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Abstract

The examination of the palladium catalysed arylation reactions of mono-iodo derivatives of the phenyl and benzyl esters of benzoic acid, phenylacetic acid and dehydrocinnamic acid has resulted in the formation of benzo[c]chromen-6-ones, unexpected cinnamate and succinate products and diphenyl dimers. Many of these products can be rationalized as arising from novel cyclic ArPd(II)-enolate intermediates, formed by intramolecular C-H activation by ArPd(II).

Keywords

Synthesis, benzo, chromen, ones, via, novel, cyclic, aryl, ester, enolate, intermediates, CMMB

Disciplines

Life Sciences | Physical Sciences and Mathematics | Social and Behavioral Sciences

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Synthesis of benzo[c]chromen-6-ones via novel cyclic aryl-Pd(II)-ester enolate intermediates

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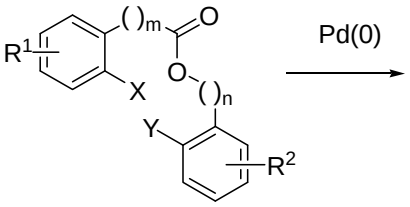
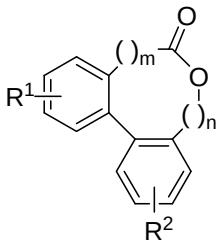
Abstract: The examination of the palladium catalysed arylation reactions of mono-iodo derivatives of the phenyl and benzyl esters of benzoic acid, phenylacetic acid and dehydrocinnamic acid has resulted in the formation of benzo[c]chromen-6-ones, unexpected cinnamate and succinate products and diphenyl dimers. Many of these products can be rationalized as arising from novel cyclic ArPd(II)-enolate intermediates, formed by intramolecular C-H activation by ArPd(II).

As part of a project concerned with the synthesis of lactones of the type **C** we have explored the palladium catalysed arylation reactions of mono-iodo di-aryl esters **A** and **B** as shown in Scheme 1. The formation of benzo[c]chromen-6-ones **C** (m = n = 0) have been readily achieved from palladium catalysed cyclization of the corresponding mono-iodophenyl benzoate derivative using this strategy.[1,2] In the successful cases reported the iodo-substituent is normally attached to the more electron deficient benzoate ring as in the case of **A** (m = n = 0). The formation of larger lactone rings have not been reported, however the palladium catalysed arylation reaction has been used to form 7-membered carbocyclic and azepine rings.[2c,3] We report here our results from the examination of the palladium catalysed arylation reactions of mono-iodo derivatives of the phenyl and benzyl esters of benzoic acid, phenylacetic acid and dehydrocinnamic acid.

Scheme 1



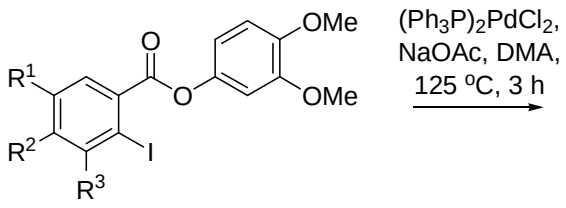
A, X = I, Y = H
B, X =H, Y = I



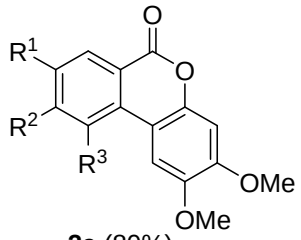
C

Treatment of the iodo-substituted phenyl benzoate derivatives **1a-c** with 26 mol % $(Ph_3P)_2PdCl_2$ in the presence of anhydrous sodium acetate (3 molar equiv.) in DMA with heating in a sealed tube at 125 ^oC for 3 h gave the benzo[c]chromen-6-ones **2a-c** in good yields (Scheme 2). In the case of **1c**, a small amount (8%) of the regioisomer **3** was also formed.

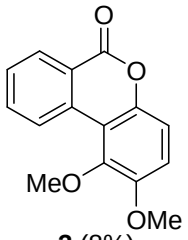
Scheme 2



1a-c



2a (80%)
2b (85%)
2c (71%)

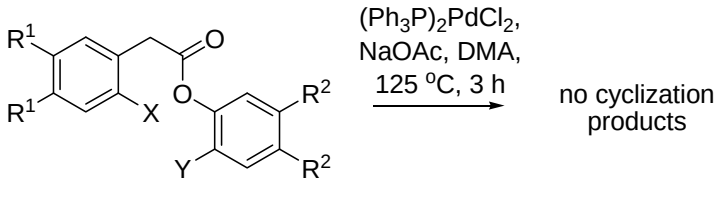


3 (8%)

a; R^1 = OMe, R^2 = OMe, R^3 = H
b; R^1 = OMe, R^2 = OMe, R^3 = OMe
c; R^1 = H, R^2 = H, R^3 = H

When the 2-iodophenyl phenyl acetates **4a-c** were treated under identical conditions to **1a-c** only products arising from hydrolysis of the ester group of **4a-c** were obtained, even though the NaOAc and DMA had been carefully dried.

Scheme 3



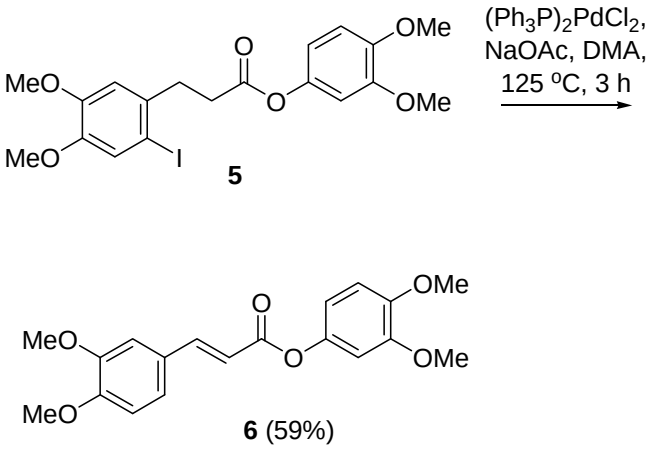
4

a; R^1 = OMe, R^2 = OMe, X = I, Y = H
b; R^1 = OMe, R^2 = H, X = H, Y = I
c; R^1 = H, R^2 = OMe, X = I, Y = H

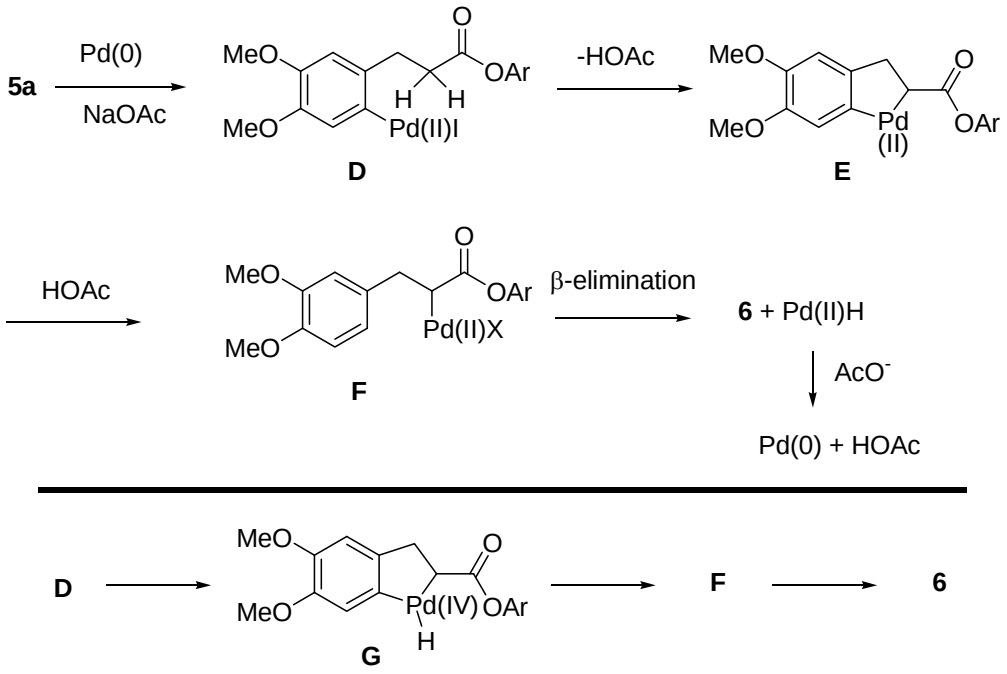
Treatment of the phenyl dihydrocinnamate **5** under these conditions resulted in formation of its cinnamate ester derivative **6** in 59% yield (Scheme 4). A possible mechanism is shown in Scheme 5.

This mechanism involves oxidative addition of the aryl iodide to Pd(0), to give the Pd(II)-intermediate **D** from which base (NaOAc) assisted cyclometallation occurs, via C-H functionalization, to give the palladacycle **E**. Intermediate **E** can undergo selective protonation to give the Pd(II)-enolate species **F** which upon β-elimination would give the cinnamate **6** and Pd(II)H. The latter species upon reaction with acetate ion would generate Pd(0) and acetic acid. The functionalization of sp^3C-H and sp^2C-H bonds by Pd(II), as in the case of the conversion of intermediate **D** to **E**, have been well documented[4] and palladium(IV) species have been suggested as intermediates in some of these reactions.[4b,h,k,p,q] Indeed oxidative addition of intermediate **D** could provide the palladium(IV) intermediate **G** which upon reductive elimination would result in intermediate **F** and thus product **6** (Scheme 5).

Scheme 4



Scheme 5 (palladium ligands not shown)



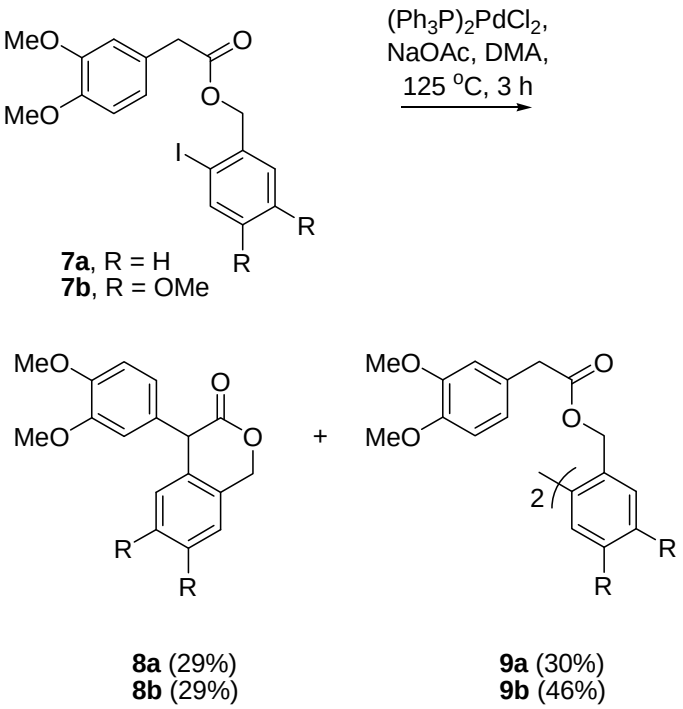
The palladium catalysed reactions of the 2-iodobenzyl 3,4-dimethoxyphenyl acetates **7a**,**b** gave a mixture of two products which consisted of the benzo[c]chromen-6-ones **8a** and **8b**, respectively and the biphenyls **9a** and **9b**, respectively (Scheme 6). These compounds were readily separated by column chromatography. The 3,4-dimethoxybenzyl 2-iodophenyl acetates **10a**,**b** gave different products. Iodide **10a** gave a separable mixture of the succinate **11** (as a 1.8 : 1 mixture of diastereomers) and the biphenyl **12**, while **10b** gave the benzo[c]chromen-6-one **8b** (Scheme 7). These unexpected products can be rationalized as arising through similar palladium intermediates to those suggested in Scheme 5. In Scheme 8, the Pd(II)-palladacycle intermediate **I** is formed from **7a,b** in an analogous fashion to **E** in Scheme 5. Reductive elimination of **I** would provide the benzo[c]chromen-6-ones **8a** or **8b**. Alternatively, dimerization of intermediate **H** would give the diphenyls **9a** or **9b**.

In Scheme 9, the Ar-Pd(II)I intermediate **J** could undergo deprotonation by NaOAc, perhaps assisted by coordination between the Pd(II) and the ester carbonyl, to give the Pd(II)-palladacycle **K** which could undergo selective protonation by HOAc to give the *O*-Pd(II)-enolate **L**. The latter would be

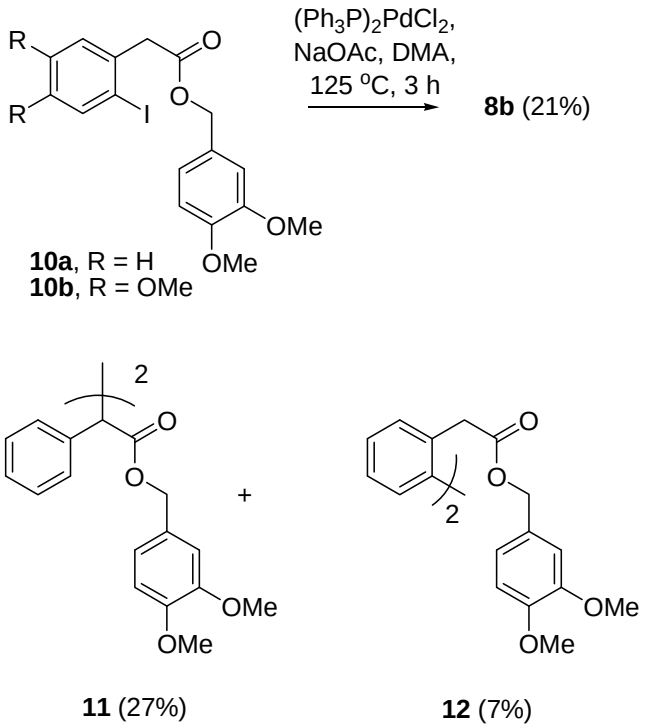
expected to be in equilibrium with the *C*-Pd(II)-enolate **M**[5] which could give rise to the same cyclic Pd(II)-enolate intermediate **I** suggested in Scheme 8 and then product **8b** via reductive elimination. Alternatively, dimerization of intermediate **M** could provide the succinate **11**. The proposed Pd(II)-palladacycle **K** is similar to that proposed as an intermediate in the Pd-catalysed intramolecular coupling ortho-bromophenylmethyl ketones to give benzofurans under basic conditions.[5] However no benzofuran products could be isolated from our reactons. We assume that because our reactions generate an equivalent of HOAc, from the transformation of intermediate **J** to **K**, that protonation of **K** to give **L** is more rapid than benzofuran formation.[6]

In conclusion, the examination of the palladium catalysed arylation reactions of mono-iodo derivatives of the phenyl and benzyl esters of benzoic acid, phenylacetic acid and dehydrocinnamic acid has resulted in the formation of benzo[c]chromen-6-ones **2a-c** and **8a,b**, the unexpected cinnamate **6** and the succinate **11** and diphenyl dimers (**9a,b** and **12**). Many of these products can be rationalized as arising from novel cyclic ArPd(II)-enolate intermediates (**E** and **I**). While the formation of ArPd(II)-enolate intermediates is well documented, these are normally generated from the intermolecular reaction of an *in situ* generated or preformed enolate anion, using a stronger base than NaOAc as in this study, and a ArPd(II)X species[7] and not by intramolecular C-H activation by ArPd(II) as we have suggested in this paper.

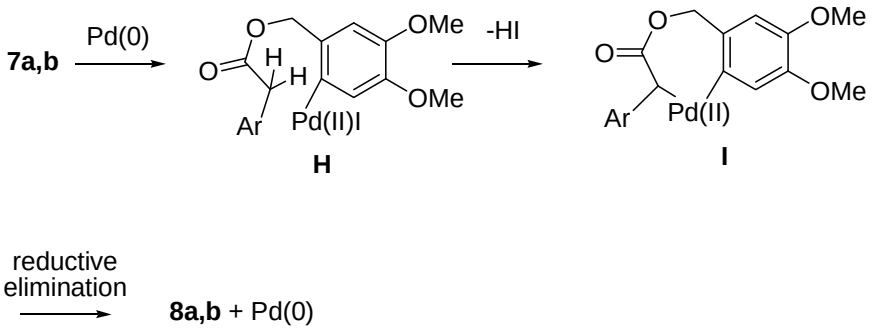
Scheme 6


(Ph3P)2PdCl2,
NaOAc, DMA,
125 °C, 3 h
MeO
MeO
O
O
I
R
R
7a, R = H
7b, R = OMe
MeO
MeO
O
O
+
MeO
MeO
O
O
2
R
R
R
R
8a (29%)
8b (29%)
9a (30%)
9b (46%)

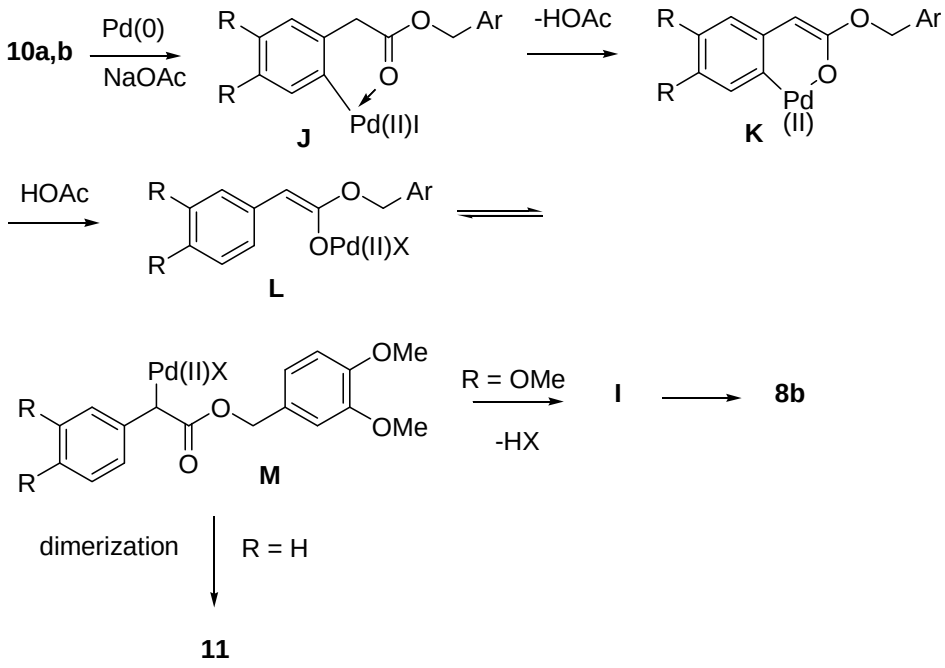
Scheme 7


(Ph3P)2PdCl2,
NaOAc, DMA,
125 °C, 3 h
8b (21%)
R
R
I
O
O
OMe
OMe
10a, R = H
10b, R = OMe
2
O
O
+
OMe
OMe
O
O
2
OMe
OMe
11 (27%)
12 (7%)

Scheme 8 (palladium ligands not shown)



Scheme 9 (palladium ligands not shown)



EXPERIMENTAL

All NMR spectra were measured in $CDCl_3$ solution at 300 MHz (^{1}H NMR) or 75 MHz (^{13}C NMR) unless otherwise indicated. NMR assignments are based on COSY, DEPT, and HSQC experiments and sometimes HMBC and NOESY experiments. DCM refers to CH_2Cl_2 and PS refers to petroleum spirit (b.p. 40-60 ^oC)

General Methods for Ester Formation

3,4-Dimethoxyphenyl 2-iodo-4,5-dimethoxybenzoate 1a

A solution of 2-iodo-4,5-dimethoxybenzoic acid (613 mg, 1.99 mmol), 3,4-dimethoxyphenol (368 mg, 2.39 mmol) and DCC (493 mg, 2.39 mmol), DMAP (73 mg, 0.59 mmol) in DCM (20 mL) was stirred at rt for 18 h under N_2, diluted with DCM (20 mL), filtered and the filtrate washed with water (20 mL) and saturated $NaHCO_3$ solution (20 mL). The organic phase was dried ($MgSO_4$), filtered, evaporated and the residue chromatographed, using EtOAc:PS (1:1) as the mobile phase, to yield the title compound as a white solid (671 mg, 76 %). M.p. 146-148 ^oC ^{1}H NMR: δ 7.64 (s, 1H, Ar-H-6), 7.45 (s, 1H, Ar-H-3), 6.89 (d, 1H, *J* = 8.0 Hz, Ar-H-5'), 6.79 (d, 1H, *J* = 2.2 Hz, Ar-H-2'), 6.78 (dd, 1H, *J* = 8.0, 2.2 Hz, Ar-H-6'), 3.95 (s, 3H, OCH$_3$-4), 3.94 (s, 3H, OCH$_3$-5), 3.89 (s, 3H, OCH$_3$-4'), 3.88 (s, 3H, OCH$_3$-3'). ^{13}C NMR: δ 164.0 (C=O), 152.2 (Ar-C-OCH$_3$-4), 149.3 (Ar-C-OCH$_3$-3'), 148.6 (Ar-C-OCH$_3$-5), 146.8 (Ar-C-OCH$_3$-4'), 144.2 (Ar-C-1'), 124.8 (Ar-C-1), 123.9 (Ar-C-H-3), 114.1 (Ar-C-H-6), 112.9 (Ar-C-H-6'), 111.1 (Ar-C-H-5'), 105.8 (Ar-C-H-2'), 85.5 (Ar-C-2), 56.2 (Ar-OCH$_3$-4), 56.1 (Ar-OCH$_3$-4'), 56.0 (Ar-OCH$_3$-5), 55.9 (Ar-OCH$_3$-3'). MS (EI+): *m/z* 444 (M^+, 8 %), 291 (100 %), HRMS (EI+): Calcd for $C_{17}H_{17}IO_6$ = 444.0069 (M^+), found 444.0053.

3,4-Dimethoxyphenyl 2-iodo-3,4,5-trimethoxybenzoate 1b

The title compound was prepared in 91 % yield (white solid, 483 mg) from 2-iodo-3,4,5-trimethoxybenzoic acid (379 mg, 1.12 mmol) and 3,4-dimethoxyphenol (207 mg, 1.34 mmol) in the presence of DCC (277 mg, 1.34 mmol), DMAP (34 mg, 0.28 mmol) and DCM (10 mL) according to the general esterification method. M.p. 98-100 ^oC. ^{1}H NMR: δ 7.39 (s, 1H, Ar-H-6), 6.90 (dd, 1H, *J* = 7.3, 2.4 Hz Ar-H-6'), 6.84 (d, 1H, *J* = 2.4 Hz Ar-H-2'), 6.82 (d, 1H, *J* = 7.3 Hz Ar-H-5'), 3.95 (s, 3H, OCH$_3$-5), 3.93 (s, 3H, OCH$_3$-4), 3.91 (s, 3H, OCH$_3$-3), 3.90 (s, 3H, OCH$_3$-3'), 3.89 (s, 3H, OCH$_3$-4'). ^{13}C NMR: δ 165.1 (C=O), 153.9 (Ar-C-OCH$_3$-3), 153.4 (Ar-C-OCH$_3$-4), 149.4 (Ar-C-OCH$_3$-4'), 147.0 (Ar-C-OCH$_3$-3'), 145.3 (Ar-C-OCH$_3$-5), 144.2 (Ar-C-1'), 129.9 (Ar-C-1), 112.8 (Ar-C-H-5'), 111.1 (Ar-C-H-6), 110.9 (Ar-C-H-6'), 105.6 (Ar-C-H-2'), 84.5 (Ar-C-2), 61.0 (OCH$_3$-5), 60.8 (OCH$_3$-3'),

56.3 (O<u>C</u>H$_3$-4), 56.1 (O<u>C</u>H$_3$-3), 55.9 (O<u>C</u>H$_3$-4'). MS: *m/z* (EI$^+$) 474 (M$^+$, 6 %), 321 (100 %) HRMS (EI$^+$): Calcd for $C_{18}H_{19}IO_7$ = 474.0175 (M$^+$), found 474.0152.

3,4-Dimethoxyphenyl 2-iodobenzoate 1c

The title compound was prepared in 93 % yield (white solid, 1.15 g) from 2-iodobenzoic acid (800 mg, 3.22 mmol) and 3,4-dimethoxyphenol (547 mg, 3.54 mmol) in the presence of DCC (732 mg, 3.54 mmol), DMAP (130 mg, 1.06 mmol) and DCM (15 mL) according to the general esterification method. M.p. 74-76 ^{o}C. ^{1}H NMR: δ 8.06 (d, 1H, *J* = 8.0 Hz, Ar-<u>H</u>-3), 8.02 (dd, 1H, *J* = 8.0, 1.5 Hz, Ar-<u>H</u>-6), 7.47 (t, 1H, *J* = 8.0 Hz, Ar-<u>H</u>-5), 7.21 (dt, 1H, *J* = 8.0, 1.5 Hz, Ar-<u>H</u>-4), 6.99 (d, 1H, *J* = 8.0 Hz, Ar-<u>H</u>-5'), 6.81 (dd, 1H, *J* = 8.0, 2.5 Hz, Ar-<u>H</u>-6'), 6.80 (d, 1H, *J* = 2.5 Hz, Ar-<u>H</u>-2'), 3.89 (s, 3H, OC<u>H</u>$_3$-3'), 3.88 (s, 3H, OC<u>H</u>$_3$-4'). ^{13}C NMR: δ 165.0 (<u>C</u>=O), 149.3 (Ar-<u>C</u>-OCH$_3$-4), 147.0 (Ar-<u>C</u>-OCH$_3$-3), 144.2 (Ar-<u>C</u>-1'), 141.5 (Ar-<u>C</u>-H-3), 134.1 (Ar-<u>C</u>-1), 133.1 (Ar-<u>C</u>-H-4), 131.4 (Ar-<u>C</u>-H-6), 127.9 (Ar-<u>C</u>-H-5), 112.8 (Ar-<u>C</u>-H-6'), 111.1 (Ar-<u>C</u>-H-5'), 105.6 (Ar-<u>C</u>-H-2'), 94.5 (Ar-<u>C</u>-2), 56.1 (Ar-O<u>C</u>H$_3$-4'), 55.9 (Ar-O<u>C</u>H$_3$-3'). MS: *m/z* (EI$^+$) 384 (M$^+$, 6 %), 125 (100 %), HRMS (EI$^+$): Calcd for $C_{15}H_{13}IO_4$ = 383.9858 (M$^+$), found 383.9862.

3,4-Dimethoxyphenyl 2-iodo-4,5-dimethoxyphenylacetate 4a

The title compound was prepared in 76 % yield (sticky white solid, 740 mg) from 2-iodo-4,5-dimethoxyphenylacetic acid (686 mg, 2.12 mmol) and 3,4-dimethoxyphenol (361 mg, 2.34 mmol) in the presence of DCC (483 mg, 2.34 mmol), DMAP (73 mg, 0.59 mmol) and DCM (10 mL) according to esterification method. M.p. 76-78 ^{o}C. ^{1}H NMR: δ 7.27 (s, 1H, Ar-<u>H</u>-3), 6.90 (s, 1H, Ar-<u>H</u>-6), 6.82 (s, 1H, Ar-<u>H</u>-5'), 6.69 (s, 1H, Ar-<u>H</u>-2'), 6.68 (s, 1H, Ar-<u>H</u>-6'), 3.95 (s, 2H, Ar-C<u>H</u>$_2$), 3.876 (s, 3H, OC<u>H</u>$_3$-3), 3.870 (s, 3H, OC<u>H</u>$_3$-5), 3.86 (s, 3H, OC<u>H</u>$_3$-4'), 3.85 (s, 3H, OC<u>H</u>$_3$-4). ^{13}C NMR: δ 169.5 (<u>C</u>=O), 149.4 (Ar-<u>C</u>-OCH$_3$-4), 149.3 (Ar-<u>C</u>-OCH$_3$-3'), 148.8 (Ar-<u>C</u>-OCH$_3$-3), 146.9 (Ar-<u>C</u>-OCH$_3$-4'), 144.3 (Ar-<u>C</u>-1'), 129.5 (Ar-<u>C</u>-1), 121.6 (Ar-<u>C</u>-H-3), 113.4 (Ar-<u>C</u>-H-6), 112.7 (Ar-<u>C</u>-H-6'), 111.1 (Ar-<u>C</u>-H-5'), 105.6 (Ar-<u>C</u>-H-2'), 88.9 (Ar-<u>C</u>-2), 56.1 (2 x O<u>C</u>H$_3$-3, 5), 55.9 (2 x O<u>C</u>H$_3$-4, 4'), 45.7 (Ar-<u>C</u>H$_2$). MS: *m/z* (EI$^+$) 458 (M$^+$, 3 %), 149 (100 %), HRMS (EI$^+$): Calcd for $C_{18}H19IO_6$ = 458.0226 (M$^+$) , found 458.0233.

2-Iodophenyl 3,4-dimethoxyphenylacetate 4b

The title compound was prepared in 91 % yield (clear oil, 1.65 g) from 3,4-dimethoxyphenylacetic acid (980 mg, 4.99 mmol) and 2-iodophenol (1.0 g, 4.54 mmol) in the presence of DCC (1.03 mg, 4.99

mmol), DMAP (166 mg, 1.36 mmol) and DCM (20 mL) according to esterification method. M.p. 52-54 ^{o}C. ^{1}H NMR: δ 7.79 (d, 1H, *J* = 8.0 Hz, Ar-H-3'), 7.32 (t, 1H, *J* = 7.5 Hz, Ar-H-5'), 7.05 (d, 1H, *J* = 7.5 Hz, Ar-H-6'), 6.96 (bs, 1H, Ar-H-2), 6.96-6.93 (m, 1H, Ar-H-6), 6.94 (t, 1H, *J* = 8.0 Hz, Ar-H-4'), 6.85 (d, 1H, *J* = 8.0 Hz, Ar-H-5), 3.89 (s, 3H, OCH$_3$-3), 3.869 (s, 3H, OCH$_3$-4), 3.864 (s, 2H, Ar-CH$_2$). ^{13}C NMR: δ 169.2 (C=O), 151.0 (Ar-C-1'), 148.8 (Ar-C-OCH$_3$-4), 148.3 (Ar-C-OCH$_3$-3), 139.3 (Ar-C-H-3'), 129.2 (Ar-C-H-5'), 127.5 (Ar-C-H-4'), 125.3 (Ar-C-1), 122.8 (Ar-C-H-6'), 121.7 (Ar-C-H-6), 112.7 (Ar-C-H-2), 111.1 (Ar-C-H-5), 90.1 (Ar-C-H-2'), 55.8 (Ar-OCH$_3$-4), 55.7 (Ar-OCH$_3$-3), 40.8 (Ar-CH$_2$). MS: *m/z* (EI$^+$) 398 (M$^+$, 46 %), 151 (100 %), HRMS (EI$^+$): Calcd for $C_{16}H_{15}IO_4$ = 398.0015 (M$^+$), found 398.0012.

3,4-Dimethoxyphenyl 2-iodophenylacetate 4c

The title compound was prepared in 92 % yield (clear oil, 1.41 g) from 2-iodophenylacetic acid (1.00 g, 3.81 mmol) and 3,4-dimethoxyphenol (647 mg, 4.19 mmol) in the presence of DCC (866 mg, 4.19 mmol), DMAP (140 mg, 1.14 mmol) and DCM (20 mL) according to esterification method. M.p. 90-92 ^{o}C. ^{1}H NMR: δ 7.87 (d, 1H, *J* = 7.5 Hz, Ar-H-3), 7.37 (d, 1H, *J* = 7.5 Hz, Ar-H-6), 7.33 (t, 1H, *J* = 7.5 Hz, Ar-H-5), 6.98 (t, 1H, *J* = 7.5 Hz, Ar-H-4), 6.81 (d, 1H, *J* = 8.0 Hz, Ar-H-5'), 6.69 (d, 1H, *J* = 1.5 Hz, Ar-H-2'), 6.68 (dd, 1H, *J* = 8.0, 1.5 Hz, Ar-H-6'), 4.01 (s, 2H, Ar-CH$_2$), 3.84 (s, 3H, OCH$_3$-3'), 3.83 (s, 3H, OCH$_3$-4'). ^{13}C NMR: δ 169.1 (C=O), 149.1 (Ar-C-OCH$_3$-3'), 146.7 (Ar-C-OCH$_3$-4'), 144.2 (Ar-C-1'), 139.4 (Ar-C-H-3), 137.2 (Ar-C-1), 130.7 (Ar-C-H-6), 129.0 (Ar-C-H-4), 128.4 (Ar-C-H-5), 112.6 (Ar-C-H-6'), 111.0 (Ar-C-H-5'), 105.5 (Ar-C-H-2'), 100.8 (Ar-C-2), 56.0 (Ar-OCH$_3$-3'), 55.8 (Ar-OCH$_3$-4'), 46.1 (Ar-CH$_2$). MS: *m/z* (EI$^+$) 398 (M$^+$, 5 %), 154 (100 %), HRMS (EI$^+$): Calcd for $C_{16}H_{15}IO_4$ = 398.0015 (M$^+$), found 398.0002.

3,4-Dimethoxyphenyl 3-(2-iodo-4,5-dimethoxyphenyl)propionate 5

The title compound was prepared in 81 % yield (cream solid, 669 mg) from 3-(2-iodo-4,5-dimethoxyphenyl)propanoic acid (566 mg, 1.68 mmol) and 3,4-dimethoxyphenol (286 mg, 1.85 mmol) in the presence of DCC (382 mg, 1.85 mmol), DMAP (51 mg, 0.42 mmol) and DCM (13 mL) according to the general esterification method. M.p. 100-102 ^{o}C. ^{1}H NMR: δ 7.22 (s, 1H, Ar-H-3), 6.83 (s, 1H, Ar-H-6), 6.81 (d, 1H, *J* = 8.7 Hz Ar-H-5'), 6.58 (dd, 1H, *J* = 8.7, 2.5 Hz Ar-H-6'), 6.55 (d, 1H, *J* = 2.5 Hz Ar-H-2'), 3.83 (s, 3H, OCH$_3$), 3.84 (s, 3H, OCH$_3$), 3.83 (s, 3H, OCH$_3$), 3.82 (s, 3H, OCH$_3$), 3.09 (t, 2H, *J* = 7.3, Ar-CH$_2$), 2.83 (t, 2H, *J* = 7.3, Ar-CH$_2$-CH$_2$). ^{13}C NMR: δ 171.3 (C=O), 149.3 (2 x Ar-C-OCH$_3$-4, 4'), 148.1 (Ar-C-OCH$_3$-5), 146.7 (Ar-C-OCH$_3$-3'), 144.1 (Ar-C-1'), 135.0 (Ar-C-1),

121.7 (Ar-C-H-3), 112.7 (Ar-C-H-6), 112.6 (Ar-C-H-6'), 111.0 (Ar-C-H-5'), 105.5 (Ar-C-H-2'), 87.7 (Ar-C-2), 56.1 (2 x Ar-OCH$_3$-3', 5), 55.8 (2 x Ar-OCH$_3$-4, 4'), 35.4 (Ar-CH$_2$), 34.6 (Ar-CH$_2$-CH$_2$). MS: *m/z* (EI$^+$) 472 (M$^+$, 19 %), 154 (100 %), HRMS (EI$^+$): Calcd for $C_{19}H_{21}IO_6$ = 472.0383 (M$^+$), found 472.0373.

2-Iodobenzyl (3,4-dimethoxyphenyl)acetate 7a

The title compound was prepared in 81 % yield (clear oil, 1.42 g) from 3,4-dimethoxyphenylacetic acid (922 mg, 4.70 mmol) and 2-iodobenzyl alcohol (1.00 g, 4.27 mmol) in the presence of DCC (969 mg, 4.70 mmol), DMAP (156 mg, 1.28 mmol) and DCM (20 mL) according to the general esterification method. M.p. 52-54 ^{o}C ^{1}H NMR: δ 7.82 (d, 1H, *J* = 7.5 Hz, Ar-H-3'), 7.30 (t, 1H, *J* = 7.5 Hz, Ar-H-5'), 7.28 (d, 1H, *J* = 7.5 Hz, Ar-H-6'), 6.99 (dt, 1H, *J* = 7.5, 2.0 Hz, Ar-H-4'), 6.84 (d, 1H, *J* = 8.5 Hz, Ar-H-6), 6.83 (bs, 1H, Ar-H-2), 6.80 (d, 1H, *J* = 8.5 Hz, Ar-H-5), 5.13 (s, 2H, Ar-CH$_2$-O), 3.85 (s, 3H, OCH$_3$-4), 3.84 (s, 3H, OCH$_3$-3), 3.63 (s, 2H, Ar-CH$_2$-CO). ^{13}C NMR: δ 171.1 (C=O), 148.8 (Ar-C-OCH$_3$-3), 148.0 (Ar-C-OCH$_3$-4), 139.3 (Ar-C-H-3'), 138.1 (Ar-C-1'), 129.7 (Ar-C-H-4'), 129.3 (Ar-C-H-6'), 128.1 (Ar-C-H-5'), 126.0 (Ar-C-1), 121.4 (Ar-C-H-6), 112.3 (Ar-C-H-2), 111.1 (Ar-C-H-5), 98.1 (Ar-C-2'), 70.1 (Ar-CH$_2$-O), 55.78 (Ar-OCH$_3$-4), 55.73 (Ar-OCH$_3$-3), 40.4 (Ar-CH$_2$-CO). MS: *m/z* (EI$^+$) 412 (M$^+$, 62 %), 151 (100 %), HRMS (EI$^+$): Calcd for $C_{17}H_{17}IO_4$ = 412.0171 (M$^+$), found 412.0151.

2-Iodo-4,5-dimethoxybenzyl 3,4-dimethoxyphenylacetate 7b

The title compound was prepared in 70 % yield (92 % brsm, orange solid, 720 mg) from 3,4-dimethoxyphenylacetic acid (474 mg, 2.41 mmol) and 2-iodo-4,5-dimethoxybenzyl alcohol (645 mg, 2.19 mmol) in the presence of DCC (498 mg, 2.41 mmol), DMAP (80 mg, 0.69 mmol) and DCM (10 mL) according to the general esterification method. (2-iodo-4,5-dimethoxybenzyl alcohol (159 mg) was recovered from the reaction.) M.p. 88-90 ^{o}C. ^{1}H NMR: δ 7.23 (s, 1H, Ar-H-3'), 6.84 (d, 1H, *J* = 7.0 Hz, Ar-H-5), 6.83 – 6.81 (m, 1H, Ar-H-6), 6.81 (d, 1H, *J* = 2.4 Hz, Ar-H-2), 6.79 (s, 1H, Ar-H-6'), 5.09 (s, 2H, Ar-CH$_2$-O), 3.86 (s, 6H, OCH$_3$-4', 5'), 3.85 (s, 3H, OCH$_3$-3), 3.76 (s, 3H, OCH$_3$-4), 3.62 (s, 1H, Ar-CH$_2$-CO). ^{13}C NMR: δ 171.3 (C=O), 149.3 (Ar-C-OCH$_3$-4), 149.2 (Ar-C-OCH$_3$-4'), 148.8 (Ar-C-OCH$_3$-5'), 148.1 (Ar-C-OCH$_3$-3), 130.6 (Ar-C-1'), 126.2 (Ar-C-1), 121.6 (Ar-C-H-3'), 121.4 (Ar-C-H-5), 112.6 (Ar-C-H-6'), 112.4 (Ar-C-H-6), 111.1 (Ar-C-H-2), 86.9 (Ar-C-2'), 70.2 (Ar-CH$_2$-O), 56.1 (Ar-OCH$_3$-3), 55.85 (2 x Ar-OCH$_3$-4, 4'), 55.83 (Ar-OCH$_3$-5'), 40.8 (Ar-CH$_2$-CO). MS: *m/z*

(EI^+) 472 (M^+, 13 %), 151 (100 %), HRMS (EI^+): Calcd for $C_{19}H_{21}IO_6$ = 472.0383 (M^+), found 472.0388.

3,4-Dimethoxybenzyl (2-iodophenyl)acetate 10a

The title compound was prepared in 91 % yield (clear oil, 1.42 g) from 2-iodophenylacetic acid **261** (1.0 g, 3.82 mmol) and 3,4-dimethoxybenzyl alcohol **231** (706 mg, 4.19 mmol) in the presence of DCC (866 mg, 4.19 mmol), DMAP (140 mg, 1.14 mmol) and DCM (20 mL) according to esterification method. ^{1}H NMR: δ 7.83 (d, 1H, *J* = 8.0 Hz, Ar-H-3), 7.29 (d, 1H, *J* = 8.0 Hz, Ar-H-6), 7.28 (t, 1H, *J* = 8.0 Hz, Ar-H-5), 6.94 (t, 1H, *J* = 8.0 Hz, Ar-H-4), 6.90 (d, 1H, *J* = 8.0 Hz, Ar-H-6'), 6.85 (bs, 1H, Ar-H-2'), 6.81 (d, 1H, *J* = 8.0 Hz, Ar-H-5'), 5.10 (s, 2H, Ar-CH_2-O), 3.86 (s, 3H, OCH_3-3'), 3.84 (s, 3H, OCH_3-4'), 3.82 (s, 2H, Ar-CH_2-CO). ^{13}C NMR: δ 170.2 (C=O), 148.9 (Ar-C-OCH_3-4'), 148.8 (Ar-C-OCH_3-3'), 139.3 (Ar-C-H-3), 137.6 (Ar-C-1), 130.5 (Ar-C-H-5), 128.7 (Ar-C-H-4), 128.3 (Ar-C-H-6), 128.1 (Ar-C-1'), 121.0 (Ar-C-H-6'), 111.5 (Ar-C-H-2'), 110.8 (Ar-C-H-5'), 100.9 (Ar-C-2), 66.7 (Ar-CH_2-O), 55.79 (Ar-OCH_3-4'), 55.78 (Ar-OCH_3-3'), 46.2 (Ar-CH_2-CO). MS: *m/z* (EI^+) 412 (M^+, 48 %), 151 (100 %), HRMS (EI^+): Calcd for $C_{17}H_{17}IO_4$ = 412.0171, found 412.0158.

3,4-Dimethoxybenzyl 2-iodo-4,5-dimethoxyphenylacetate 10b

The title compound was prepared in 77 % yield (white solid, 452 mg) from 2-iodo-3,4-dimethoxyphenylacetic acid **254** (400 mg, 1.24 mmol) and 3,4-dimethoxybenzyl alcohol **231** (229 mg, 1.36 mmol) in the presence of DCC (282 mg, 1.36 mmol), DMAP (45 mg, 0.37 mmol) and DCM (10 mL) according to esterification method. M.p. 96-98 ^{o}C. ^{1}H NMR: δ 7.23 (s, 1H, Ar-H-3), 6.91 (dd, 1H, *J* = 8.0, 2.0 Hz, Ar-H-6'), 6.88 (d, 1H, *J* = 2.0 Hz, Ar-H-2'), 6.83 (d, 1H, *J* = 8.0 Hz, Ar-H-5'), 6.78 (s, 1H, Ar-H-6), 5.11 (s, 2H, Ar-CH_2-O), 3.87 (s, 3H, OCH_3-3'), 3.86 (s, 3H, OCH_3-4'), 3.84 (s, 3H, OCH_3-5), 3.81 (s, 3H, OCH_3-4), 3.76 (s, 2H, Ar-CH_2-CO). ^{13}C NMR: δ 170.6 (C=O), 149.0 (Ar-C-OCH_3-4), 148.9 (2 x Ar-C-OCH_3-4', 5'), 148.6 (Ar-C-OCH_3-5), 129.9 (Ar-C-1), 128.2 (Ar-C-1'), 121.5 (Ar-C-H-3), 121.1 (Ar-C-H-6'), 113.2 (Ar-C-H-6), 111.6 (Ar-C-H-5'), 110.8 (Ar-C-H-2'), 88.8 (Ar-C-2), 66.7 (Ar-CH_2-O), 56.1 (Ar-OCH_3-5'), 55.87 (2 x Ar-OCH_3-4, 4'), 55.86 (Ar-OCH_3-3'), 45.7 (Ar-CH_2-CO). MS: *m/z* (EI^+) 472 (M^+, 9 %), 151 (100 %) HRMS (ES^+): Calcd for $C_{19}H_{22}IO_6$ = 473.0461 ($M+H^+$), found 473.0443.

General Method For Palladium-Mediated Arylation

2,3,8,9-Tetramethoxy-6*H*-benzo[c]chromen-6-one 2a

Compound **1a** (100 mg, 0.22 mmol), $(Ph_3P)_2PdCl_2$ (41 mg, 0.058 mmol), anhydrous NaOAc (55 mg, 0.67 mmol) and DMA (25 mL) were combined in an ACE® pressure tube. The solution was degassed for 20 min with Ar, the vessel sealed and heated at 120 ^{0}C for 3 h. The tube was cooled to RT and the solid residue removed by filtration. The filtrate was diluted with 20 mL of 10 % HCl solution and extracted with EtOAc (2 x 20 mL). The combined extracts were washed with H_2O (4 x 20 mL), dried ($MgSO_4$), filtered, evaporated and the title compound was isolated as a white film (57.2 mg, 80 %) by flash silica gel chromatography using DCM:PS:EtOAc (2:2:1) as the eluent. M.p. 217-219 ^{o}C ^{1}H NMR: δ 7.69 (s, 1H, Ar-H-7), 7.24 (s, 1H, Ar-H-10), 7.22 (s, 1H, Ar-H-1), 6.83 (s, 1H, Ar-H-4), 4.11 (s, 3H, OCH$_3$-8), 4.02 (s, 3H, OCH$_3$-2), 3.99 (s, 3H, OCH$_3$-9), 3.94 (s, 3H, OCH$_3$-3). ^{13}C NMR: δ 161.4 (C=O), 155.1 (Ar-C-OCH$_3$-8), 150.9 (Ar-C-OCH$_3$-3), 149.3 (Ar-C-OCH$_3$-9), 146.3 (Ar-C-4a), 146.0 (Ar-C-OCH$_3$-2), 130.3 (Ar-C-7a), 113.3 (Ar-C-10a), 110.5 (Ar-C-H-7), 110.0 (Ar-C-1a), 103.8 (Ar-C-H-10), 102.0 (Ar-C-H-1), 100.8 (Ar-C-H-4), 56.6 (Ar-OCH$_3$-2), 56.3 (Ar-OCH$_3$-8), 56.2 (Ar-OCH$_3$-9), 56.1 (Ar-OCH$_3$-3). MS: *m/z* (EI$^+$) 316 (M$^+$, 100 %) HRMS (CI$^+$): Calcd for $C_{17}H_{17}O_6$ = 317.1025 (M+H$^+$), found 317.1026 (M$^+$).

2,3,8,9,10-Pentamethoxy-6*H*-benzo[c]chromen-6-one 2b

The title compound was prepared in 85 % yield (white solid, 63 mg) from **1b** (100 mg, 0.21 mmol), in the presence of $(Ph_3P)_2PdCl_2$ (39 mg, 0.055 mmol), NaOAc (52 mg, 0.63 mmol) and DMA (25 mL) according to the general arylation method described above. M.p. 148-150 ^{o}C. ^{1}H NMR: δ 8.39 (s, 1H, Ar-H-7), 7.72 (s, 1H, Ar-H-1), 6.86 (s, 1H, Ar-H-4), 4.05 (s, 3H, OCH$_3$-8), 4.00 (s, 3H, OCH$_3$-9), 3.99 (s, 3H, OCH$_3$-10), 3.98 (s, 3H, OCH$_3$-3), 3.94 (s, 3H, OCH$_3$-2). ^{13}C NMR: δ 161.3 (C=O), 152.8 (Ar-C-OCH$_3$-10), 150.1 (Ar-C-OCH$_3$-9), 149.9 (Ar-C-OCH$_3$-2), 148.9 (Ar-C-OCH$_3$-3), 145.7 (Ar-C-OCH$_3$-8), 145.4 (Ar-C-4a), 123.1 (Ar-C-7a), 116.2 (Ar-C-10a), 109.4 (Ar-C-1a), 108.1 (Ar-C-H-7), 107.9 (Ar-C-H-1), 100.3 (Ar-C-H-4), 61.1 (Ar-OCH$_3$-8), 60.6 (Ar-OCH$_3$-3), 56.2 (Ar-OCH$_3$-9), 56.1 (Ar-OCH$_3$-10), 56.0 (Ar-OCH$_3$-2). MS: *m/z* (CI$^+$) 347 (M+H$^+$, 100 %) HRMS (CI$^+$): Calcd for $C_{18}H_{19}O_7$ = 347.1131 (M+H$^+$), found 347.1132.

2,3-Dimethoxy-6*H*-benzo[c]chromen-6-one 2c and 1,2-Dimethoxy-6*H*-benzo[c]chromen-6-one 3

Compound **2c** was prepared in 71 % yield (white solid, 47.3 mg) from **1c** (100 mg, 0.26 mmol), in the presence of $(Ph_3P)_2PdCl_2$ (39 mg, 0.067 mmol), NaOAc (64 mg, 0.78 mmol) and DMA (25 mL) according to the general arylation method described above. Regioisomer **3** was also isolated from the reaction as a white solid (9.2 mg, 8 %). NMR data was consistent with the literature for **2c** and **3**.[8]

3,4-Dimethoxyphenyl (2*E*)-3-(3,4-dimethoxyphenyl)acrylate 6

The title compound was prepared in 59 % yield (yellow film, 43 mg) from **5** (100 mg, 0.20 mmol), in the presence of $(Ph_3P)_2PdCl_2$ (37 mg, 0.053 mmol), NaOAc (51 mg, 0.61 mmol) and DMA (25 mL) according to the general arylation method described above. While this is a known compound NMR data was not reported.[9] ^{1}H NMR: δ 7.80 (d, 1H, *J* = 15.9 Hz, Ar-C<u>H</u>=CH), 7.16 (dd, 1H, *J* = 8.1, 1.5 Hz, Ar-<u>H</u>-6), 7.10 (d, 1H, *J* = 1.5 Hz, Ar-<u>H</u>-2), 6.89 (d, 1H, *J* = 8.1 Hz, Ar-<u>H</u>-5), 6.86 (d, 1H, *J* = 9.3 Hz, Ar-<u>H</u>-5'), 6.72 (d, 1H, *J* = 2.7 Hz, Ar-<u>H</u>-2'), 6.71 (dd, 1H, *J* = 9.3, 2.7 Hz, Ar-<u>H</u>-6'), 6.48 (d, 1H, *J* = 15.9 Hz, Ar-CH=C<u>H</u>), 3.92 (s, 6H, 2 x OC<u>H</u>$_3$-3, 4), 3.88 (s, 3H, OC<u>H</u>$_3$-3'), 3.86 (s, 3H, OC<u>H</u>$_3$-4').
^{13}C NMR: δ 166.0 (<u>C</u>=O), 151.4 (Ar-<u>C</u>-OCH$_3$-3), 149.3 (Ar-<u>C</u>-OCH$_3$-4), 149.2 (Ar-<u>C</u>-OCH$_3$-4'), 146.7 (Ar-<u>C</u>-OCH$_3$-3'), 146.4 (Ar-<u>C</u>H=CH), 144.4 (Ar-<u>C</u>-1'), 127.1 (Ar-<u>C</u>-CH=CH), 122.9 (Ar-<u>C</u>-H-6), 114.7 (Ar-CH=<u>C</u>H), 112.9 (Ar-<u>C</u>-H-6'), 111.1 (Ar-<u>C</u>-H-5), 111.0 (Ar-<u>C</u>-H-5'), 109.7 (Ar-<u>C</u>-H-2), 105.8 (Ar-<u>C</u>-H-2'), 56.1 (Ar-O<u>C</u>H$_3$), 55.96 (Ar-O<u>C</u>H$_3$), 55.94 (Ar-O<u>C</u>H$_3$), 55.8 (Ar-O<u>C</u>H$_3$). MS: *m/z* (EI$^+$) 344 (M$^+$, 13 %), 191 (100 %) HRMS (EI$^+$): Calcd for $C_{19}H_{20}O_6$ = 344.1260 (M$^+$), found 344.1256.

4-(3,4-Dimethoxyphenyl)-1,4-dihydro-3*H*-isochromen-3-one 8a and 2,2'-(dimethylenebiphenyl-2,2'-diyl) [di(3,4-dimethoxyphenyl)]diacetate 9a

Compounds **8a** (white film, 20 mg, 29 %) and **9a** (white film, 31 mg, 30%) were prepared from **7a** (100 mg, 0.24 mmol), in the presence of $(Ph_3P)_2PdCl_2$ (44 mg, 0.063 mmol), NaOAc (60 mg, 0.73 mmol) and DMA (25 mL) according to the general arylation method described above.

8a: ^{1}H NMR: δ 7.38 (d, 1H, *J* = 8.4 Hz, Ar-<u>H</u>-5), 7.37 (t, 1H, *J* = 8.4 Hz, Ar-<u>H</u>-7), 7.29 (d, 1H, *J* = 8.4 Hz, Ar-<u>H</u>-8), 7.15 (t, 1H, *J* = 8.4 Hz, Ar-<u>H</u>-6), 6.81 (d, 1H, *J* = 2.1 Ar-<u>H</u>-2'), 6.78 (d, 1H, *J* = 8.2 Hz, Ar-<u>H</u>-5'), 6.53 (dd, 1H, *J* = 8.2, 2.1 Hz, Ar-<u>H</u>-6'), 5.23 (ABq, 2H, *J* = 16.5 Hz, Ar-C<u>H</u>$_2$-O), 4.95 (Ar-C<u>H</u>-CO), 3.85 (s, 3H, OC<u>H</u>$_3$-4'), 3.82 (s, 3H, OC<u>H</u>$_3$-3'). ^{13}C NMR: δ 171.6 (<u>C</u>=O), 149.6 (Ar-<u>C</u>-OCH$_3$-3'), 149.0 (Ar-<u>C</u>-OCH$_3$-4'), 134.4 (Ar-<u>C</u>-5a), 132.2 (Ar-<u>C</u>-8a), 129.2 (Ar-<u>C</u>-H-5), 128.2 (Ar-<u>C</u>-H-6), 128.0 (Ar-<u>C</u>-H-7), 126.7 (Ar-<u>C</u>-1'), 125.0 (Ar-<u>C</u>-H-8), 120.5 (Ar-<u>C</u>-H-6'), 111.7 (Ar-<u>C</u>-H-2'), 111.3

(Ar-C-H-5'), 69.7 (Ar-CH_2-O), 56.1 (2 x Ar-OCH_3-3, 4), 51.5 (Ar-CH-CO). MS: *m/z* (EI^+) 284 (M^+, 73 %), 209 (100 %), HRMS (EI^+): Calcd for $C_{17}H_{16}O_4$ = 284.1048 (M^+), found 284.1057.

9a: ^{1}H NMR: δ 7.37 (dd, 2H, *J* = 7.5, 1.5 Hz, Ar-H-3'), 7.33 (dt, 2H, *J* = 7.5, 1.5 Hz, Ar-H-5'), 7.28 (dt, 2H, *J* = 7.5, 1.5 Hz, Ar-H-4'), 7.11 (dd, 2H, *J* = 7.5, 1.0 Hz, Ar-H-6'), 6.78 (d, 2H, *J* = 9.0 Hz, Ar-H-5), 6.74 (dd, 2H, *J* = 9.0, 1.5 Hz, Ar-H-6), 6.73 (bs, 2H, Ar-H-2), 4.83 (ABq, 4H, *J* = 12.5, Hz Ar-CH_2-O), 3.85 (s, 6H, OCH_3-4), 3.81 (s, 6H, OCH_3-3), 3.48 (s, 4H, Ar-CH_2-CO). ^{13}C NMR: δ 171.2 (C=O), 148.8 (Ar-C-OCH_3-3), 148.1 (Ar-C-OCH_3-4), 139.6 (Ar-C-H-3'), 133.7 (Ar-C-1'), 129.9 (Ar-C-2'), 128.9 (Ar-C-H-3'), 127.9 (2 x Ar-C-H-4', 5'), 126.2 (Ar-C-1), 121.4 (Ar-C-H-6), 112.3 (Ar-C-H-2), 111.1 (Ar-C-H-5), 64.5 (Ar-CH_2-O), 55.8 (Ar-OCH_3-4), 55.7 (Ar-OCH_3-3), 40.7 (Ar-CH_2-CO). MS: *m/z* (EI^+) 570 (M^+, 47 %), 151 (100 %), HRMS (EI^+): Calcd for $C_{34}H_{34}O_8$ = 570.2254 (M^+), found 570.2271.

4-(3,4-Dimethoxyphenyl)-6,7-dimethoxy-1,4-dihydro-3*H*-isochromen-3-one 8b and 2,2'-[dimethylene(4,4',5,5'-tetramethoxybiphenyl-2,2'-diyl](di(3,4-dimethoxyphenyl))diacetate 9b

Compounds **8b** (yellow film, 21 mg, 29 %) and **9b** (orange film, 39 mg, 46%) were prepared from **7b** (115 mg, 0.24 mmol), in the presence of $(Ph_3P)_2PdCl_2$ (44 mg, 0.063 mmol), NaOAc (60 mg, 0.73 mmol) and DMA (25 mL) according to the general arylation method described above.

8b: see following procedure for spectral data of this compound.

9b: ^{1}H NMR: δ 6.84 (s, 2H, Ar-H-6'), 6.78 (d, 2H, *J* = 9.0 Hz, Ar-H-5), 6.76 (d, 2H, *J* = 9.0 Hz, Ar-H-6), 6.75 (bs, 2H, Ar-H-2), 6.69 (s, 2H, Ar-H-3'), 4.81 (ABq, 4H, *J* = 12.0 Hz, Ar-CH_2-O), 3.85 (s, 6H, OCH_3-5'), 3.84 (s, 6H, OCH_3-4'), 3.81 (s, 6H, OCH_3-3), 3.80 (s, 6H OCH_3-4), 3.51 (s, 4H Ar-CH_2-CO). ^{13}C NMR: δ 171.3 (C=O), 148.9 (Ar-C-OCH_3-4'), 148.4 (2x Ar-C-OCH_3-3, 4), 148.3 (Ar-C-OCH_3-3'), 132.3 (Ar-C-1'), 126.3 (Ar-C-2'), 126.2 (Ar-C-1), 121.3 (Ar-C-H-6), 113.1 (Ar-C-H-3), 112.3 (Ar-C-H-2), 111.9 (Ar-C-H-6), 111.1 (Ar-C-H-5), 64.4 (Ar-CH_2-O), 56.0 (Ar-OCH_3-3), 55.9 (Ar-OCH_3-4), 55.8 (Ar-OCH_3-4'), 55.7 (Ar-OCH_3-3'), 40.8 (Ar-CH_2-CO). MS: *m/z* (EI^+) 690 (M^+, 11 %), 368 (100 %), HRMS (EI^+): Calcd for $C_{38}H_{42}O_{12}$ = 690.2676 (M^+), found 690.2679.

4-(3,4-Dimethoxyphenyl)-6,7-dimethoxy-1,4-dihydro-3*H*-isochromen-3-one 8b

The title compound was also prepared in 21 % yield (yellow film, 15 mg) from 3,4-dimethoxybenzyl (2-iodo-4,5-dimethophenyl)acetate (115 mg, 0.24 mmol), in the presence of $(Ph_3P)_2PdCl_2$ (44 mg, 0.063 mmol), NaOAc (60 mg, 0.73 mmol) and DMA (25 mL) according to the general arylation method described above. ^{1}H NMR: δ 6.84 (d, 1H, *J* = 2.0 Ar-H-2'), 6.77 (s, 1H, Ar-H-5), 6.78 (d, 1H, *J*

= 8.7 Hz, Ar-H-5'), 6.65 (s, 1H, Ar-H-8), 6.51 (dd, 1H, *J* = 8.7, 2.0 Hz, Ar-H-6'), 5.17 (ABq, 2H, *J* = 13.5 Hz, Ar-CH_2-O), 4.89 (Ar-CH-CO), 3.92 (s, 3H, OCH_3-6), 3.85 (s, 3H, OCH_3-7), 3.84 (s, 3H, OCH_3-3'), 3.83 (s, 3H, OCH_3-4'). ^{13}C NMR: δ 171.5 (C=O), 149.8 (Ar-C-OCH_3-3), 149.6 (Ar-C-OCH_3-4'), 149.0 (Ar-C-OCH_3-4), 148.8 (Ar-C-OCH_3-5'), 127.0 (Ar-C-5a), 126.2 (Ar-C-1'), 124.3 (Ar-C-8a), 120.2 (Ar-C-H-6'), 111.5 (Ar-C-H-2'), 111.3 (Ar-C-H-5'), 111.2 (Ar-C-H-8), 108.1 (Ar-C-H-5), 69.6 (Ar-CH_2-O), 56.4 (Ar-OCH_3), 56.3 (Ar-OCH_3), 56.2 (Ar-OCH_3), 56.1 (Ar-OCH_3), 50.9 (Ar-CH-CO). MS: *m/z* (EI^+) 344 (M^+, 46 %), 269 (100 %), HRMS (CI^+): Calcd for $C_{19}H_{21}O_6$ = 345.1338 ($M+H^+$), found 345.1327.

Di-(3,4-dimethoxybenzyl) 2,3-diphenylsuccinate 11 and di-(3,4-dimethoxybenzyl) 2,2'-biphenyl-2,2'-diylacetate 12

Compound **11** was prepared in 27 % yield (clear film, 19 mg) from **10a** (100 mg, 0.24 mmol), in the presence of $(Ph_3P)_2PdCl_2$ (65 mg, 0.093 mmol), NaOAc (60 mg, 0.73 mmol) and DMA (25 mL) according to the general arylation method described above, and with HPLC separation of **12** (clear film, 4 mg, 7 %) from the reaction mixture. The major and minor diastereomers could not be separated by HPLC and are reported together. The diastereomeric ratio was major: minor = 1.8:1. NMR signals for the minor diastereomer are shown in brackets.

11: ^{1}H NMR: δ 7.47 (dd, 2H, *J* = 7.5, 2.1 Hz, Ar-H-4), 7.13 (t, 4H, *J* = 7.5 Ar-H-3,5), 7.03 (dd, 4H, Ar-H-2,6), 6.73 (d, 2H, *J* = 7.8 Hz, Ar-H-5'), 6.59 (dd, 2H, *J* = 7.8, 2.1 Hz, Ar-H-6'), 6.48 (d, 2H, *J* = 2.1 Hz, Ar-H-2'), 5.04 (4.76) (ABq, 4H, *J* = 12.3 Hz, (ABq, 4H, *J* = 12.0 Hz), Ar-CH_2-O), 4.30 (4.43) (s, 2H, Ar-CH-CO), 3.85 (3.85) (s, 3H, OCH_3-3'), 3.74 (3.69) (s, 3H, OCH_3-4'). ^{13}C NMR: δ 172.8 (171.4) (C=O), 148.9 (Ar-C-OCH_3-3'), 148.8 (Ar-C-OCH_3-4'), 135.5 (136.1) (Ar-C-H-2'), 128.5 (128.6) (Ar-C-H-4), 128.3 (128.2) (Ar-C-H-3,5), 128.4 (Ar-C-1), 128.0 (127.9) (Ar-C-1'), 127.4 (127.8) (Ar-C-H-2,6), 120.8 (120.5) (Ar-C-H-6'), 110.9 (111.2) (Ar-C-H-2'), 110.7 (110.9) (Ar-C-H-5'), 66.6 (Ar-CH_2-O), 55.8 (Ar-OCH_3), 55.7 (55.6) (Ar-OCH_3), 54.8 (54.9) (Ar-CH-CO). MS: *m/z* (EI^+) 570 (M^+, 10 %), 151 (100 %), HRMS (EI^+): Calcd for $C_{34}H_{34}O_8$ = 570.2253 (M^+), found 570.2231.

12: ^{1}H NMR: δ 7.30-7.26 (m, 4H, Ar-H-5,6), 7.22-7.16 (m, 4H, Ar-H-3,4), 7.07 (d, 2H, *J* = 7.2 Hz, Ar-H-5), 6.78 (d, 2H, *J* = 1.2 Hz, Ar-H-2'), 6.72 (dd, 2H, *J* = 7.2, 1.2 Hz, Ar-H-6'), 4.91 (s, 4H Ar-CH_2-O), 3.85 (s, 6H, OCH_3-3'), 3.80 (s, 6H OCH_3-4'), 3.36 (ABq, 4H, *J* = 16.0 Hz, Ar-CH_2-CO).

^{13}C NMR: δ 171.4 (C=O), 149.0 (Ar-C-OCH_3-4'), 148.9 (Ar-C-OCH_3-3'), 140.6 (Ar-C-H-3), 132.4 (Ar-C-1'), 130.2 (Ar-C-H-5), 130.1 (Ar-C-H-4), 128.5 (Ar-C-1), 127.7 (Ar-C-H-6), 126.9 (Ar-C-2'),

121.1 (Ar-C-H-6'), 111.6 (Ar-C-H-2'), 110.8 (Ar-C-H-5'), 66.9 (Ar-CH_2-O), 55.9 (Ar-OCH_3-4'), 55.8 (Ar-OCH_3-3'), 38.7 (Ar-CH_2-CO). MS: *m/z* (EI^+) 570 (M^+, 5 %), 151 (100 %), HRMS (EI^+): Calcd for $C_{34}H_{34}O_8$ = 570.2253 (M^+), found 570.2239.

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GRAPHICAL ABSTRACT

Synthesis of benzo[c]chromen-6-ones via novel cyclic aryl-Pd(II)-ester enolate intermediates

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