_f = 0.3 in 50% EtOAc in hexane; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.01 (s, 1H), 6.91 (d, *J* = 1.7 Hz, 1H), 6.88 (dd, *J* = 8.3, 1.9 Hz, 1H), 6.79 (dt, *J* = 14.3, 7.1 Hz, 4H), 6.45 (s, 1H), 6.37 (s, 1H), 3.88 (s, 3H), 3.86 (s, 3H), 3.85 (s, 3H), 3.82 (s, 6H), 3.70 (s, 3H), 3.32 (s, 3H); **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 152.3, 149.0, 148.6, 148.5, 148.5, 148.2, 142.2, 140.3, 136.8, 133.5, 123.3, 120.7, 120.6, 118.4, 113.8, 113.1, 111.3, 110.9, 110.7, 96.9, 56.6, 56.0, 56.0, 55.9, 55.9, 55.9, 55.7; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{27}H_{31}O_7$ 467.2064, found 467.2078.



Synthesis of 7 and 8

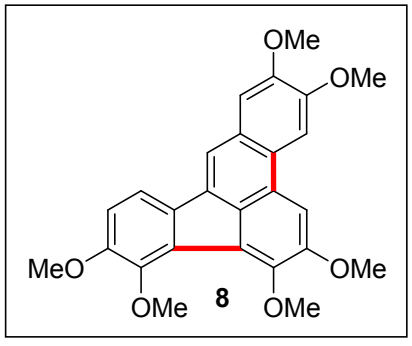
7 and **8** were synthesized by following the reported procedure (Zhai, L.; Shukla, R.; Rathore, R. *Org. Lett.* **2009**, *11*, 3474.). A solution of olefin **6c** (50 mg, 0.11 mmol, 1 equiv) in dichloromethane (10 mL) was added BF_3-Et_2O (~10 equiv) and DDQ (1 equiv) at 0 °C. The progress of the reaction was monitored by TLC. After completion of the reaction, it was quenched with a saturated aqueous solution of $NaHCO_3$ (20 mL). The dichloromethane layer was separated and washed with water and brine solution, dried over anhydrous $MgSO_4$, and filtered. Removal of the solvent in *vacuo* afforded the crude product which was purified by silica gel column chromatography (20 % EtOAc/Hexane) to afford **7**.

9-(3,4-Dimethoxyphenyl)-2,3,6,7-tetramethoxyphenanthrene (7). White solid (49 mg, 100%); mp: 186-188 °C; R_f = 0.3 in 50% EtOAc in hexane; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 19.8 Hz, 2H), 7.51 (s, 1H), 7.36 (s, 1H), 7.28 – 6.95 (m, 4H), 4.14 (s, 6H), 4.02 (s, 3H), 3.98 (s, 3H), 3.91 (s, 3H), 3.84 (s, 3H); **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 149.3, 149.1, 149.1, 148.7, 148.6, 148.3, 136.2, 134.1, 126.3, 125.5, 125.0, 125.0, 123.9, 122.2, 113.3, 111.2, 108.4, 107.1, 103.1, 102.8, 56.2, 56.2, 56.2, 56.1, 56.0, 55.8; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{26}H_{27}O_6$ 435.1802, found 435.1814.



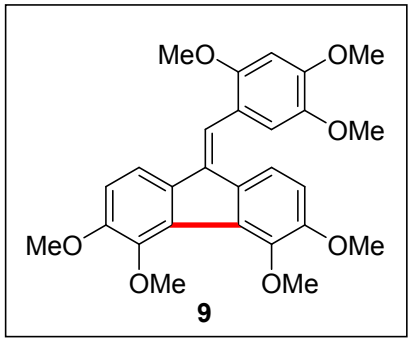
DDQ (3 equiv) was used for the synthesis of **8**.

1,2,5,6,11,12-Hexamethoxybenzo[*e*]acephenanthrylene (8). Yellow solid (46 mg, 92%); mp: 232-234 °C; R_f = 0.25 in 50% EtOAc in hexane; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.86 (s, 1H), 7.73 (s, 1H), 7.67 (s, 1H), 7.55 (s, 1H), 7.42 (s, 1H), 7.29 (s, 1H), 4.12 (s, 3H), 4.12 (s,



6H), 4.05 (s, 3H), 4.04 (s, 3H), 4.03 (s, 3H); **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 154.7, 149.3, 149.3, 149.1, 148.8, 145.1, 133.2, 132.3, 131.8, 128.9, 127.7, 127.2, 124.5, 123.3, 117.9, 109.9, 107.7, 104.8, 103.5, 102.4, 61.2, 56.6, 56.4, 56.3, 56.2, 55.9; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{26}H_{25}O_6$ 433.1646, found 433.1655.

3,4,5,6-Tetramethoxy-9-(2,4,5-trimethoxybenzylidene)-9*H*-fluorene (9). Yellow solid (45 mg, 90%); mp: 210-212 °C; R_f = 0.25 in 50% EtOAc in hexane; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.42 (s, 1H), 7.29 (d, *J* = 7.7 Hz, 2H), 7.23 (s, 1H), 7.08 (d, *J* = 4.5 Hz, 2H), 6.62 (s, 1H), 4.01 (s, 3H), 3.98 (s, 6H), 3.97 (s, 3H), 3.89 (s, 3H), 3.79 (s, 3H), 3.64 (s, 3H); **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 152.5, 150.1, 149.9, 148.2, 147.2, 142.7, 135.3, 135.2, 132.7, 132.4, 129.4, 120.6, 116.7, 114.5, 108.3, 104.1, 101.9, 97.3, 56.6, 56.6, 56.4, 56.3, 56.2, 56.2, 56.1; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{27}H_{29}O_7$ 465.1908, found 465.1899.

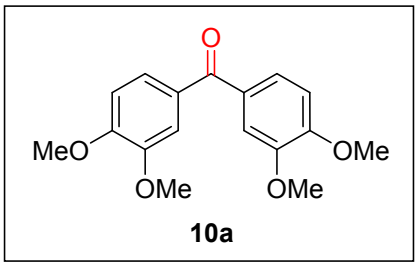


9

General Procedure for the Synthesis of Benzophenones (10)

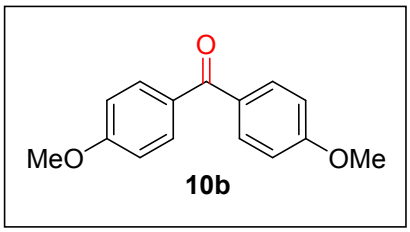
To a solution of diarylmethylphosphonate (100 mg) in THF (2 mL) was added potassium *tert*-butoxide (5 equiv) and the mixture was stirred under air at room temperature for 14 h. The reaction mixture was quenched with aqueous HCl (5N, 1 mL) and extracted with EtOAc (3 × 10 mL). The combined organic layer was washed with brine, dried over Mg_2SO_4, filtered, and concentrated *in vauo*. The crude product was purified by silica gel on column chromatography to obtain **10**.

Bis(3,4-dimethoxyphenyl)methanone (10a). White solid (66 mg, 92%); mp: 138-140 °C; R_f = 0.4 in 50% EtOAc in hexane; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.42 (d, *J* = 1.4 Hz, 1H), 7.37 (dd, *J* = 8.3, 1.7 Hz, 1H), 6.90 (d, *J* = 8.3 Hz, 1H), 3.95 (s, 6H), 3.93 (s, 6H); **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 194.6, 152.7, 149.0, 130.9, 124.9, 112.4, 109.8, 56.2, 56.2; **HRMS** (ESI-QTOF) *m/z* $[M+Na]^+$ calcd for $C_{17}H_{18}NaO_5$ 325.1046, found 325.1066.



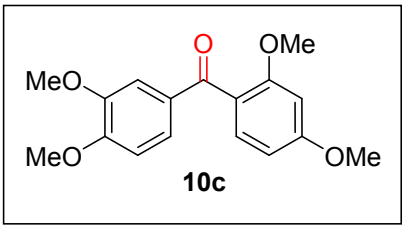
10a

Bis(4-methoxyphenyl)methanone (10b). White solid (59 mg, 90%); mp: 142-144 °C; R_f = 0.4 in 20% EtOAc in hexane; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.6 Hz, 4H), 6.96 (d, *J* = 8.6 Hz, 4H), 3.88 (s, 6H); **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 194.6, 162.9, 132.3, 130.8, 113.6, 55.6; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{15}H_{15}O_3$ 243.1016, found 243.1023.



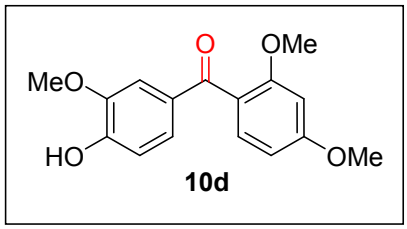
10b

(2,4-Dimethoxyphenyl)(3,4-dimethoxyphenyl)methanone (10c). White solid (63 mg, 88%); mp: 118-120°C; R_f = 0.4 in 50% EtOAc in hexane; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.43 (s, 1H), 7.38 (dd, *J* = 8.3, 1.5 Hz, 1H), 6.90 (d, *J* = 8.3 Hz, 1H), 6.78 (d, *J* = 8.2 Hz, 1H), 6.66 (s, 1H), 6.59 (d, *J* = 8.2 Hz, 1H), 3.96 (s, 3H), 3.94 (s, 3H), 3.85 (s, 3H), 3.76 (s, 3H); **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 194.6, 152.7, 148.9, 148.8, 147.5, 137.0, 130.9, 124.9, 121.4, 112.7, 112.4, 110.9, 109.8, 56.2, 56.1, 55.9, 55.9; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{17}H_{19}O_5$ 303.1227, found 303.1236.



10c

(2,4-Dimethoxyphenyl)(4-hydroxy-3-methoxyphenyl)methanone (10d). White solid (53 mg, 68%); mp: 120-122 °C; R_f = 0.3 in 50% EtOAc in hexane; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.53 (d, *J* = 1.6 Hz, 1H), 7.31 (d, *J* = 8.2 Hz, 1H), 7.23 (dd, *J* = 8.2, 1.7 Hz, 1H), 6.87 (d, *J* = 8.3 Hz, 1H), 6.53 (dd, *J* = 10.4, 1.9 Hz, 2H), 6.21 (s, 1H), 3.92 (s, 3H), 3.86 (s, 3H), 3.72 (s, 3H); **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 194.5, 162.9, 159.2, 150.3, 146.5, 131.5, 131.2, 126.3, 121.9, 113.6, 111.1, 104.4, 98.9, 56.2, 55.7, 55.6; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{16}H_{17}O_5$ 289.1071, found 289.1087.

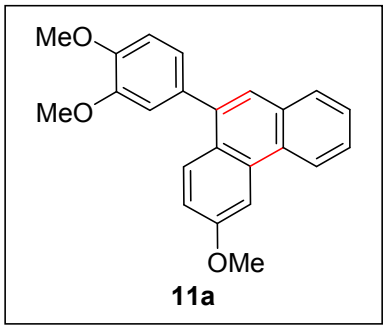


10d

General Procedure for the Synthesis of Phenanthrenes (11) via a Tandem SM-HWE Reaction

To a stirred solution of phosphonate **5g** (100 mg, 0.22 mmol, 1 equiv), (2-formylphenyl)boronic acid (48 mg, 0.32 mmol, 1.5 equiv), and potassium *tert*-butoxide (123 mg, 1.1 mmol, 5 equiv) in dioxane (4 mL) was added $PdCl_2$(dppf)-CH_2Cl_2 (9 mg, 0.0105 mmol, 0.05 equiv). The resultant mixture was degassed for 15 min and stirred at 100 °C under nitrogen atmosphere for 18 h. The reaction mixture was cooled and filtered through a pad of Celite. The filtrate was diluted with CH_2Cl_2 (30 mL) and washed with brine and water. The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure to give the crude product. Purification by flash chromatography on silica gel (hexanes:EtOAc, 9:1) afforded **11a**.

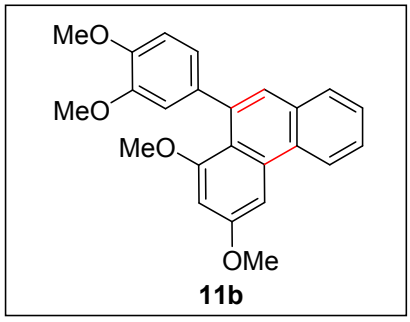
10-(3,4-Dimethoxyphenyl)-3-methoxyphenanthrene (11a). White solid (57 mg, 78%); mp: 117-119 °C; R_f = 0.2 in 10% EtOAc in hexane; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.64 (d, *J* = 7.8 Hz, 1H), 8.14 (d, *J* = 1.9 Hz, 1H), 7.89 (t, *J* = 7.3 Hz, 2H),



11a

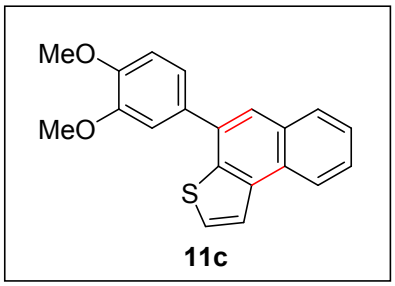
7.68 – 7.58 (m, 2H), 7.56 (s, 1H), 7.19 (dd, *J* = 9.0, 2.3 Hz, 1H), 7.06 (dt, *J* = 24.0, 8.1 Hz, 3H), 4.04 (s, 3H), 3.99 (s, 3H), 3.92 (s, 3H); **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 158.4, 148.8, 148.5, 138.5, 133.7, 132.3, 132.2, 129.4, 128.7, 128.6, 127.1, 126.2, 126.1, 125.2, 122.7, 122.3, 116.4, 113.4, 111.1, 104.4, 56.1, 56.1, 55.6; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{23}H_{21}O_3$ 345.1485, found 345.1495.

10-(3,4-Dimethoxyphenyl)-1,3-dimethoxyphenanthrene (11b). White solid (52 mg, 70%); mp: 131-133 °C; R_f = 0.2 in 10% EtOAc in hexane; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.59 (d, *J* = 7.7 Hz, 1H), 7.86 – 7.79 (m, 1H), 7.77 (d, *J* = 1.9 Hz, 1H), 7.60 (p, *J* = 7.0 Hz, 2H), 7.43 (s, 1H), 6.93 (dd, *J* = 14.3, 7.6 Hz, 3H), 6.64 (d, *J* = 1.9 Hz, 1H), 4.05 (s, 3H), 3.97 (s, 3H), 3.87 (s, 3H), 3.53 (s, 3H); **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 159.0, 158.6, 147.6, 147.3, 138.9, 136.8, 133.8, 132.0, 129.2, 128.5, 127.3, 127.2, 126.2, 123.1, 120.31, 117.3, 112.6, 109.9, 99.4, 96.5, 56.1, 56.0, 55.6, 55.6; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{24}H_{23}O_4$ 375.1591, found 375.1601.



11b

4-(3,4-Dimethoxyphenyl)naphtho[2,1-b]thiophene (11c). Colorless liquid (52 mg, 73%); R_f = 0.2 in 10% EtOAc in hexane; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.36 (d, *J* = 8.0 Hz, 1H), 8.08 (dd, *J* = 5.4, 1.4 Hz, 1H), 7.98 (d, *J* = 8.0 Hz, 1H), 7.74 (s, 1H), 7.65 – 7.52 (m, 3H), 7.38 (d, *J* = 10.1 Hz, 2H), 7.04 (dd, *J* = 8.0, 1.0 Hz, 1H), 3.98 (s, 6H); **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 149.2, 149.1, 137.8, 136.7, 134.9, 133.4, 131.9, 128.6,



11c

128.5, 126.4, 126.4, 125.8, 124.0, 123.7, 122.6, 120.8, 111.7, 111.5, 56.1, 56.1; **HRMS** (ESI-QTOF) *m/z* $[M+Na]^+$ calcd for $C_{20}H_{16}NaO_2S$ 343.0763, found 343.0771.

Supporting Information

The Supporting Information is available free of charge on the ACS Publication website at DOI:

^1H and ^{13}C NMR spectra of the synthesized compounds.

Notes

The authors declare no competing financial interest.

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References

[1] Singh, D. K.; Prasad, S. S.; Kim, J.; Kim, I. One-pot, Three-component Approach to Diarylacetonitriles. *Org. Chem. Front.* **2019**, *6*, 669-673.

[2] Suzuki, T.; Moriya, M.; Sakamoto, T.; Suga, T.; Kishino, H.; Takahashi, H.; Ishikawa, M.; Nagai, K.; Imai, Y.; Sekino, E.; Ito, M.; Iwaasa, H.; Ishihara, A.; Tokita, S.; Kanatani, A.; Sato, N.; Fukami, T. Discovery of Novel Spiro-piperidine Derivatives as Highly Potent and Selective Melanin-concentrating Hormone 1 Receptor Antagonists. *Bioorg. Med. Chem. Lett.* **2009**, *19*, 3072-3077.

[3] (a) Palchaudhuri, R.; Nesterenko, V.; Hergenrother, P. J. The Complex Role of the Triphenylmethyl Motif in Anticancer Compounds. *J. Am. Chem. Soc.* **2008**, *130*, 10274-10281. (b) Montel, S.; Raffier, L.; He, Y.; Walsh, P. J. Palladium-Catalyzed α-Arylation of Benzylic Phosphonates. *Org. Lett.* **2014**, *16*, 1446-1449. (c) Huang, H.; Kang, J. Y. Organocatalytic Phosphonylation of in Situ Formed o-Quinone Methides. *Org. Lett.* **2017**, *19*, 5988-5991. (d) Chen, L.; Fang, X.-Y.; Zou, Y.-X. A Highly Efficient Nucleophilic Substitution Reaction Between $R_2P(O)H$ and Triarylmethanols to Synthesize Phosphorus-substituted Triarylmethanes. *Org. Biomol. Chem.* **2018**, *16*, 951-956. (e) Fathalla, W.; Pazdera, P.; El-Rayes, S.; Ali, I. A. I. Efficient Synthesis of α-Substituted-α-arylmethyl Phosphonates Using Trichloroacetimidate C-C Coupling Method. *Tetrahedron* **2018**, *74*, 1681-1691. (f) Matsude, A.; Hirano, K.; Miura, M. Palladium-Catalyzed Benzylic Phosphorylation of Diarylmethyl Carbonates. *Org. Lett.* **2018**, *20*, 3553-3556. (g) Yang, B.; Yao, W.; Xia, X.-F.; Wang, D. Mn-Catalyzed 1,6-Conjugate Addition/Aromatization of para-Quinone Methides. *Org. Biomol. Chem.* **2018**, *16*, 4547-4557.

[4] (a) Wadsworth, W. S., Jr.; Emmons, W. D. The Utility of Phosphonate Carbanions in Olefin Synthesis. *J. Am. Chem. Soc.* **1961**, *83*, 1733-1738. (b) Engel, R. Phosphonates as Analogues of Natural Phosphates. *Chem. Rev.* **1977**, *77*, 349-367. (c) Schwender, C. F.; Beers, S. A.; Malloy, E. A.; Cinicola, J. J.;Wustrow, D. J.; Demarest, K. D.; Jordan, J. Benzylphosphonic Acid Inhibitors of Human Prostatic Acid Phosphatase. *Bioorg. Med. Chem. Lett.* **1996**, *6*, 311-314. (d) Moonen, K.; Laureyn, I.; Stevens, C. V. Synthetic Methods for Azaheterocyclic Phosphonates and Their Biological Activity. *Chem. Rev.* **2004**, *104*, 6177-6216. (e) Cattani-Scholz, A. Functional Organophosphonate Interfaces for Nanotechnology: A Review. *ACS Appl. Mater. Interfaces* **2017**, *9*, 25643-25655.

[5] When diethyl phosphite was used instead of triethyl phosphite, **5a** was obtained in 81% yield.

[6] See the Experimental Section for details.

[7] Even resubjection of the isolated compounds (**4a'-1** and **4a'-2**) to 1,3-dimethoxybenzene (1.2 equiv) and BF_3-OEt_2 (1 equiv) in DCE at 80 °C for prolonged time did not give the desired products. Further optimization for unreactive aldehydes is required.

[8] (a) Khalid Baig, M. Z.; Sahu, P. K.; Sarkar, M.; Chakravarty, M. Haloarene-Linked Unsymmetrically Substituted Triarylethenes: Small AIEgens To Detect Nitroaromatics and Volatile Organic Compounds. *J. Org. Chem.* **2017**, *82*, 13359-13367. (b) Li, J.; Huang, W.; Chen, J.; He, L.; Cheng, X.; Li, G. Electrochemical Aziridination by Alkene Activation Using a Sulfamate as the Nitrogen Source. *Angew. Chem., Int. Ed.* **2018**, *57*, 5695-5698.

[9] (a) Miller, R. B.; Al-Hassan, M. I. Stereospecific Synthesis of (Z)-Tamoxifen via Carbometallation of Alkynylsilanes. *J. Org. Chem.* **1985**, *50*, 2121-2123. (b) Stüdemann, T.;

Knochel, P. New Nickel-Catalyzed Carbozincation of Alkynes: A Short Synthesis of (Z)-Tamoxifen. *Angew. Chem., Int. Ed.* **1997**, *36*, 93-95. (c) Zhou, C.; Larock, R. C. Regio- and Stereoselective Route to Tetrasubstituted Olefins by the Palladium-Catalyzed Three-Component Coupling of Aryl Iodides, Internal Alkynes, and Arylboronic Acids. *J. Org. Chem.* **2005**, *70*, 3765-3777. (d) Shimizu, M.; Nakamaki, C.; Shimono, K.; Schelper, M.; Kurahashi, T.; Hiyama, T. Stereoselective Cross-Coupling Reaction of 1,1-Diboryl-1-alkenes with Electrophiles: A Highly Stereocontrolled Approach to 1,1,2-Triaryl-1-alkenes. *J. Am. Chem. Soc.* **2005**, *127*, 12506-12507.

[10] (a) Wiseman, H. *Tamoxifen: Molecular Basis of Use in Cancer Treatment and Prevention*; Wiley: Chichester, U.K., 1994. (b) Jordan, V. C. Antiestrogens and Selective Estrogen Receptor Modulators as Multifunctional Medicines. 2. Clinical Considerations and New Agents. *J. Med. Chem.* **2003**, *46*, 1081-1111. (c) Itami, K.; Ohashi, Y.; Yoshida, J.-i. Triarylethene-Based Extended π-Systems: Programmable Synthesis and Photophysical Properties. *J. Org. Chem.* **2005**, *70*, 2778-2792.

[11] (a) Harvey, R. G. *Polycyclic Aromatic Hydrocarbons*; Wiley-VCH: New York, 1997. (b) Ito, H.; Ozaki, K.; Itami, K. Annulative π-Extension (APEX): Rapid Access to Fused Arenes, Heteroarenes, and Nanographenes. *Angew. Chem., Int. Ed.* **2017**, *56*, 11144-11164. (c) Ito, H.; Segawa, Y.; Murakami, K.; Itami, K. Polycyclic Arene Synthesis by Annulative π-Extension. *J. Am. Chem. Soc.* **2019**, *141*, 3-10.

[12] For our work on polyaromatic compounds, see: (a) Park, S.; Kwon D. I.; Lee, J.; Kim, I. When Indolizine Meets Quinoline: Diversity-Oriented Synthesis of New Polyheterocycles and Their Optical Properties. *ACS Comb. Sci.* **2015**, *17*, 459-469. (b) Jung, Y.; Kim, I.

Deformylative Intramolecular Hydroarylation: Synthesis of Benzo[e]pyrido[1,2-a]indoles. *Org. Lett.* **2015**, *17*, 4600-4603. (c) Jung, Y.; Kim, I. Synthesis of 6-Aryl-5-iodobenzo[e]pyrido[1,2-a]indoles by 6-endo-dig Iodocyclization. *Asian J. Org. Chem.* **2016**, *5*, 147-152. (d) Nayak, M.; Singh, D. K.; Kim, I. Polyaromatic Heterocycles through Intramolecular Alkyne Carbonyl Metathesis: 5-Acylnaphtho[2,1-b]benzofurans. *Tetrahedron* **2017**, *73*, 1831-1840. (e) Nayak, M.; Singh, D. K.; Kim, I. Regiospecific Synthesis of 5- and 6-Acylated Naphtho[1,2-b]benzofurans via Intramolecular Alkyne Carbonyl Metathesis. *Synthesis* **2017**, *49*, 2063-2073.

[13] For reviews, see: (a) Watson, M. D.; Fechtenkötter, A.; Müllen, K. Big Is Beautiful−"Aromaticity" Revisited from the Viewpoint of Macromolecular and Supramolecular Benzene Chemistry. *Chem. Rev.* **2001**, *101*, 1267-1300. (b) King, B. T.; Kroulik, J.; Robertson, C. R.; Rempala, P.; Hilton, C. L.; Korinek, J. D.; Gortari, L. M. Controlling the Scholl Reaction. *J. Org. Chem.* **2007**, *72*, 2279-2288. (c) Grzybowski, M.; Skonieczny, K.; Butenschön, H.; Gryko, D. T. Comparison of Oxidative Aromatic Coupling and the Scholl Reaction. *Angew. Chem., Int. Ed.* **2013**, *52*, 9900-9930. (d) Li, C.; Yang, Y.; Miao, Q. Recent Progress in Chemistry of Multiple Helicenes. *Chem. Asian J.* **2018**, *13*, 884-894.

[14] (a) Churruca, F.; SanMartin, R.; Tellitu, I.; Domínguez, E. A New, Expeditious Entry to the Benzophenanthrofuran Framework by a Pd-Catalyzed C- and O-Arylation/PIFA-Mediated Oxidative Coupling Sequence. *Eur. J. Org. Chem.* **2005**, 2481-2490. (b) Zhai, L.; Shukla, R.; Rathore, R. Oxidative C−C Bond Formation (Scholl Reaction) with DDQ as an Efficient and Easily Recyclable Oxidant. *Org. Lett.* **2009**, *11*, 3474-3477. (c) Fujimoto, S.; Matsumoto, K.;

Shindo, M. Aerobic Oxidative Intramolecular Aromatic Coupling via Heterogeneous Metal Catalysts. *Adv. Synth. Catal.* **2016**, *358*, 3057-3061. (d) Matsushima, T.; Kobayashi, S.; Watanabe, S. Air-Driven Potassium Iodide-Mediated Oxidative Photocyclization of Stilbene Derivatives. *J. Org. Chem.* **2016**, *81*, 7799-7806. (e) Ye, Q.; Zhang, Z.; Png, Z. M.; Neo, W. T.; Lin, T.; Zeng, H.; Xu, H.; Xu, J. Cyclization of Tetraaryl-Substituted Benzoquinones and Hydroquinones through the Scholl Reaction. *J. Org. Chem.* **2016**, *81*, 9219-9226. (f) Ip, H.-W.; Ng, C.-F.; Chow, H.-F.; Kuck, D. Three-Fold Scholl-Type Cycloheptatriene Ring Formation around a Tribenzotriquinacene Core: Toward Warped Graphenes. *J. Am. Chem. Soc.* **2016**, *138*, 13778-13781. (g) Kawamura, M.; Tsurumaki, E.; Toyota, S. Facile Synthesis of Rubicenes by Scholl Reaction. *Synthesis* **2018**, *50*, 134-138. (h) Gupta, V.; Pandey, S. K.; Singh, R. P. Facile Synthesis of Triphenylenes and Triphenylene/Phenanthrene Fused Heteroaromatics. *Org. Biomol. Chem.* **2018**, *16*, 7134-7138.

[15] (a) Khalid, M. B. Z.; Pallikonda, G.; Tulichala, R. N. P.; Chakravarty, M. Oxy-Wittig Reactions of 1-Naphthyl(aryl)methylphosphonates: a New Approach to Naphthylarylketones. *Tetrahedron* **2016**, *72*, 2094-2101. (b) Huang, T.; Chen, T.; Han, L.-B. Oxidative Dephosphorylation of Benzylic Phosphonates with Dioxygen Generating Symmetrical trans-Stilbenes. *J. Org. Chem.* **2018**, *83*, 2959-2965.

[16] (a) Floyd, A. J.; Dyke, S. F.; Ward, S. E. The Synthesis of Phenanthrenes. *Chem. Rev.* **1976**, *76*, 509-562. (b) Jana, R.; Biswas, A.; Samanta, S.; Ray, J. K. Synthesis of Phenanthrene and Alkyl Phenanthrenes by Palladium(0)-Catalyzed Pericyclic Reactions. *Synthesis* **2010**, 2092-2100. (c) Kondoh, A.; Aoki, T.; Terada, M. Synthesis of Phenanthrene Derivatives by Intramolecular Cyclization Utilizing the [1,2]-Phospha-Brook Rearrangement Catalyzed by a

Brønsted Base. *Chem. Eur. J.* **2015**, *21*, 12577-12580. (d) Nagata, T.; Satoh, T.; Nishii, Y.; Miura, M. Rhodium-Catalyzed Oxidative Annulation of (2-Arylphenyl)boronic Acids with Alkynes: Selective Synthesis of Phenanthrene Derivatives. *Synlett* **2016**, *27*, 1707-1710. (e) Fujita, T.; Takahashi, I.; Hayashi, M.; Wang, J.; Fuchibe, K.; Ichikawa, J. Facile Synthesis of Polycyclic Aromatic Hydrocarbons: Brønsted Acid Catalyzed Dehydrative Cycloaromatization of Carbonyl Compounds in 1,1,1,3,3,3-Hexafluoropropan-2-ol. *Eur. J. Org. Chem.* **2017**, 262-265.

[17] For synthesis of phenanthrenes via Suzuki-Miyaura coupling/aldol condensation cascade reaction, see: Kim, Y. H.; Lee, H.; Kim, Y. J.; Kim, B. T.; Heo, J.-N. Direct One-Pot Synthesis of Phenanthrenes via Suzuki−Miyaura Coupling/Aldol Condensation Cascade Reaction. *J. Org. Chem.* **2008**, *73*, 495-501.