

1-1-2007

## Intramolecular versus intermolecular oxidative couplings of ester tethered di-aryl ethers

Stephen R. Taylor  
*University of Wollongong*


Alison T. Ung  
*University of Wollongong, [alison\\_ung@uow.edu.au](mailto:alison_ung@uow.edu.au)*

Stephen G. Pyne  
*University of Wollongong, [spyne@uow.edu.au](mailto:spyne@uow.edu.au)*

Brian W. Skelton  
*University of Western Australia*

Allan H. White  
*University of Western Australia*

Follow this and additional works at: <https://ro.uow.edu.au/scipapers>

 Part of the [Life Sciences Commons](#), [Physical Sciences and Mathematics Commons](#), and the [Social and Behavioral Sciences Commons](#)

---

### Recommended Citation

Taylor, Stephen R.; Ung, Alison T.; Pyne, Stephen G.; Skelton, Brian W.; and White, Allan H.: Intramolecular versus intermolecular oxidative couplings of ester tethered di-aryl ethers 2007, 11377-11385.  
<https://ro.uow.edu.au/scipapers/4046>

---

## Intramolecular versus intermolecular oxidative couplings of ester tethered di-aryl ethers

### Abstract

The oxidative cyclization of 3,4-dimethoxyphenyl 3,4-dimethoxyphenylacetate, through intramolecular biphenyl bond formation, was successful and gave the target seven-membered lactone in good yield (85–86%). All other ester substrates gave biphenyl products or their further oxidized products via intermolecular coupling of their radical cation intermediate with the neutral substrate. It appears that matching of the oxidation potentials and nucleophilicity of the two phenyl rings, the positioning of the ring substituents and the ease of *E* to *Z* isomerization about the ester C–O bond are important factors contributing to these product outcomes.

### Keywords

Intramolecular, versus, intermolecular, oxidative, couplings, ester, tethered, aryl, ethers, CMMB

### Disciplines

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

### Publication Details

Taylor, S. R., Ung, A. T., Pyne, S. G., Skelton, B. W. & White, A. H. (2007). Intramolecular versus intermolecular oxidative couplings of ester tethered di-aryl ethers. *Tetrahedron*, (63), 11377-11385.

# Intramolecular versus intermolecular oxidative couplings of ester tethered di-aryl ethers

Stephen R. Taylor, Alison T. Ung<sup>\*</sup> and Stephen G. Pyne<sup>\*</sup> Brian W. Skelton<sup>b</sup> and Allan H. White<sup>b</sup>

<sup>a</sup>*Department of Chemistry, University of Wollongong, Wollongong, NSW, 2522, Australia*

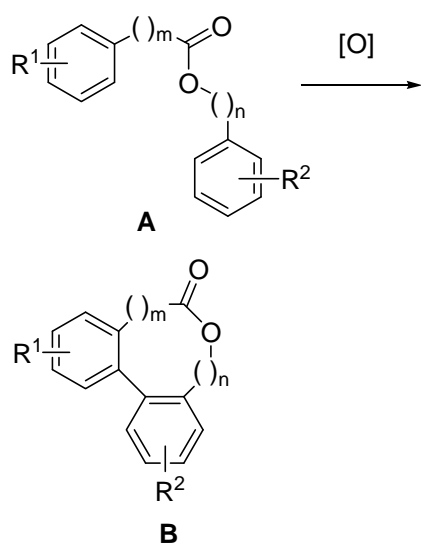
<sup>b</sup>*Chemistry M313, School of Biomedical, Biomolecular and Chemical Sciences, University of Western Australia, Crawley, Western Australia, 6009, Australia*

**Abstract:** The oxidative cyclization of 3,4-dimethoxyphenyl 3,4-dimethoxyphenylacetate, through intramolecular biphenyl bond formation, was successful and gave the target 7-membered lactone in good yield (85-86%). All other ester substrates gave biphenyl products or their further oxidized products via intermolecular coupling of their radical cation intermediate with the neutral substrate. It appears that matching of the oxidation potentials and nucleophilicity of the two phenyl rings, the positioning of the ring substituents and the ease of *E* to *Z* isomerization about the ester C-O bond are important factors contributing to these product outcomes.

As part of a medicinal chemistry project we have explored the oxidative coupling reactions of the ester tethered di-aryl esters **A** aimed at the synthesis of lactones of the type **B** as shown in Scheme 1. While both the intramolecular and intermolecular oxidative couplings of phenyl ethers to give biphenyls using one electron oxidants have been reported, these have generally been restricted to electron rich substrates.<sup>1-28</sup> The intramolecular versions of these reactions have been used to prepare 6-<sup>29-32</sup> and 7-membered<sup>24</sup> carbocyclic ring products using an all-

carbon tether between the two participating aryl ethers,<sup>33</sup> while 6,<sup>32</sup> 7-<sup>24,34,35</sup> and 8-membered<sup>34,35</sup> heterocyclic ring products have been obtained when the tether contains a heteroatom (N, O, S and Si). The use of an ester tether in these types of reaction has not been reported.<sup>36</sup> It was thus of interest to explore the oxidative coupling reactions of **A** with single electron oxidants and to determine the effects of ring size and the electronic properties of the two coupling partners of the efficiencies and product distributions of such reactions.

Scheme 1



### Oxidative coupling reactions of substituted phenyl phenylacetates

Initial experiments focussed on a study of the oxidative coupling reactions of the tetramethoxy substituted phenyl phenylacetate derivative **1a** with the one electron oxidants,  $\text{FeCl}_3/\text{SiO}_2$ ,<sup>1,2</sup>  $\text{MoCl}_5$ ,<sup>3-8</sup>  $\text{VOF}_3$ ,<sup>9-15</sup> thallium(III) trifluoroacetate (TTFA),<sup>16-21</sup>  $\text{Ce}(\text{OH})_4$ ,<sup>22,23</sup> and phenyl iodine(III) bis(trifluoroacetate) (PIFA)<sup>24-28</sup> using literature procedures (Scheme 2). Reactions with the latter three oxidizing reagents required the addition of  $\text{BF}_3 \cdot \text{Et}_2\text{O}$ . The results of these reactions are summarized in Table 1.

Scheme 2

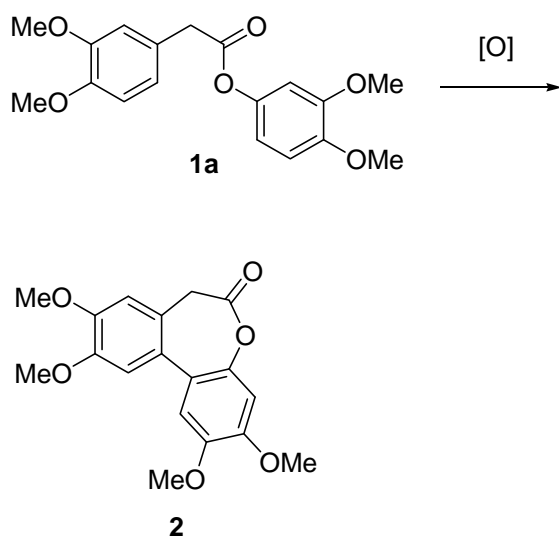


Table 1.

Entry	Oxidant	Conditions	Time	Yield of <b>2</b> (%)
1	FeCl <sub>3</sub> /SiO <sub>2</sub>	CH <sub>2</sub> Cl <sub>2</sub> , rt	6 h	0
2	MoCl <sub>5</sub>	CH <sub>2</sub> Cl <sub>2</sub> , 0° C to rt	2 h	26
3	VOF <sub>3</sub>	TFA, TFAA, CH <sub>2</sub> Cl <sub>2</sub> , EtOAc, 0° C	1 h	60
4	TTFA <sup>1</sup>	TFAA, 0° C	1 h	60
5	TTFA	MeCN, BF <sub>3</sub> .Et <sub>2</sub> O, 0° C	1 h	74
6	Ce(OH) <sub>4</sub>	CH <sub>2</sub> Cl <sub>2</sub> , TFA, BF <sub>3</sub> .Et <sub>2</sub> O, 0° C	6 h	86
7	PIFA <sup>2</sup>	MeCN, BF <sub>3</sub> .Et <sub>2</sub> O, rt	10 min	85

<sup>1</sup> TTFA is thallium(III) trifluoroacetate

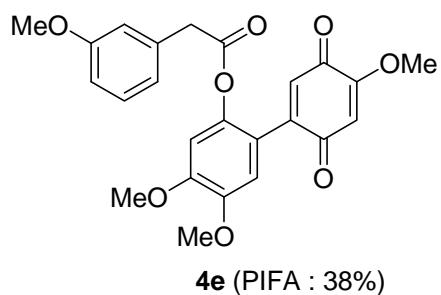
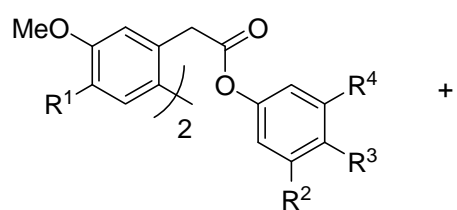
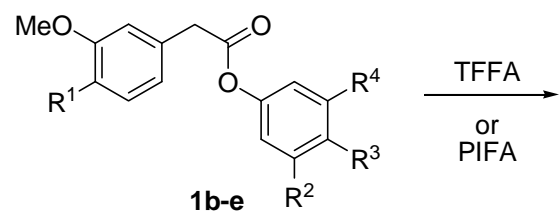
<sup>2</sup> PIFA is phenyl iodine(III) bis(trifluoroacetate)

Clearly the use of PIFA, BF<sub>3</sub>.Et<sub>2</sub>O in MeCN solution at rt for 10 min (Table 1, entry 7) gave the best overall performance in terms of the yield (85%) of **2** and reaction time. This

procedure was far more convenient than the one using hygroscopic  $\text{Ce}(\text{OH})_4$ , even though this reagent gave a slightly higher yield (86%) of **2** (Table 1, entry 6). Thus the PIFA method and that using TTFA (Table 1, entry 5) were employed in subsequent oxidative coupling reactions.

The results of the oxidative couplings of the substituted phenyl phenylacetates **1b-f** with TTFA or PIFA, under the conditions shown in Table 1, are summarized in Scheme 3 (the yields in brackets refer to the reactions with TTFA and PIFA, respectively). Unlike the reactions of **1a**, none of these substrates gave the desired intramolecular cyclization product (**B**,  $m = 1$ ,  $n = 0$ ). Esters **1b-d** ( $\text{R}^1 = \text{OMe}$ ) gave the biphenyl products **3b-d**, through intermolecular coupling of the phenylacetate rings of **1b-d**, while the ester **1e** ( $\text{R}^1 = \text{H}$ ) gave the biphenyl **4e**, formed via the intermolecular coupling of the more electron rich dimethoxy-substituted phenoxy ring, followed by further oxidation of the biphenyl ring system and then hydrolysis to give a *para*-quinone (see Scheme 4 for more details).<sup>36</sup> The ester **1f**, having only one methoxy group on each aromatic ring, was unreactive to the PIFA oxidative conditions. The structure of **3c** was confirmed by a single crystal X-ray study (Figure 1; CCDC 647893). The simpler esters **5** and **7**, representing the phenylacetate and phenoxy ring moieties of **1a-d** and **1e**, respectively gave the related biphenyl product **6** and the *para*-quinone **8**, respectively, upon treatment with TTFA or PIFA (Scheme 4). The structure of **8** was confirmed by a single crystal X-ray study (Figure 2, CCDC 647894). These results indicated that both aromatic rings of **1a** are readily oxidized. This was further supported by the measurements of the oxidation potentials ( $E^0$ ) of compounds **5** and **7** (see Supporting Information for details) which were 1.40 V and 1.41 V, respectively.

**Scheme 3** (the yields in brackets refer to the reactions with TTFA and PIFA, respectively)



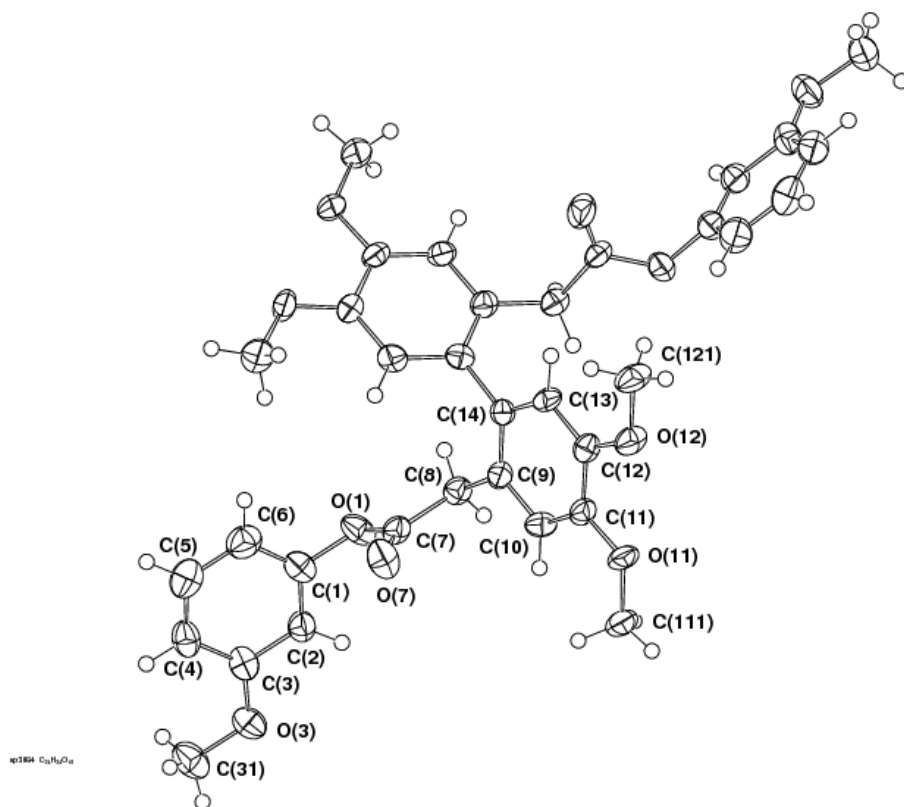
**b**; R<sup>1</sup> = OMe, R<sup>2</sup> = OMe, R<sup>3</sup> = H, R<sup>4</sup> = OMe

**c**; R<sup>1</sup> = OMe, R<sup>2</sup> = OMe, R<sup>3</sup> = H, R<sup>4</sup> = H

**d**; R<sup>1</sup> = OMe, R<sup>2</sup> = H, R<sup>3</sup> = OMe, R<sup>4</sup> = H

**e**; R<sup>1</sup> = H, R<sup>2</sup> = OMe, R<sup>3</sup> = OMe, R<sup>4</sup> = H

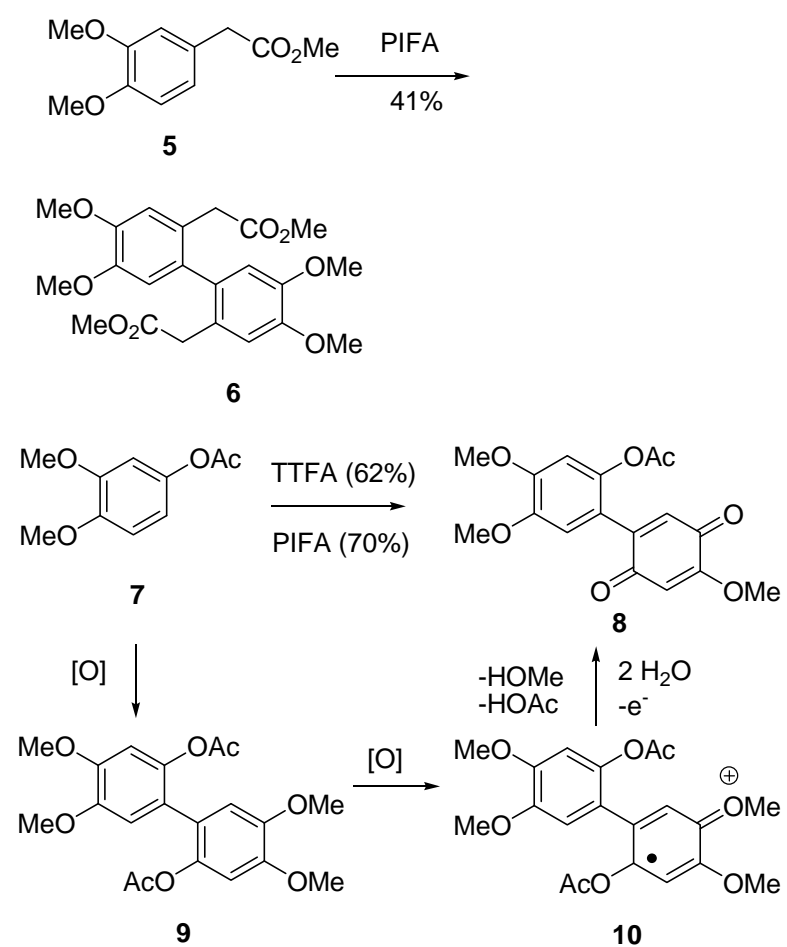
**f**; R<sup>1</sup> = H, R<sup>2</sup> = OMe, R<sup>3</sup> = H, R<sup>4</sup> = H

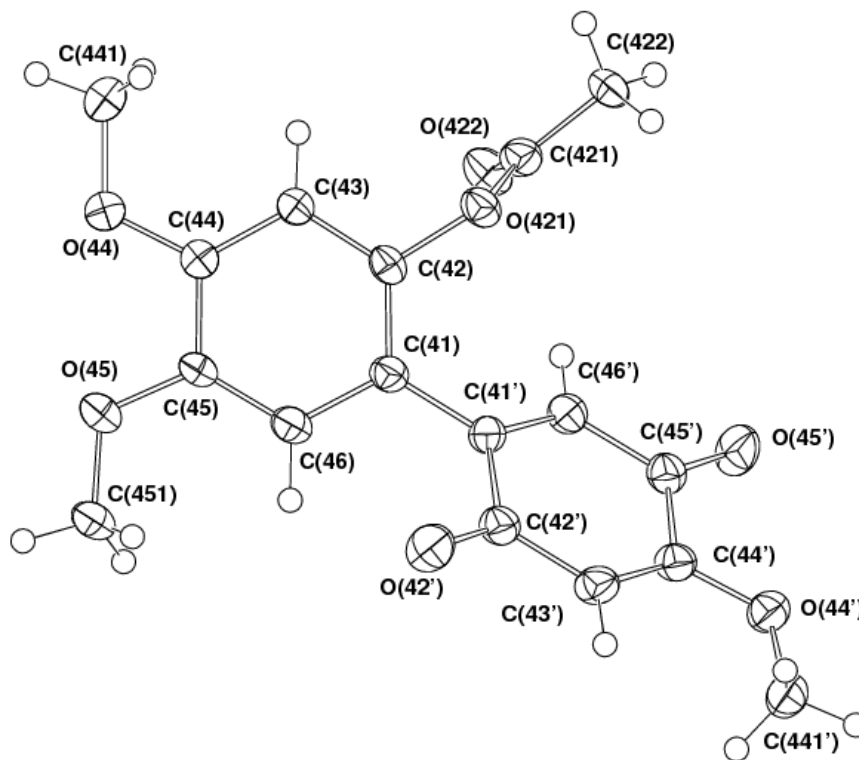


**Figure 1.** Molecular projection of **3c** (50% probability displacement amplitude ellipsoids for non-hydrogen atoms, hydrogen atoms having arbitrary radii of 0.1 Å, here and in Figures 2 and 3).



## Scheme 4



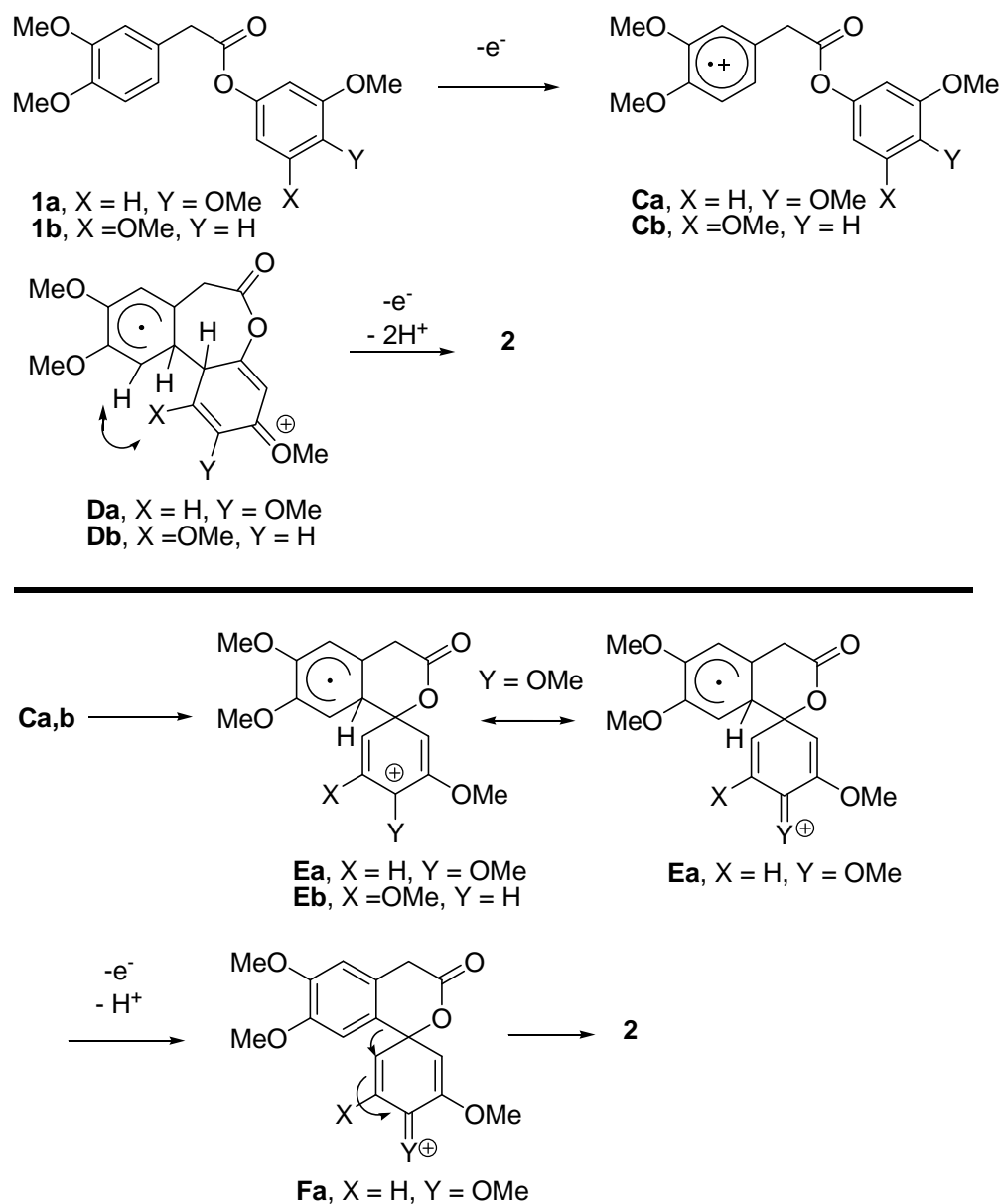


**Figure 2.** Molecular projection of **8** (molecule 1; there are four molecules in the asymmetric unit, molecules 3,4 differing from molecules 1,2 by rotation of *ca* 180 ° about the pendant acetate bond).

Notably, **1b**, the isomeric 3,5-dimethoxyphenyl ester of **1a** failed to provide the corresponding cyclization product analogous to **2**, even though the phenoxy ring of **1b** had the same number of activating methoxy groups as **1a**. Two possible mechanisms for the formation of **2** from **1a** are shown in Scheme 5. In the first mechanism, the radical cation intermediate **Ca** undergoes intramolecular electrophilic attack by the 3,4-dimethoxyphenoxyacyl ring, *para* to the activating methoxy group which also stabilizes intermediate **Da**. While such stabilization is also possible in intermediate **Db**, derived from cyclization of **1b**, this intermediate would be destabilized relative to **Da** due to an unfavourable steric interaction between X (X = OMe) and the CH of the adjoining 6-membered ring (Scheme 5). An alternative mechanism involving the intermediate **E** followed

by a dienone-phenol-like rearrangement is possible for **Ea** but not for **Eb** in which  $Y = H$  because of the relatively poorer stabilization of the intermediate cation.<sup>34</sup>

Scheme 5

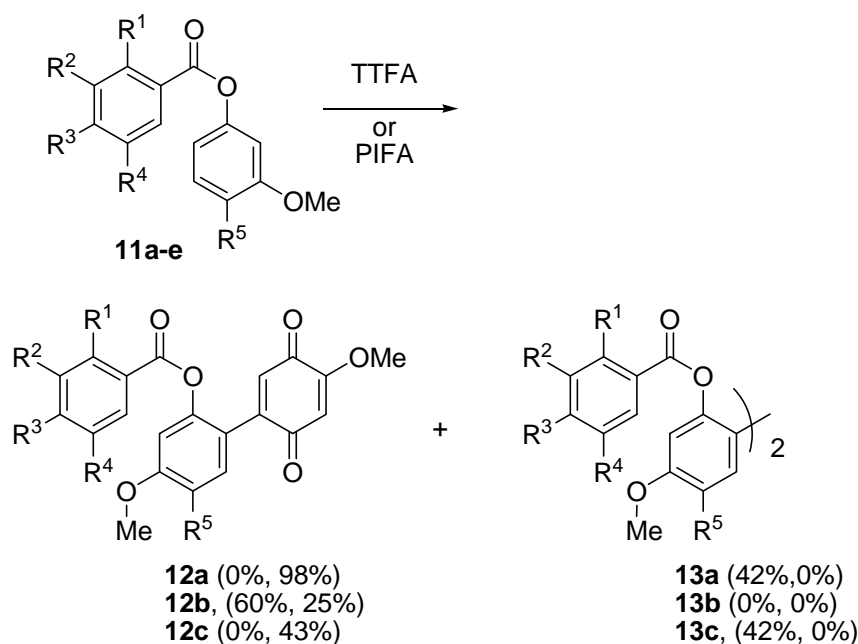


An alternative path, involving oxidation of the phenoxy ring of **1a** first is also possible. Cyclization would lead to an intermediate related to **Da** in which the two 6-membered rings had the reverse electronic nature.

### Oxidative coupling reactions of substituted phenyl benzoates

Treatment of the substituted phenyl benzoates **11a-c** ( $R^5 = \text{OMe}$ ) with PIFA under similar reaction conditions as applied to **1a-f**, provided the *para*-quinones **12 a-c** in variable yields (Scheme 6). Treatment of **11b** with TTFA also provided the quinone **12b**, whereas the esters **11a** and **11c** gave the corresponding biphenyls **13a** and **13c**, respectively (Scheme 6). These products were a result of the initial oxidation and dimerization of the more electron rich 3,4-dimethoxyphenoxy ring. In contrast the esters **11d,e** ( $R^5 = \text{H}$ ) having only one methoxy group of the phenoxy ring, but in the case of **11d** three methoxys on the benzoate ring, gave no isolable oxidation products and in each case the starting ester was recovered (24-57%). These latter results indicated that both the trimethoxybenzoate and the 3-methoxyphenoxy rings in **11d,e** were too deactivated (the former by the carboxylate group) to undergo smooth oxidation.

**Scheme 6** (the yields in brackets refer to the reactions with TTFA and PIFA, respectively)

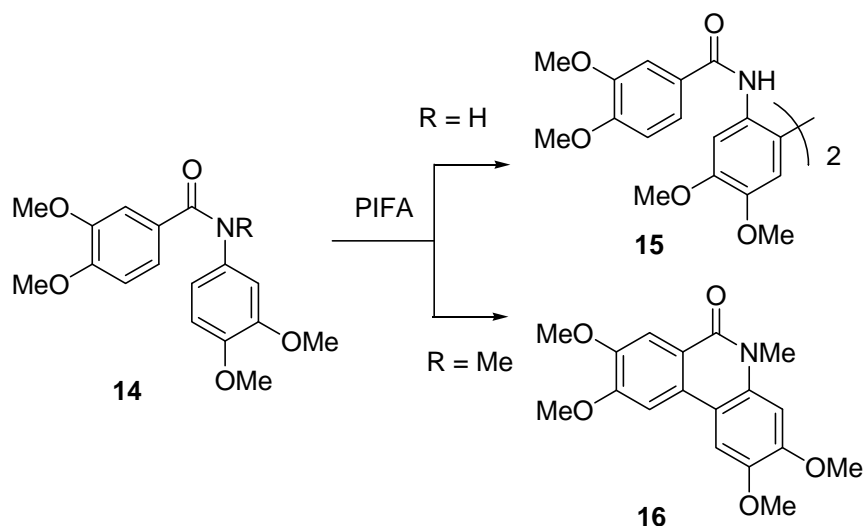


- a**; R<sup>1</sup> = H, R<sup>2</sup> = OMe, R<sup>3</sup> = OMe, R<sup>4</sup> = H, R<sup>5</sup> = OMe  
**b**; R<sup>1</sup> = OMe, R<sup>2</sup> = OMe, R<sup>3</sup> = OMe, R<sup>4</sup> = H, R<sup>5</sup> = OMe  
**c**; R<sup>1</sup> = H, R<sup>2</sup> = OMe, R<sup>3</sup> = OMe, R<sup>4</sup> = OMe, R<sup>5</sup> = OMe  
**d**; R<sup>1</sup> = OMe, R<sup>2</sup> = OMe, R<sup>3</sup> = OMe, R<sup>4</sup> = H, R<sup>5</sup> = H  
**e**; R<sup>1</sup> = H, R<sup>2</sup> = OMe, R<sup>3</sup> = OMe, R<sup>4</sup> = OMe, R<sup>5</sup> = H

The analogous tetramethoxy substituted benzamide **14** (R = H) to **11a** was reported to give the corresponding biphenyl **15** (R = H) through dimerization of the more electron rich aniline ring, while its *N*-methyl derivative **14** (R = Me) gave the cyclization product **16** (Scheme 7).<sup>32</sup> The unsuccessful cyclization of **14** (R = H) has been attributed to the inaccessibility of the *s-cis* (*E*) amide isomer that is required for cyclization. While oxidative cyclization of the esters **1** and **11** would also require them to adopt the energetically less favourable *s-cis* (*E*) isomer this isomer is more readily accessible in the case of esters (*E-Z* energy difference 18-22 kcal mol<sup>-1</sup> for amides and 5-6 kcal mol<sup>-1</sup> for esters)<sup>37</sup> but may also be a contributing factor in the lack of cyclization products being produced from oxidation of these ester substrates. This effect would be more pronounced in the phenyl benzoate ester **11a** when compared to **1a**,

since the *s-cis* (*-E*) isomer would be of higher energy due to the closer proximity of the two phenyl groups.

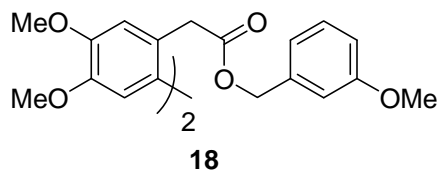
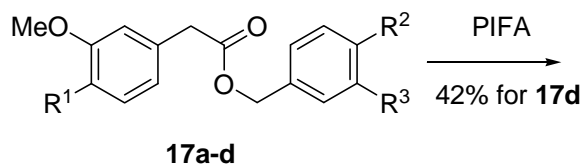
### Scheme 7



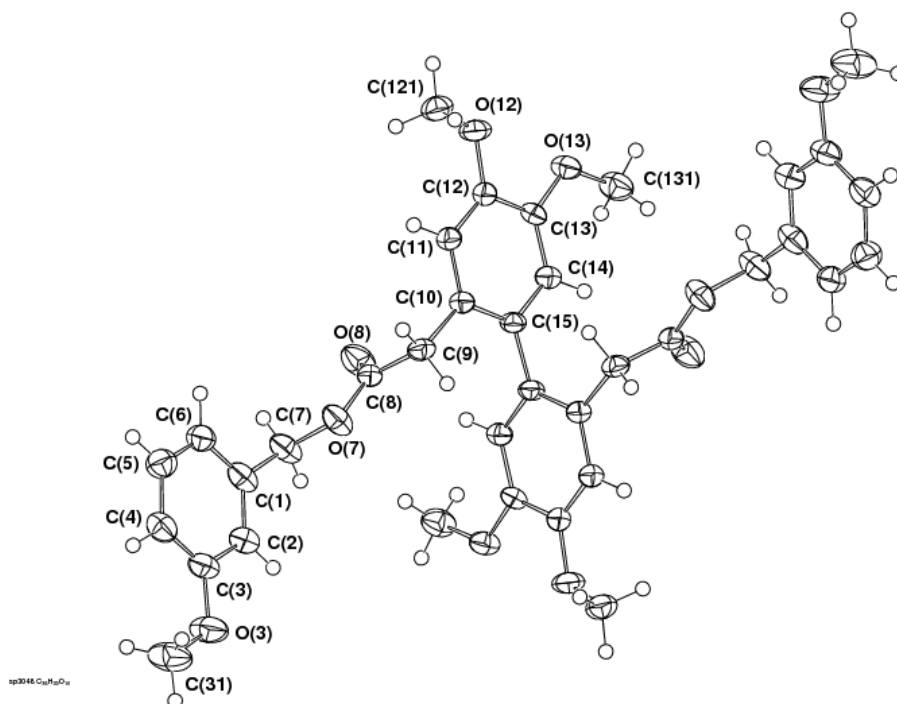
### Oxidative coupling reactions of substituted benzyl phenylacetates

Not surprisingly, exposure of the methoxy substituted benzyl phenylacetates **17a-c** to the above oxidative conditions resulted in oxidative cleavage of the *O*-benzyl group and formation of 3,4-dimethoxy- or 4-methoxybenzaldehyde (Scheme 8). None of the desired cyclization products, or the corresponding biphenyls could be detected from analysis of the crude reaction mixtures. In contrast, the 3-methoxybenzyl ester **17d** was less prone to oxidative cleavage and gave the biphenyl **18** in 45% yield using PIFA. Oxidative coupling of **17d** had occurred through the more electron rich 3,4-dimethoxyphenylacetate aromatic ring. The structure of **18** was confirmed by a single crystal X-ray analysis (Figure 3; CCDC 647895).

## Scheme 8



- a; R<sup>1</sup> = OMe, R<sup>2</sup> = OMe, R<sup>3</sup> = OMe  
 b; R<sup>1</sup> = OMe, R<sup>2</sup> = OMe, R<sup>3</sup> = H  
 c; R<sup>1</sup> = H, R<sup>2</sup> = H, R<sup>3</sup> = OMe  
 d; R<sup>1</sup> = OMe, R<sup>2</sup> = H, R<sup>3</sup> = OMe

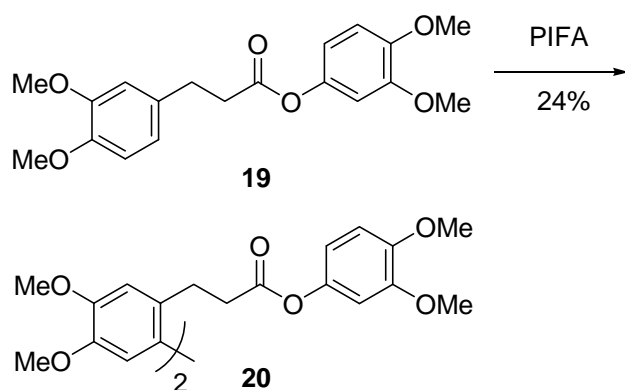


**Figure 3.** Molecular projection of **18**.

The dihydrocinnamate ester **19**, the homologue of **1a**, underwent intermolecular oxidative coupling through the cinnamate aryl ring to give the biphenyl **20** and none of the desired cyclized product, although this would require cyclization through an unfavourable, 8-

membered ring transition state or a less likely 7-membered spiro-intermediate, a homologue of intermediate **E** (Scheme 5). Notably, intramolecular biaryl couplings to form 8-membered heterocyclic rings have been reported using  $-\text{CH}_2\text{N}(\text{TFA})\text{CH}_2\text{CH}_2-$  as a tether on substrates that have the same or less number of methoxy groups as **19** (Scheme 9).<sup>34</sup>

### Scheme 9



In conclusion, the oxidative cyclization of the ester **1a**, through intramolecular biphenyl bond formation, was successful and the target 7-membered lactone **2** was obtained in good yield (85-86%). All other ester substrates gave biphenyl products or their further oxidized products via intermolecular coupling of their radical cation intermediate with the neutral substrate. It appears that matching of the oxidation potentials and nucleophilicity of the two phenyl rings, the positioning of the ring substituents and the ease of *E* to *Z* isomerization about the ester C-O bond are important factors contributing to these product outcomes.

## EXPERIMENTAL

PS refers to the fraction of petroleum spirit with a boiling point of 40-60 °C. DCM refers to dichloromethane. All <sup>1</sup>H NMR spectra were measured at 300 MHz and all <sup>13</sup>C NMR (DEPT) spectra at 75 MHz in CDCl<sub>3</sub> solution, unless otherwise noted. All spectra were referenced to CDCl<sub>3</sub> (<sup>1</sup>H δ 7.26 ppm and <sup>13</sup>C NMR δ 77.00 ppm). <sup>1</sup>H NMR assignments were achieved with the aid of gCOSY, and in some cases NOESY and TOCSY experiments. <sup>13</sup>C NMR



assignments were based upon DEPT, gHSQC and gHMBC experiments. In the NMR assignments Q refers to quinone NMR signals.

### **General Methods for Ester Formation (see Supporting Information for data and procedures for other esters)**

#### **3,4-Dimethoxyphenyl 3,4-dimethoxyphenylacetate 1a.**

To a stirred solution of 3,4-dimethoxyphenyl acetic acid (500 mg, 2.54 mmol), DCC (578 mg, 2.80 mmol) and DMAP (77 mg, 0.637 mmol) in dry DCM (10 mL) was added a solution of 3,4-dimethoxyphenol (373 mg, 2.42 mmol) in dry DCM (2 mL). The reaction was stirred at rt for 18 h under N<sub>2</sub>, diluted with DCM (20 mL), filtered and the filtrate washed with water (20 mL) and saturated NaHCO<sub>3</sub> solution (20 mL). The organic phase was dried over MgSO<sub>4</sub>, filtered, evaporated and the residue chromatographed, using EtOAc:PS (1:1) as the mobile phase, to yield the title compound as a white solid (727 mg, 90 %). Spectral data was consistent with that reported in the literature.<sup>38</sup> M.p. 110-112 °C (lit.<sup>38</sup> m.p. 109-110 °C).

### **General Methods for Oxidative Couplings**

#### **Method A – Hypervalent iodine (PIFA)**

##### **2,3,9,10-Tetramethoxydibenzo[b,d]oxepin-6(7H)-one 2.**

To a solution of **1a** (61 mg, 0.18 mmol) and PIFA (82 mg, 0.19 mmol) in dry MeCN (2 mL) at 0 °C under N<sub>2</sub> was added BF<sub>3</sub>·Et<sub>2</sub>O (100 µL). After 10 min the mixture was diluted with water (15 mL) and extracted with DCM (2 x 20 mL). The extracts were combined, washed with sat. aqueous NaHCO<sub>3</sub> (20 mL), dried over MgSO<sub>4</sub>, filtered and evaporated. Purification by flash silica gel chromatography using EtOAc:PS (1:1) as the eluent, yielded the title compound as a white solid (52 mg, 85 %). This compound was also prepared by oxidative coupling methods B, C, D and E.

#### **Method B – Thallium trifluoroacetate (TTFA)**

To a solution of **1a** (100 mg, 0.30 mmol) and TTFA (163 mg, 0.30 mmol) in dry MeCN (4 mL) at 0 °C under N<sub>2</sub> was added BF<sub>3</sub>·Et<sub>2</sub>O (200 µL). After 1 h the mixture was diluted with water (15 mL) and extracted with DCM (2 x 20 mL). The extracts were combined, washed with sat. aqueous NaHCO<sub>3</sub> (20 mL), dried over MgSO<sub>4</sub>, filtered and evaporated. Purification

by flash silica gel chromatography using EtOAc:PS (1:1) as the eluent yielded the title compound as a white solid (74 mg, 74 %).

#### Method C – MoCl<sub>5</sub>

Compound **1a** (50 mg, 0.15 mmol) was dissolved in dry DCM (2 mL) and was stirred with powdered molecular sieves (4 Å, 100 mg) for 30 min, then the mixture was cooled to 0 °C. MoCl<sub>5</sub> (90 mg, 0.33 mmol) was added to the reaction mixture and stirring was continued at 0 °C for 2 h after which the mixture was diluted with water (15 mL) and extracted with DCM (2 x 20 mL). The extracts were combined, washed with sat. aqueous NaHCO<sub>3</sub> (20 mL), dried over MgSO<sub>4</sub>, filtered and evaporated. Purification by flash silica gel chromatography using EtOAc:PS (1:1) as the eluent yielded the title compound as a white solid (13 mg, 26 %).

#### Method D – Ce(OH)<sub>4</sub>

To a solution of **1a** (50 mg, 0.15 mmol), Ce(OH)<sub>4</sub> (156 mg, 0.75 mmol), TFA (2 mL) and trifluoroacetic anhydride (0.4 mL) in dry DCM (7 mL) at 0 °C under N<sub>2</sub> was added BF<sub>3</sub>·Et<sub>2</sub>O (38 μL). The ice bath was removed and the reaction warmed to RT over 6 h. The reaction was quenched with water (15 mL) and extracted with DCM (2 x 20 mL). The combined extracts were washed with sat. aqueous NaHCO<sub>3</sub> (20 mL), dried over MgSO<sub>4</sub>, filtered and evaporated. Purification by flash silica gel chromatography using EtOAc:PS (1:1) as the eluent yielded the title compound as a white solid (43 mg, 86 %).

#### Method E – VOF<sub>3</sub>

To a solution of TFA:trifluoroacetic anhydride (20:1, 1.5 mL) in dry EtOAc (1.5 mL) at 0 °C was added VOF<sub>3</sub> (47 mg, 0.37 mmol), followed by a solution of **1a** (50 mg, 0.15 mmol) in dry DCM (3 mL). The ice bath was removed and the reaction warmed to RT over 3 h. The reaction was quenched with water (15 mL) and extracted with DCM (2 x 20 mL). The extracts were combined, washed with sat. aqueous NaHCO<sub>3</sub> (20 mL), dried over MgSO<sub>4</sub>, filtered and evaporated. Purification by flash silica gel chromatography using EtOAc:PS (1:1) as the eluent yielded the title compound as a white solid (30 mg, 60 %). Starting material (14 mg, 28 %) was also obtained from the column. M.p. 176-178 °C. <sup>1</sup>H NMR: δ 7.02 (s, 1H, Ar-H-11), 6.94 (s, 1H, Ar-H-1), 6.82 (s, 1H, Ar-H-8), 6.76 (s, 1H, Ar-H-4), 3.92 (s, 6H, OCH<sub>3</sub>-2, 3), 3.88 (s, 3H, OCH<sub>3</sub>-10), 3.87 (s, 3H, OCH<sub>3</sub>-9), 3.51 (ABq, 2H *J* = 12.6 Hz, Ar-CH<sub>2</sub>). <sup>13</sup>C

NMR:  $\delta$  169.4 ( $\underline{\text{C}}=\text{O}$ ), 149.6 (Ar- $\underline{\text{C}}-\text{OCH}_3$ -9), 149.3 (Ar- $\underline{\text{C}}-\text{OCH}_3$ -2), 149.2 (Ar- $\underline{\text{C}}-\text{OCH}_3$ -3), 146.5 (Ar- $\underline{\text{C}}-\text{OCH}_3$ -10), 143.5 (Ar- $\underline{\text{C}}$ -4a), 127.4 (Ar- $\underline{\text{C}}$ -11a), 123.1 (Ar- $\underline{\text{C}}$ -8a), 121.2 (Ar- $\underline{\text{C}}$ -1a), 111.1 (Ar- $\underline{\text{C}}$ -H-8), 110.9 (Ar- $\underline{\text{C}}$ -H-1), 110.2 (Ar- $\underline{\text{C}}$ -H-11), 104.3 (Ar- $\underline{\text{C}}$ -H-4), 56.4 (Ar- $\underline{\text{OCH}}_3$ -2), 56.2 (Ar- $\underline{\text{OCH}}_3$ -3), 56.1 (Ar- $\underline{\text{OCH}}_3$  10), 56.0 (Ar- $\underline{\text{OCH}}_3$  9), 39.6 (Ar- $\underline{\text{CH}}_2$ ). MS (CI<sup>+</sup>):  $m/z$  331 (M+1, 100%), HRMS (EI<sup>+</sup>): Calcd for C<sub>18</sub>H<sub>18</sub>O<sub>6</sub> = 330.1103 (M<sup>+</sup>), found 330.1102.

**(Di-3,5-dimethoxyphenyl)2,2'-(4,4',5,5'-tetramethoxybiphenyl-2,2'-diyl)diacetate 3b.**

The title compound was prepared in 39 % yield (white solid, 37 mg) from **1b** (100 mg, 0.30 mmol) in the presence of PIFA (129 mg, 0.30 mmol), BF<sub>3</sub>·Et<sub>2</sub>O (100  $\mu$ L) and MeCN (3 mL) according to oxidative coupling method A. M.p. 114-116 °C. <sup>1</sup>H NMR:  $\delta$  6.97 (s, 2H, Ar- $\underline{\text{H}}$ -6), 6.79 (s, 2H, Ar- $\underline{\text{H}}$ -3), 6.29 (t, 2H,  $J$  = 2.2 Hz, Ar- $\underline{\text{H}}$ -4'), 6.13 (d, 4H,  $J$  = 2.1 Hz, Ar- $\underline{\text{H}}$ -2', 6'), 3.94 (s, 6H,  $\underline{\text{OCH}}_3$ ), 3.81 (s, 6H,  $\underline{\text{OCH}}_3$ ), 3.71 (s, 12H, 4 x  $\underline{\text{OCH}}_3$ ), 3.61 (ABq, 4H,  $J$  = 15.0 Hz, Ar- $\underline{\text{CH}}_2$ ). <sup>13</sup>C NMR:  $\delta$  170.2 ( $\underline{\text{C}}=\text{O}$ ), 161.0 (2x Ar- $\underline{\text{C}}-\text{OCH}_3$ -3', 5'), 152.1 (Ar- $\underline{\text{C}}$ -1'), 148.4 (Ar- $\underline{\text{C}}-\text{OCH}_3$ -4), 147.8 (Ar- $\underline{\text{C}}-\text{OCH}_3$ -5), 133.0 (Ar- $\underline{\text{C}}$ -1), 124.3 (Ar- $\underline{\text{C}}$ -2), 113.4 (Ar- $\underline{\text{C}}$ -H-3), 112.7 (Ar- $\underline{\text{C}}$ -H-6), 99.9 (2 x Ar- $\underline{\text{C}}$ -H-2', 6'), 98.1 (Ar- $\underline{\text{C}}$ -H-4'), 55.98 (Ar- $\underline{\text{OCH}}_3$ ), 55.92 (Ar- $\underline{\text{OCH}}_3$ ), 55.37 (2x Ar- $\underline{\text{OCH}}_3$ ), 38.3 (Ar- $\underline{\text{CH}}_2$ ). MS (ES<sup>+</sup>):  $m/z$  663 (M+H, 100 %), HRMS (ES<sup>+</sup>): Calcd for C<sub>36</sub>H<sub>39</sub>O<sub>12</sub> = 663.2442 (M+H<sup>+</sup>), found 663.2438.

**Di-(3-methoxyphenyl)2,2'-(4,4',5,5'-tetramethoxybiphenyl-2,2'-diyl)diacetate 3c.**

The title compound was prepared in 81 % yield (pale yellow solid, 107 mg) from **1c** (150 mg, 0.49 mmol) in the presence of PIFA (227 mg, 0.53 mmol), BF<sub>3</sub>·Et<sub>2</sub>O (130  $\mu$ L) and MeCN (5 mL) according to oxidative coupling method A. The title compound was prepared in 97 % yield (yellow film, 116 mg) from **1c** (117 mg, 0.38 mmol) in the presence of TTFA (210 mg, 0.38 mmol), BF<sub>3</sub>·Et<sub>2</sub>O (2000  $\mu$ L) and MeCN (4 mL) according to oxidative coupling method B. M.p. 122-124 °C. <sup>1</sup>H NMR:  $\delta$  7.20 (t, 2H,  $J$  = 8.1 Hz, Ar- $\underline{\text{H}}$ -5'), 6.97 (s, 2H, Ar- $\underline{\text{H}}$ -6), 6.79 (s, 2H, Ar- $\underline{\text{H}}$ -3), 6.74 (dd, 2H,  $J$  = 8.1, 2.1 Hz, Ar- $\underline{\text{H}}$ -6'), 6.54 (dd, 2H,  $J$  = 8.1, 2.1 Hz, Ar- $\underline{\text{H}}$ -4'), 6.50 (t, 2H,  $J$  = 2.1 Hz, Ar- $\underline{\text{H}}$ -2'), 3.94 (s, 6H,  $\underline{\text{OCH}}_3$ -4), 3.79 (s, 6H,  $\underline{\text{OCH}}_3$ -3), 3.73 (s, 6H,  $\underline{\text{OCH}}_3$ -3'), 3.62 (ABq, 4H,  $J$  = 16.2 Hz, Ar- $\underline{\text{CH}}_2$ ). <sup>13</sup>C NMR:  $\delta$  170.3 ( $\underline{\text{C}}=\text{O}$ ), 160.3 (Ar- $\underline{\text{C}}-\text{OCH}_3$ -3'), 151.5 (Ar- $\underline{\text{C}}$ -1'), 148.4 (Ar- $\underline{\text{C}}-\text{OCH}_3$ -3), 147.7 (Ar- $\underline{\text{C}}-\text{OCH}_3$ -4), 132.9 (Ar- $\underline{\text{C}}$ -1), 129.6 (Ar- $\underline{\text{C}}$ -H-5'), 124.3 (Ar- $\underline{\text{C}}$ -2), 113.5 (Ar- $\underline{\text{C}}$ -H-5), 113.4 (Ar- $\underline{\text{C}}$ -H-4'), 112.7 (Ar- $\underline{\text{C}}$ -H-2), 111.5 (Ar- $\underline{\text{C}}$ -H-6'), 107.4 (Ar- $\underline{\text{C}}$ -H-2'), 55.9 (Ar- $\underline{\text{OCH}}_3$ -4), 55.8 (Ar- $\underline{\text{OCH}}_3$ -3), 55.2 (Ar-

OCH<sub>3</sub>-3'), 38.3 (Ar-CH<sub>2</sub>-CO). MS (EI<sup>+</sup>): *m/z* 602 (M<sup>+</sup>, 10 %), 299 (100 %), HRMS (EI<sup>+</sup>): Calcd for C<sub>34</sub>H<sub>34</sub>O<sub>10</sub> = 602.2151 (M<sup>+</sup>), found 602.2160.

**Di-(4-methoxyphenyl)2,2'-(4,4',5,5'-tetramethoxybiphenyl-2,2'-diyl)diacetate 3d.**

The title compound was prepared in 50 % yield (white solid, 49.5 mg) from **1d** (100 mg, 0.28 mmol) in the presence of PIFA (149 mg, 0.34 mmol), BF<sub>3</sub>.Et<sub>2</sub>O (83 μL) and MeCN (5 mL) according to oxidative coupling method A. The title compound was also prepared in 63 % yield (clear film, 49.5 mg) from **1d** (50 mg, 0.14 mmol) in the presence of TTFA (44 mg, 0.082 mmol), BF<sub>3</sub>.Et<sub>2</sub>O (100 μL) and MeCN (1 mL) according to oxidative coupling method B. M.p. 102-104 °C. <sup>1</sup>H NMR: δ 6.97 (s, 2H, Ar-H-6), 6.86 (d, 4H, *J* = 9.0 Hz, Ar-H-2', 6'), 6.82 (d, 4H, *J* = 9.0 Hz, Ar-H-3', 5'), 6.79 (s, 2H, Ar-H-3), 3.95 (s, 6H, OCH<sub>3</sub>), 3.79 (s, 6H, OCH<sub>3</sub>), 3.77 (s, 6H, OCH<sub>3</sub>), 3.59 (ABq, 4H, *J* = 16.2 Hz, Ar-CH<sub>2</sub>). <sup>13</sup>C NMR: δ 170.8 (C=O), 157.1 (Ar-C-OCH<sub>3</sub>-4'), 148.3 (Ar-C-OCH<sub>3</sub>-5), 147.6 (Ar-C-OCH<sub>3</sub>-4), 144.0 (Ar-C-1'), 132.9 (Ar-C-1), 124.3 (Ar-C-2), 122.1 (2 x Ar-C-H-2' 6'), 114.2 (2x Ar-C-H-3', 5'), 113.3 (Ar-C-H-3), 112.6 (Ar-C-H-6), 55.9 (Ar-OCH<sub>3</sub>), 55.8 (Ar-OCH<sub>3</sub>), 55.4 (Ar-OCH<sub>3</sub>), 38.2 (Ar-CH<sub>2</sub>-CO). MS (EI<sup>+</sup>): *m/z* 602 (M<sup>+</sup>, 2 %), HRMS (EI<sup>+</sup>): Calcd for C<sub>34</sub>H<sub>34</sub>O<sub>10</sub> = 602.2151 (M<sup>+</sup>), found 602.2182.

**4,5-Dimethoxy-2-(4-methoxy-3,6-dioxocyclohexa-1,4-dien-1-yl)phenyl (3-methoxyphenyl)acetate 4e.**

The title compound was prepared in 38 % yield (pale film, 34 mg) from 3,4-dimethoxyphenyl (3-methoxyphenyl)acetate **1e** (123 mg, 0.41 mmol) in the presence of PIFA (184 mg, 0.43 mmol), BF<sub>3</sub>.Et<sub>2</sub>O (104 μL) and MeCN (5 mL) according to oxidative coupling method A. <sup>1</sup>H NMR: δ 7.16 (t, 1H, *J* = 7.8 Hz, Ar-H-5), 6.82 (dd, 1H, *J* = 7.8, 2.7 Hz, Ar-H-6), 6.79 (d, 1H, *J* = 2.1 Hz, Ar-H-2), 6.76 (dd, 1H, *J* = 7.8, 2.7 Hz, Ar-H-4), 6.71 (s, 1H, Ar-H-6'), 6.65 (s, 1H, Ar-H-3'), 6.52 (s, 1H, Q-H-b), 5.78 (s, 1H, Q-H-e), 3.87 (s, 3H, OCH<sub>3</sub>-5'), 3.83 (s, 3H, OCH<sub>3</sub>-4'), 3.81 (s, 3H, OCH<sub>3</sub>-3), 3.77 (s, 3H, Q-OCH<sub>3</sub>), 3.66 (s, 2H, Ar-CH<sub>2</sub>). <sup>13</sup>C NMR: δ 185.5 (Q-C=O-c), 181.4 (Q-C=O-f), 169.3 (C=O), 159.6 (Ar-C-OCH<sub>3</sub>-3), 158.0 (Q-C-OCH<sub>3</sub>-d), 150.5 (Ar-C-OCH<sub>3</sub>-4'), 146.7 (Ar-C-OCH<sub>3</sub>-5'), 144.0 (Ar-C-1'), 141.8 (Q-C-a), 134.2 (Ar-C-1), 132.4 (Q-C-H-b), 129.7 (Ar-C-H-5), 121.5 (Ar-C-H-6), 117.4 (Ar-C-2'), 114.5 (Ar-C-H-2), 113.1 (Ar-C-H-4), 112.5 (Ar-C-H-3'), 107.5 (Q-C-H-e), 106.4 (Ar-C-H-6'), 56.2 (Ar-OCH<sub>3</sub>-4'), 56.1 (Ar-OCH<sub>3</sub>-5'), 56.0 (Ar-OCH<sub>3</sub>-3), 55.1 (Q-OCH<sub>3</sub>), 41.3 (Ar-CH<sub>2</sub>). MS

(EI+):  $m/z$  438 ( $M^+$ , 16 %), 292 (100 %) HRMS (EI+): Calcd for  $C_{24}H_{22}O_8 = 438.1314$  ( $M^+$ ), found 438.1331.

#### Dimethyl 2,2'-(4,4',5,5'-tetramethoxybiphenyl-2,2'-diyl)diacetate **6**.<sup>39</sup>

The title compound was prepared in 41 % yield (clear crystals, 53 mg) from **5** (129 mg, 0.62 mmol) in the presence of PIFA (250 mg, 0.58 mmol),  $BF_3 \cdot Et_2O$  (150  $\mu$ L) and MeCN (10 mL) according to oxidative coupling method A. M.p. 142-144 °C (lit.<sup>39</sup> m.p. 145 °C).  $^1H$  NMR:  $\delta$  6.84 (s, 2H, Ar-H-6), 6.72 (s, 2H, Ar-H-3), 3.92 (s, 6H,  $OCH_3$ -5), 3.83 (s, 6H,  $OCH_3$ -4), 3.60 (s, 6H,  $CO_2CH_3$ ), 3.35 (ABq, 4H,  $J = 16.5$  Ar- $\underline{CH_2}$ ).  $^{13}C$  NMR:  $\delta$  172.4 ( $\underline{C=O}$ ), 148.1 (Ar- $\underline{C-OCH_3}$ -4), 147.4 (Ar- $\underline{C-OCH_3}$ -5), 132.8 (Ar- $\underline{C-1}$ ), 124.6 (Ar- $\underline{C-2}$ ), 113.2 (Ar- $\underline{C-H-3}$ ), 112.5 (Ar- $\underline{C-H-6}$ ), 55.8 (Ar- $\underline{OCH_3}$ ), 55.7 (Ar- $\underline{OCH_3}$ ), 51.8 ( $CO_2\underline{CH_3}$ ), 37.9 (Ar- $\underline{CH_2}$ ). MS (CI+):  $m/z$  419 (M+H, 100 %), HRMS (EI+): Calcd for  $C_{22}H_{26}O_8 = 418.1627$  ( $M^+$ ), found 418.1615.

#### 4,5-Dimethoxy-2-(4-methoxy-3,6-dioxocyclohexa-1,4-dien-1-yl)phenyl acetate **8**.

The title compound was prepared in 70 % yield (cloudy film, 49 mg) from **7** (100 mg, 0.51 mmol) in the presence of PIFA (227 mg, 0.53 mmol),  $BF_3 \cdot Et_2O$  (130  $\mu$ L) and MeCN (5 mL) according to oxidative coupling method A. The title compound was also prepared in 62 % yield (clear film, 44 mg) from 3,4-dimethoxyphenylacetate (100 mg, 0.51 mmol) in the presence of TTFA (44 mg, 0.082 mmol),  $BF_3 \cdot Et_2O$  (100  $\mu$ L) and MeCN (1 mL) according to oxidative coupling method B.  $^1H$  NMR:  $\delta$  6.75 (s, 1H, Ar-H-3), 6.73 (s, 1H, Ar-H-6), 6.72 (s, 1H, Q-H-b), 6.03 (s, 1H, Q-H-e), 3.89 (s, 3H,  $-OCH_3$ -5), 3.87 (s, 3H,  $OCH_3$ -4), 3.86 (s, 3H, Q- $\underline{OCH_3}$ ), 2.16 (s, 3H,  $CO\underline{CH_3}$ ).  $^{13}C$  NMR:  $\delta$  185.4 (Q- $\underline{C=O}$ -c), 181.8 (Q- $\underline{C=O}$ -f), 168.9 ( $\underline{C=O}$ ), 158.4 (Q- $\underline{C-OCH_3}$ ), 150.6 (Ar- $\underline{C-OCH_3}$ -5), 146.5 (Ar- $\underline{C-OCH_3}$ -4), 144.2 (Ar- $\underline{C-1}$ ), 142.1 (Q- $\underline{C-a}$ ), 132.2 (Q- $\underline{C-H-b}$ ), 117.1 (Ar- $\underline{C-2}$ ), 112.8 (Ar- $\underline{C-H-3}$ ), 107.7 (Q- $\underline{C-H-e}$ ), 106.6 (Ar- $\underline{C-H-6}$ ), 56.2 (Ar- $\underline{OCH_3}$ -5), 56.1 (Ar- $\underline{OCH_3}$ -4), 56.0 (Q- $\underline{OCH_3}$ ), 20.8 ( $CO\underline{CH_3}$ ). MS (EI+):  $m/z$  332 ( $M^+$ , 16 %), 292 (100 %), HRMS (EI+): Calcd for  $C_{17}H_{16}O_7 = 332.0896$  ( $M^+$ ), found 332.0896.

#### 4,5-Dimethoxy-2-(4-methoxy-3,6-dioxocyclohexa-1,4-dien-1-yl)phenyl 3,4-dimethoxybenzoate **12a**.

The title compound was prepared in 98 % yield (red crystals, 55 mg) from **11a** (79 mg, 0.25 mmol) in the presence of PIFA (112 mg, 0.26 mmol),  $BF_3 \cdot Et_2O$  (63  $\mu$ L) and DCM (5 mL) according to oxidative coupling method A. M.p. 196-198 °C.  $^1H$  NMR:  $\delta$  7.71 (dd, 1H,  $J =$

8.7, 2.1 Hz, Ar-H-6), 7.54 (d, 1H,  $J = 2.1$  Hz, Ar-H-2), 6.91 (d, 1H,  $J = 8.7$  Hz, Ar-H-5), 6.84 (s, 1H, Ar-H-6'), 6.81 (s, 1H, Ar-H-3'), 6.79 (s, 1H, Q-H-b), 5.94 (s, 1H, Q-H-e), 3.95 (s, 3H, OCH<sub>3</sub>), 3.93 (s, 3H, OCH<sub>3</sub>), 3.91 (s, 3H, OCH<sub>3</sub>), 3.90 (s, 3H, OCH<sub>3</sub>), 3.79 (s, 3H, Q-OCH<sub>3</sub>). <sup>13</sup>C NMR:  $\delta$  185.5 (Q-C=O-c), 181.7 (Q-C=O-f), 164.4 (C=O), 158.3 (Q-C-OCH<sub>3</sub>), 153.6 (Ar-C-OCH<sub>3</sub>-3), 150.7 (Ar-C-OCH<sub>3</sub>-4'), 148.7 (Ar-C-OCH<sub>3</sub>-4), 146.6 (Ar-C-OCH<sub>3</sub>-5'), 144.3 (Ar-C-1'), 142.5 (Q-C-a), 132.5 (Q-C-H-b), 124.3 (Ar-C-H-6), 121.1 (Ar-C-1), 117.4 (Ar-C-2'), 112.8 (Ar-C-H-3'), 112.2 (Ar-C-H-2), 110.4 (Ar-C-H-5), 107.7 (Q-C-H-e), 106.7 (Ar-C-H-6'), 56.3 (Ar-OCH<sub>3</sub>), 56.2 (Ar-OCH<sub>3</sub>), 56.1 (Ar-OCH<sub>3</sub>), 56.0 (Ar-OCH<sub>3</sub>), 55.9 (Q-OCH<sub>3</sub>). MS (EI<sup>+</sup>):  $m/z$  454 (M<sup>+</sup>, 2 %), HRMS (EI<sup>+</sup>): Calcd for C<sub>24</sub>H<sub>22</sub>O<sub>9</sub> = 454.1263 (M<sup>+</sup>), found 454.1256.

**4,5-Dimethoxy-2-(4-methoxy-3,6-dioxocyclohexa-1,4-dien-1-yl)phenyl 2,3,4-trimethoxybenzoate 12b.**

The title compound was prepared in 25 % yield (white film, 17 mg) from **11b** (100 mg, 0.28 mmol) in the presence of PIFA (132 mg, 0.35 mmol), BF<sub>3</sub>.Et<sub>2</sub>O (73  $\mu$ L) and MeCN (4 mL) according to method A; and in 60 % yield (42 mg, 97 % brsm) from **11b** (100 mg, 0.28 mmol) in the presence of TTFA (93 mg, 0.17 mmol), BF<sub>3</sub>.Et<sub>2</sub>O (73  $\mu$ L) and MeCN (4 mL) according to oxidative coupling method B. <sup>1</sup>H NMR:  $\delta$  7.63 (d, 1H,  $J = 8.7$  Hz, Ar-H-6), 6.83 (s, 1H, Ar-H-6'), 6.79 (s, 1H, Ar-H-3'), 6.78 (s, 1H, Q-H-b), 6.70 (d, 1H,  $J = 8.7$  Hz, Ar-H-5), 5.95 (s, 1H, Q-H-e), 3.91 (s, 3H, OCH<sub>3</sub>-3), 3.90 (s, 3H, OCH<sub>3</sub>-5'), 3.89 (s, 3H, OCH<sub>3</sub>-2), 3.88 (s, 3H, OCH<sub>3</sub>-4), 3.85 (s, 3H, OCH<sub>3</sub>-4'), 3.79 (s, 3H, Q-OCH<sub>3</sub>). <sup>13</sup>C NMR:  $\delta$  185.5 (Q-C=O-c), 181.8 (Q-C=O-f), 163.1 (C=O), 158.2 (Q-C-OCH<sub>3</sub>-d), 157.8 (Ar-C-OCH<sub>3</sub>-4), 155.3 (Ar-C-OCH<sub>3</sub>-2), 150.6 (Ar-C-OCH<sub>3</sub>-4'), 146.5 (Ar-C-OCH<sub>3</sub>-5'), 144.2 (Ar-C-1'), 142.9 (Q-C-a), 142.5 (Ar-C-OCH<sub>3</sub>-3), 132.4 (Q-C-H-b), 127.3 (Ar-C-H-6), 117.5 (Ar-C-2'), 116.1 (Ar-C-1), 112.9 (Ar-C-H-3'), 107.7 (Q-C-H-e), 106.9 (Ar-C-H-5), 106.8 (Ar-C-H-6'), 61.6 (Ar-OCH<sub>3</sub>-2), 60.8 (Ar-OCH<sub>3</sub>-4), 56.3 (Ar-OCH<sub>3</sub>-4'), 56.2 (Ar-OCH<sub>3</sub>-5'), 56.1 (Ar-OCH<sub>3</sub>-3), 56.0 (Q-OCH<sub>3</sub>). MS (EI<sup>+</sup>):  $m/z$  484 (M<sup>+</sup>, 4 %), 195 (100 %) HRMS (EI<sup>+</sup>): Calcd for C<sub>25</sub>H<sub>25</sub>O<sub>10</sub> = 484.1447 (M<sup>+</sup>), found 484.1459.

**4,5-Dimethoxy-2-(4-methoxy-3,6-dioxocyclohexa-1,4-dien-1-yl)phenyl 3,4,5-trimethoxybenzoate 12c.**

The title compound was prepared in 43 % yield (white solid, 70 mg) from **11c** (100 mg, 0.28 mmol) in the presence of PIFA (132 mg, 0.35 mmol),  $\text{BF}_3 \cdot \text{Et}_2\text{O}$  (73  $\mu\text{L}$ ) and MeCN (4 mL) according to oxidative coupling method A.  $^1\text{H}$  NMR:  $\delta$  7.29 (s, 2H, Ar-H-2,6), 6.82 (s, 1H, Ar-H-6'), 6.80 (s, 1H, Ar-H-3'), 6.79 (s, 1H, Q-H-b), 5.93 (s, 1H, Q-H-e), 3.91 (s, 3H,  $\text{OCH}_3$ -4), 3.90 (s, 3H,  $\text{OCH}_3$ -5'), 3.89 (s, 9H,  $\text{OCH}_3$ -3, 5, 4'), 3.78 (s, 3H, Q- $\text{OCH}_3$ ).  $^{13}\text{C}$  NMR:  $\delta$  185.5 (Q-C=O-c), 181.7 (Q-C=O-f), 164.3 (C=O), 158.4 (Q-C- $\text{OCH}_3$ ), 153.0 (2 x Ar-C- $\text{OCH}_3$ -3, 5), 150.8 (Ar-C- $\text{OCH}_3$ -4'), 146.7 (Ar-C- $\text{OCH}_3$ -5'), 144.3 (Ar-C-1'), 142.9 (Ar-C- $\text{OCH}_3$ -4), 142.4 (Q-C-a), 132.6 (Q-C-H-b), 123.6 (Ar-C-1), 117.4 (Ar-C-2'), 112.8 (Ar-C-H-3'), 107.7 (Q-C-H-e), 107.2 (2 x Ar-C-H-2, 6), 106.7 (Ar-C-H-6'), 60.9 (Ar- $\text{OCH}_3$ -4), 56.3 (Ar- $\text{OCH}_3$ -5'), 56.2 (3 x Ar- $\text{OCH}_3$ -3, 5, 4'), 56.1 (Q- $\text{OCH}_3$ ). MS (EI+):  $m/z$  484 ( $\text{M}^+$ , 24 %), HRMS (EI+): Calcd for  $\text{C}_{25}\text{H}_{24}\text{O}_{10}$  = 484.1369 ( $\text{M}^+$ ), found 484.1367.

#### **4,4',5'5'-Tetramethoxybiphenyl-2,2'-diyl di-(3,4-dimethoxydibenzoate) 13a.**

The title compound was prepared in 42 % yield (clear film, 41 mg) from **11a** (100 mg, 0.29 mmol) in the presence of TTFA (86 mg, 0.16 mmol),  $\text{BF}_3 \cdot \text{Et}_2\text{O}$  (73  $\mu\text{L}$ ) and MeCN (5 mL) according to oxidative coupling method B.  $^1\text{H}$  NMR:  $\delta$  7.65 (dd, 2H,  $J$  = 8.4, 2.1 Hz, Ar-H-6), 7.46 (d, 2H,  $J$  = 2.1 Hz, Ar-H-2), 6.85 (s, 2H, Ar-H-3'), 6.84 (d, 2H,  $J$  = 8.4 Hz, Ar-H-5), 6.81 (s, 2H, Ar-H-6'), 3.91 (s, 6H,  $\text{OCH}_3$ -3), 3.85 (s, 6H,  $\text{OCH}_3$ -5'), 3.84 (s, 6H,  $\text{OCH}_3$ -4'), 3.73 (s, 6H,  $\text{OCH}_3$ -4).  $^{13}\text{C}$  NMR:  $\delta$  165.0 (C=O), 153.3 (Ar-C- $\text{OCH}_3$ -3), 148.6 (Ar-C- $\text{OCH}_3$ -4'), 148.5 (Ar-C- $\text{OCH}_3$ -5'), 146.3 (Ar-C- $\text{OCH}_3$ -4), 141.7 (Ar-C-2'), 124.1 (Ar-C-H-6), 121.6 (Ar-C-1, Ar-C-1'), 113.0 (Ar-C-H-5), 112.1 (Ar-C-H-2), 110.2 (Ar-C-H-6'), 106.3 (Ar-C-H-3'), 55.9 (3 x Ar- $\text{OCH}_3$ -3, 4', 5'), 55.8 (Ar- $\text{OCH}_3$ -4). MS (EI+):  $m/z$  634 ( $\text{M}^+$ , 9 %), 167 (100 %), HRMS (EI+): Calcd for  $\text{C}_{34}\text{H}_{34}\text{O}_{12}$  = 634.2050 ( $\text{M}^+$ ), found 634.2047.

#### **4,4',5,5'-Tetramethoxy-2,2'-diyl di-(3,4,5-trimethoxydibenzoate) 13c.**

The title compound was prepared in 42 % yield (clear film, 41 mg) from **11c** (100 mg, 0.29 mmol) in the presence of TTFA (86 mg, 0.16 mmol),  $\text{BF}_3 \cdot \text{Et}_2\text{O}$  (73  $\mu\text{L}$ ) and MeCN (5 mL) according to oxidative coupling method B.  $^1\text{H}$  NMR:  $\delta$  7.22 (s, 4H, Ar-H-2, 6), 6.86 (s, 4H, Ar-H-3', 6'), 3.89 (s, 6H,  $\text{OCH}_3$ -4), 3.86 (s, 6H,  $\text{OCH}_3$ -5'), 3.81 (s, 12H,  $\text{OCH}_3$ -3, 5), 3.78 (s, 6H,  $\text{OCH}_3$ -4').  $^{13}\text{C}$  NMR:  $\delta$  164.8 (C=O), 152.9 (2 x Ar-C- $\text{OCH}_3$ -3, 5), 148.8 (Ar-C- $\text{OCH}_3$ -5'), 146.5 (Ar-C- $\text{OCH}_3$ -4'), 142.6 (Ar-C- $\text{OCH}_3$ -4), 141.8 (Ar-C-2'), 124.2 (Ar-C-1), 121.6 (Ar-C-1'), 113.1 (Ar-C-H-6'), 107.2 (2 x Ar-C-H-2, 6), 106.1 (Ar-C-H-3'), 60.9 (Ar- $\text{OCH}_3$ -

5'), 56.2 (Ar-OCH<sub>3</sub>-4'), 56.1 (2 x Ar-OCH<sub>3</sub>-3, 5), 56.0 (Ar-OCH<sub>3</sub>-4). MS (EI<sup>+</sup>): *m/z* 694 (M<sup>+</sup>, 18 %), 195 (100 %), HRMS (EI<sup>+</sup>): Calcd for C<sub>36</sub>H<sub>38</sub>O<sub>14</sub> = 694.2262 (M<sup>+</sup>), found 694.2282.

**[Di-(3-methoxybenzyl)]-(4,4',5,5'-tetramethoxybiphenyl-2,2'-diyl)diacetate 18.**

The title compound was prepared in 42 % yield (white solid, 41 mg) from **17d** (100 mg, 0.28 mmol) in the presence of PIFA (142 mg, 0.33 mmol), BF<sub>3</sub>.Et<sub>2</sub>O (73 μL) and MeCN (4 mL) according to oxidative coupling method A. M.p. 102-104 °C. <sup>1</sup>H NMR: δ 7.22 (t, 2H, *J* = 7.8 Hz, Ar-H-5'), 6.84-6.80 (m, 4H, Ar-H-4', 6'), 6.82 (s, 2H, Ar-H-6), 6.76 (t, 2H, *J* = 2.1 Hz, Ar-H-2'), 6.70 (s, 2H, Ar-H-3), 5.00 (ABq, 4H, *J* = 12.3 Hz, Ar-CH<sub>2</sub>-O), 3.86 (s, 6H, OCH<sub>3</sub>-4), 3.75 (s, 6H, OCH<sub>3</sub>-3'), 3.72 (s, 6H, OCH<sub>3</sub>-3), 3.36 (s, 4H, Ar-CH<sub>2</sub>-CO). <sup>13</sup>C NMR: δ 171.7 (C=O), 159.6 (Ar-C-OCH<sub>3</sub>-3'), 148.2 (Ar-C-OCH<sub>3</sub>-4), 147.4 (Ar-C-OCH<sub>3</sub>-3), 137.2 (Ar-C-1'), 132.8 (Ar-C-1), 129.5 (Ar-C-H-5'), 124.6 (Ar-C-2), 120.1 (Ar-C-H-6'), 113.6 (Ar-C-H-4'), 113.4 (Ar-C-H-3), 113.2 (Ar-C-H-6), 112.5 (Ar-C-H-2'), 66.2 (Ar-CH<sub>2</sub>-O), 55.8 (Ar-OCH<sub>3</sub>-4), 55.7 (Ar-OCH<sub>3</sub>-3), 55.1 (Ar-OCH<sub>3</sub>-3'), 38.1 (Ar-CH<sub>2</sub>-CO). MS (EI<sup>+</sup>): *m/z* 630 (M<sup>+</sup>, 10 %), 121 (100 %), HRMS (EI<sup>+</sup>): Calcd for C<sub>36</sub>H<sub>38</sub>O<sub>10</sub> = 630.2465 (M<sup>+</sup>), found 630.2439.

**Di-(3,4-dimethoxyphenyl) 3,3'-(4,4',5,5'-tetramethoxybiphenyl-2,2'-diyl)dipropionate 20.**

The title compound was prepared in 24 % yield (yellow film, 24 mg) from **19** (100 mg, 0.28 mmol) in the presence of PIFA (130 mg, 0.30 mmol), BF<sub>3</sub>.Et<sub>2</sub>O (100 μL) and MeCN (3 mL) according to oxidative coupling method A. <sup>1</sup>H NMR: δ 6.88 (s, 2H, Ar-H-6), 6.78 (d, 2H, *J* = 8.7 Hz, Ar-H-5'), 6.72 (s, 2H, Ar-H-3), 6.49 (dd, 2H, *J* = 8.7, 2.4 Hz, Ar-H-6'), 6.45 (d, 2H, *J* = 2.4 Hz, Ar-H-2'), 3.91 (s, 6H, OCH<sub>3</sub>), 3.85 (s, 6H, OCH<sub>3</sub>), 3.84 (s, 6H, OCH<sub>3</sub>), 3.80 (s, 6H, OCH<sub>3</sub>), 2.93-2.72 (m, 4H, Ar-CH<sub>2</sub>), 2.64 (t, 4H, *J* = 7.2 Hz, Ar-CH<sub>2</sub>-CH<sub>2</sub>). <sup>13</sup>C NMR: δ 171.6 (C=O), 149.2 (Ar-C-OCH<sub>3</sub>-3'), 148.2 (Ar-C-OCH<sub>3</sub>-3), 147.0 (Ar-C-OCH<sub>3</sub>-4), 146.7 (Ar-C-OCH<sub>3</sub>-4'), 144.1 (Ar-C-1'), 132.5 (Ar-C-1), 130.2 (Ar-C-2), 113.4 (Ar-C-H-3), 112.6 (Ar-C-H-6'), 112.1 (Ar-C-H-6), 111.0 (Ar-C-H-5'), 105.5 (Ar-C-H-2'), 56.0 (Ar-OCH<sub>3</sub>), 55.9 (2 x Ar-OCH<sub>3</sub>), 55.8 (Ar-OCH<sub>3</sub>), 35.3 (Ar-CH<sub>2</sub>-CH<sub>2</sub>), 28.2 (Ar-CH<sub>2</sub>). MS (EI<sup>+</sup>): *m/z* 690 (M<sup>+</sup>, 14 %), HRMS (EI<sup>+</sup>): Calcd for C<sub>38</sub>H<sub>43</sub>O<sub>12</sub> = 691.2755 (M<sup>+</sup>), found 691.2726.



**REFERENCES**

1. Jempty, T. C.; Gogins, K. A. Z.; Mazur, Y.; Miller, L. L. *J. Org. Chem.* **1981**, *46*, 4545-4551.
2. Jempty, T. C.; Miller, L. L.; Mazur, Y. *J. Org. Chem.* **1980**, *45*, 749-751.
3. Waldvogel, S. R. *Synlett* **2002**, *4*, 622-624.
4. Kramer, B.; Frohlich, R.; Bergander, K.; Waldvogel, S. R. *Synthesis* **2003**, *1*, 91-96.
5. Kumar, S.; Manickam, M. *Chem. Commun.* **1997**, 1615-1616.
6. Mirk, D.; Wibbeling, B.; Frohlich, R.; Waldvogel, S. R. *Synlett* **2004**, *11*, 1970-1974.
7. Waldvogel, S. R.; Aits, E.; Holst, C.; Frohlich, R. *Chem. Commun.* **2002**, 1278-127.
8. Kumar, S.; Manickam, M. *Chem. Commun.* **1997**, 1615-1616.
9. Schwartz, M. A.; Rose, B. F.; Holton, R. A.; Scott, S. W.; Vishnuvajjala, B. *J. Am. Chem. Soc.* **1977**, *99*, 2571-2578.
10. Elliot, I. W. *J. Org. Chem.* **1977**, *42*, 1090-1093.
11. Kupchan, S. M.; Liepa, A. J.; Kameswaran, V.; Bryan, R. F. *J. Am. Chem. Soc.* **1973**, *95*, 6861-6863.
12. Damon, R. E.; Schlessinger, R. H.; Blount, J. F. *J. Org. Chem.* **1976**, *41*, 3772-3773.
13. Kupchan, S. M.; Dhingra, O. P.; Kim, C-K.; Kameswaran, V. *J. Org. Chem.* **1976**, *41*, 4047-4049.
14. Kupchan, S. M.; Dhingra, O. P.; Kim, C-K.; Kameswaran, V. *J. Org. Chem.* **1978**, *43*, 2521-2529.
15. Kupchan, S. M.; Kameswaran, V.; Lynn, J. T.; Williams, D. K.; Liepa, A. J. *J. Am. Chem. Soc.* **1975**, *97*, 5622-5623.
16. Morimoto, T.; Chiba, M.; Achiwa, K. *Tetrahedron* **1993**, *49*, 1793-1806.
17. Kende, A. S.; Liebeskind, L. S.; Mills, J. E.; Rutledge, P. S.; Curran, D. P. *J. Am. Chem. Soc.* **1977**, *99*, 7082-7083.
18. Evans, D. A.; Cain, P. A.; Wong, R. Y. *J. Am. Chem. Soc.* **1977**, *99*, 7083-7085.

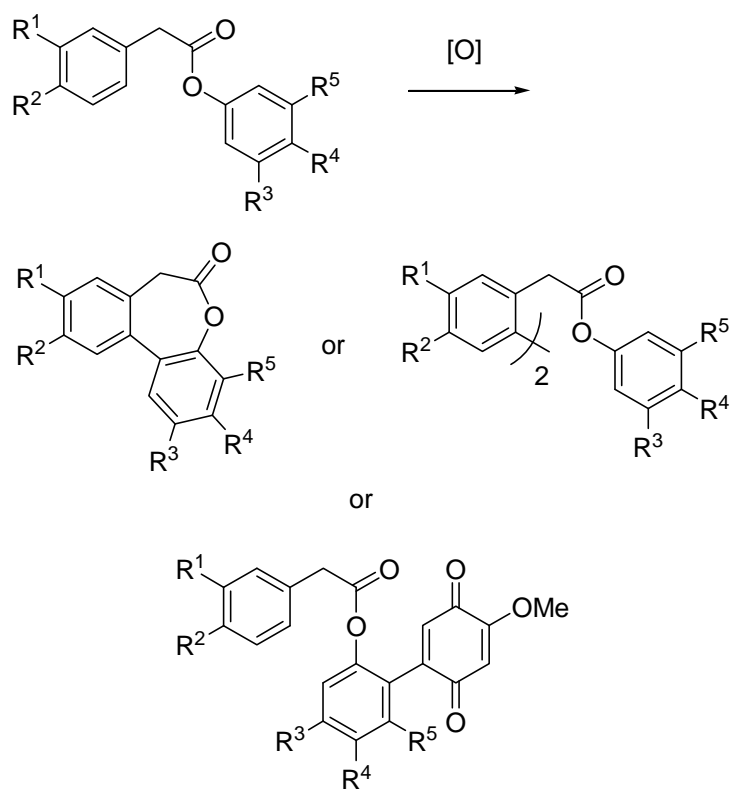
19. McKillop, A.; Turrell, A. G.; Young, D. W.; Taylor, E. C. *J. Am. Chem. Soc.* **1980**, *102*, 6504-6512.
20. Taylor, E. C.; Andrade, J. G.; Rall, G. J. H.; McKillop, A. *J. Am. Chem. Soc.* **1980**, *102*, 6513-6519.
21. Lau, W.; Kochi, J. K. *J. Am. Chem. Soc.* **1984**, *106*, 7100-7112.
22. Norman, R. O. C.; Thomas, C. B.; Ward, P. J. *J. Chem. Soc. Perkin Trans. 1* **1973**, 2914-2917.
23. Planchenault, D.; Dhal, R.; Robin, J-P. *Tetrahedron* **1993**, *49*, 5823-5830.
24. Tohma, H.; Morioka, H.; Takizawa, S.; Arisawa, M.; Kita, Y. *Tetrahedron* **2001**, *57*, 345-352.
25. Arisawa, M.; Utsumi, S.; Nakajima, M.; Ramesh, N. G.; Tohma, H.; Kita, Y. *Chem. Commun* **1999**, 469-470.
26. Kita, Y.; Takada, T.; Gyoten, M.; Tohma, H.; Zenk, M. H.; Eichhorn, J. *J. Org. Chem.* **1996**, *61*, 5857-5864.
27. Hamamoto, H.; Anilkumar, G.; Tohma, H.; Kita, Y. *Chem. Commun.* **2002**, 450-451
28. Tohma, H.; Kita, Y. *Top. Curr. Chem.* **2003**, *224* (Hypervalent iodine chemistry), 209-248
29. Olivera, R.; San Martin, R.; Dominguez, E. *J. Org. Chem.* **2000**, *65*, 7010-7019.
30. Churruca, F.; San Martin, R.; Tellitu, I.; Dominguez, E. *Eur. J. Org. Chem.* **2005**, 2481-2490.
31. Moreno, I.; Tellitu, I.; Dominguez, E.; San Martin, R. *Eur. J. Org. Chem.* **2002**, 2126-2135.
32. Moreno, I.; Tellitu, I.; Etayo, J.; San Martin, R.; Dominguez, E. *Tetrahedron* **2001**, *57*, 5403-5411.

33. Carbocycles have also been generated from bis(3,4-dimethoxyphenyl) alkanes phenyl ethers by electrochemical oxidation, see: Ronlan, A.; Parker V. D. *J. Am. Chem. Soc.* **1974**, *39*, 1014-1016.
34. Hamamoto, H.; Anilkumar, G.; Tohma, H.; Kita, Y. *Chem. Eur. J.* **2002**, *8*, 5377-5383.
35. Takada, T.; Arisawa, M.; Gyoten, M.; Hamada, R.; Tohma, H.; Kita, Y. *J. Org. Chem.* **1998**, *63*, 7698-7706.
36. The electrochemical oxidation of diaryl esters has been shown to give in one case a diphenyl derivative from intermolecular coupling. Further oxidation of this compound gave a *para*-quinone product. Other esters gave oligomeric products, see: Sainsbury, M.; Wyatt, J. *J. Chem. Soc. Perkin Trans. 1* **1979**, 108-114.
37. *Stereochemistry of Organic Compounds*, Eliel, E. L.; Wilen, S. H.; Editors, Wiley, New York, 1994, pp 618-620.
38. Elliott, I. W.; Sloan, M. J.; Tate, E. *Tetrahedron* **1996**, *52*, 8063-8072.
39. Cromartje, R. I. T.; Harley-Mason, J.; Wannigama, D. G. P. *J. Chem. Soc.* **1958**, 1981-198.

**Acknowledgments:**

We thank Johnson and Johnson Research Pty. Limited, Sydney and the University of Wollongong for supporting this research and Dr. Wayne Gerlach for encouragement and support.

## GRAPHICAL ABSTRACT

**Intramolecular versus intermolecular oxidative couplings of ester tethered di-aryl ethers**Stephen R. Taylor, Alison T. Ung and Stephen G. Pyne Brian W. Skelton and Allan H. White<sup>b</sup>*Department of Chemistry, University of Wollongong, Wollongong, NSW, 2522, Australia**Chemistry M313, School of Biomedical, Biomolecular and Chemical Sciences, University of Western Australia, Crawley, Western Australia, 6009, Australia*

## **Intramolecular versus intermolecular oxidative couplings of ester tethered di-aryl ethers**

Stephen R. Taylor, Alison T. Ung<sup>\*</sup> and Stephen G. Pyne<sup>\*</sup> Brian W. Skelton<sup>b</sup> and Allan H. White<sup>b</sup>

<sup>a</sup>*Department of Chemistry, University of Wollongong, Wollongong, NSW, 2522, Australia*

<sup>b</sup>*Department of Chemistry, University of Western Australia, Crawley, Western Australia, 6009, Australia*

### **Supporting Information**

#### **Structure determinations**

Full spheres of 'low-temperature' CCD area-detector diffractometer data were measured (Bruker AXS instrument,  $\omega$ -scans; monochromatic Mo K $\alpha$  radiation;  $\lambda = 0.71073 \text{ \AA}$ ;  $T \text{ ca. } 153 \text{ K}$ ), yielding  $N_{\text{(total)}}$  reflections, these merging to  $N$  unique ( $R_{\text{int}}$  cited) after 'empirical'/multiscan absorption correction,  $N_0$  with  $F > 4\sigma(F)$  considered 'observed'. Conventional residuals  $R$ ,  $R_w$  (weights:  $(\sigma^2(F^2) + n F^2)^{-1}$ ) are cited on the latter convergence, the full matrix least squares refinement refining anisotropic displacement parameters for C, O,  $(x,y,z,U_{\text{iso}})_H$  being included, constrained at estimates. Neutral atom complex scattering factors were employed within the XTAL 3.7 program system.\* Molecular projections are shown in the Figures, C, O with 50% probability amplitude displacement envelopes, H

---

\* S.R. Hall, D.J. du Boulay, R. Olthof-Hazekamp (eds.), 'The Xtal 3.7 System', University of Western Australia, 2001.

having arbitrary radii of 0.1 Å. Full .cif depositions (excluding structure factor amplitudes) reside with the Cambridge Crystallographic Data Base, CCDC 647893-647895; the results are consistent with the stoichiometries and connectivities as presented.

### Crystal/refinement data

**3c.**  $C_{34}H_{34}O_{10}$ ,  $M = 602.7$ . Orthorhombic, space group  $Pba2$  ( $C_{2v}^8$ , No. 32),  $a = 13.074(8)$ ,  $b = 23.014(12)$ ,  $c = 4.844(2)$  Å,  $V = 1457$  Å<sup>3</sup>.  $D_c$  ( $Z = 2$ ) = 1.37<sub>3</sub> g cm<sup>-3</sup>.  $\mu_{Mo} = 0.10$  mm<sup>-1</sup>; specimen: 0.16 x 0.15 x 0.15 mm;  $T_{min/max} = 0.80$ .  $2\theta_{max} = 50^\circ$ ;  $N_t = 5224$ ,  $N = 1330$  ( $R_{int} = 0.060$ ),  $N_o = 981$ ;  $R = 0.048$ ,  $R_w$  ( $n = 5$ ) = 0.098;  $S = 0.98$ .  $|\Delta\rho_{max}| = 0.35$  e Å<sup>-3</sup>.

*Comment.* The molecule is disposed about a crystallographic 2-axis, one half comprising the asymmetric unit of the structure. In the present and following structure, 'Friedel' data were merged in the refinement.

**8.**  $C_{17}H_{16}O_7$ ,  $M = 332.3$ . Monoclinic, space group  $Cc$  ( $C_s^4$ , No. 9),  $a = 23.144(4)$ ,  $b = 18.658(3)$ ,  $c = 15.415(3)$  Å,  $\beta = 110.525(4)^\circ$ ,  $V = 6234$  Å<sup>3</sup>.  $D_c$  ( $Z = 16$ ) = 1.37<sub>3</sub> g cm<sup>-3</sup>.  $\mu_{Mo} = 0.11$  mm<sup>-1</sup>; specimen: 0.50 x 0.34 x 0.32 mm;  $T_{min/max} = 0.92$ .  $2\theta_{max} = 65^\circ$ ;  $N_t = 43567$ ,  $N = 11364$  ( $R_{int} = 0.040$ ),  $N_o = 8198$ ;  $R = 0.065$ ,  $R_w$  ( $n = 25$ ) = 0.14;  $S = 1.02$ .  $|\Delta\rho_{max}| = 0.56$  e Å<sup>-3</sup>.

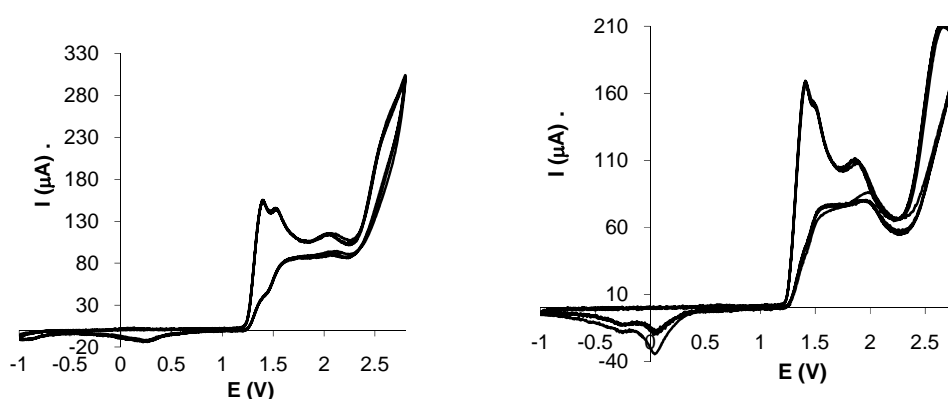
*Comment.* The crystal packing is spectacular, molecular planes being disposed quasi-normal to  $a^*$  with pseudo-symmetry evident among the four molecules of the asymmetric unit. The latter may be partitioned as molecules, 1,2 // 3,4 depending on the orientation of the pendant acetate groups. Relevant dihedral angles (degree) are as follows:

Mol	1	2	3	4
C(n2)-C(n1)-O(n1')-C(n2')	138.7(3)	134.3(4)	128.5(4)	133.3(4)
C(n1)-C(n2)-O(n21)-C(n21)	-103.(3)	-95.5(4)	103.4(4)	106.9(4)
C(n3')-C(n4')-O(n4')-C(n41')	0.0(6)	-3.4(6)	-4.5(6)	-1.9(6)
$\theta(\text{ar}(C_6)/\text{ar}'(C_6))$	40.0(2)	46.6(2)	52.2(2)	46.9(2)

18.  $C_{36}H_{38}O_{10}$ ,  $M = 630.7$ . Monoclinic, space group  $P2/c$  ( $C_{2h}^4$ , No.13),  $a = 11.716(3)$ ,  $b = 5.249(1)$ ,  $c = 25.763(7)$  Å,  $\beta = 110.311(5)^\circ$ ,  $V = 1559$  Å<sup>3</sup>.  $D_c$  ( $Z = 2$ ) =  $1.34_4$  g cm<sup>-3</sup>.  $\mu_{Mo} = 0.10$  mm<sup>-1</sup>; specimen: 0.16 x 0.16 x 0.10 mm;  $T_{min/max} = 0.86$ .  $2\theta_{max} = 50^\circ$ ;  $N_t = 11791$ ,  $N = 2753$  ( $R_{int} = 0.074$ ),  $N_o = 1729$ ;  $R = 0.055$ ,  $R_w$  ( $n_w = 9$ );  $S = 0.98$ .  $|\Delta\rho_{max}| = 0.47$  e Å<sup>-3</sup>.

### Cyclic Voltammetry

Compounds were dissolved in degassed MeCN containing 0.1 M LiClO<sub>4</sub> and diluted to 0.01 M, and then subjected to anodic oxidation in an undivided beaker-type cell (50 mL). The working electrode was a 1 mm platinum disk, the auxiliary electrode was platinum mesh and the reference was an Ag/Ag<sup>+</sup> (Ag wire dipped in to a solution containing 0.01 M AgNO<sub>3</sub> and 0.1 M tetrabutylammonium perchlorate in MeCN). Scan rates were 100 mV/s.



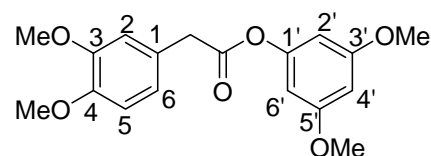
**Figure** The Cyclic Voltammograms obtained following the electrochemical oxidation of compounds a) **6** and b) **7** as 0.01 M solutions in MeCN.

### Synthesis of Esters

All <sup>1</sup>H NMR spectra were performed at 300 MHz and all <sup>13</sup>C NMR (DEPT) spectra at 75 MHz in CDCl<sub>3</sub> solution, unless otherwise noted. All spectra were referenced to CDCl<sub>3</sub> (<sup>1</sup>H δ 7.26 ppm and <sup>13</sup>C

NMR  $\delta$  77.00 ppm).  $^1\text{H}$  NMR assignments were achieved with the aid of gCOSY, and in some cases NOESY and TOCSY experiments.  $^{13}\text{C}$  NMR assignments were based upon DEPT, gHSQC and gHMBC experiments. \* Indicates individual OMe resonances were not assigned.

### 3,4-Dimethoxyphenyl 3,5-dimethoxyphenylacetate **1b**



The title compound was prepared in 92 % yield (cream solid, 497 mg) from 3,4-dimethoxyphenylacetic acid (318 mg, 1.6 mmol) and 3,5-dimethoxyphenol (300 mg 1.94 mmol) in the presence of DCC (367 mg, 1.78 mmol), DMAP (47 mg, 0.38 mmol) and DCM (6 mL) as for **1a**.

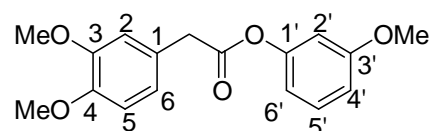
m.p. 94-96 °C

$^1\text{H}$  NMR:  $\delta$  6.91 (d, 1H,  $J = 2.0$  Hz, Ar-H-2), 6.90 (dd, 1H,  $J = 8.9, 2.0$  Hz, Ar-H-6), 6.83 (d, 1H,  $J = 8.9$  Hz, Ar-H-5), 6.31 (t, 1H,  $J = 2.1$  Hz, Ar-H-4'), 6.23 (d, 2H,  $J = 2.1$  Hz, Ar-H-2', 6'), 3.87 (s, 3H, OCH<sub>3</sub>), 3.86 (s, 3H, OCH<sub>3</sub>), 3.76 (s, 2H, Ar-CH<sub>2</sub>), 3.72 (s, 6H, OCH<sub>3</sub>).

$^{13}\text{C}$  NMR:  $\delta$  169.8 (C=O), 160.9 (2 x Ar-C-OCH<sub>3</sub>-3', 5'), 152.0 (Ar-C-OCH<sub>3</sub>-1'), 148.7 (Ar-C-OCH<sub>3</sub>-3), 148.1 (Ar-C-OCH<sub>3</sub>-4), 125.5 (Ar-C-1'), 121.3 (Ar-C-H-6), 112.1 (Ar-C-H-5), 111.0 (Ar-C-H-2), 99.8 (2x Ar-C-H-2', 6'), 97.9 (Ar-C-H-4'), 55.6 (Ar-OCH<sub>3</sub>)\*, 55.2 (Ar-OCH<sub>3</sub>)\*, 40.6 (Ar-CH<sub>2</sub>-).

MS (CI<sup>+</sup>):  $m/z$  333 (M+H<sup>+</sup>, 100 %), HRMS (CI<sup>+</sup>): Calcd for C<sub>18</sub>H<sub>21</sub>O<sub>6</sub> = 333.1338 (M+H<sup>+</sup>), found 333.1332.

### 3,4-Dimethoxyphenyl 3-methoxyphenylacetate **1c**



The title compound was prepared in 83 % yield (clear oil, 822 mg) from 3,4-dimethoxyphenylacetic acid (640 mg, 3.26 mmol) and 3-methoxyphenol (0.524 mL, 4.83 mmol) in the presence of DCC (740 mg, 3.58 mmol), DMAP (100 mg, 8.18 mmol) and DCM (12 mL) as for **1a**.

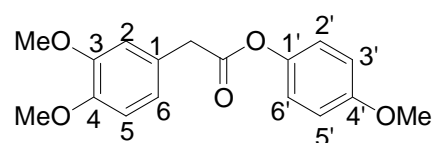
$^1\text{H}$  NMR:  $\delta$  7.24 (t, 1H,  $J = 8.1$  Hz, Ar-H-5'), 6.91-6.89 (m, 2H, Ar-H-2, 6), 6.84 (d, 1H,  $J = 8.6$  Hz, Ar-H-5), 6.75 (dd, 1H,  $J = 8.1, 2.1$  Hz, Ar-H-6'), 6.65 (dd, 1H,  $J = 8.1, 2.1$  Hz, Ar-H-4'), 6.62 (t, 1H,  $J = 2.1$  Hz, Ar-H-2'), 3.87 (s, 3H, OCH<sub>3</sub>)\*, 3.85 (s, 3H, OCH<sub>3</sub>)\*, 3.77 (s, 2H, Ar-CH<sub>2</sub>), 3.74 (s, 3H, OCH<sub>3</sub>-3').



$^{13}\text{C}$  NMR:  $\delta$  169.9 ( $\text{C}=\text{O}$ ), 160.2 ( $\text{Ar}-\text{C}-\text{OCH}_3-3'$ ), 151.4 ( $\text{Ar}-\text{C}-1'$ ), 148.7 ( $\text{Ar}-\text{C}-\text{OCH}_3-3$ ), 148.0 ( $\text{Ar}-\text{C}-\text{OCH}_3-4$ ), 129.5 ( $\text{Ar}-\text{C}-\text{H}-5'$ ), 125.6 ( $\text{Ar}-\text{C}-1$ ), 121.3 ( $\text{Ar}-\text{C}-\text{H}-6$ ), 113.4 ( $\text{Ar}-\text{C}-\text{H}-5$ ), 112.1 ( $\text{Ar}-\text{C}-\text{H}-4'$ ), 111.4 ( $\text{Ar}-\text{C}-\text{H}-6'$ ), 111.0 ( $\text{Ar}-\text{C}-\text{H}-2$ ), 107.3 ( $\text{Ar}-\text{C}-\text{H}-2'$ ), 55.6 (2 x  $\text{Ar}-\text{OCH}_3-3, 4$ ), 55.1 ( $\text{Ar}-\text{OCH}_3-3'$ ), 40.6 ( $\text{Ar}-\text{CH}_2-\text{CO}$ ).

MS (EI+):  $m/z$  302 ( $\text{M}^+$ , 39 %), 151 (100 %), HRMS (EI+): Calcd for  $\text{C}_{17}\text{H}_{18}\text{O}_5 = 302.1154$  ( $\text{M}^+$ ), found 302.1148.

### 3,4-Dimethoxyphenyl 4-methoxyphenylacetate **1d**



The title compound was prepared in 86 % yield (white solid, 848 mg) from 3,4-dimethoxyphenylacetic acid (640 mg, 3.26 mmol) and 4-methoxyphenol (600 mg 4.83 mmol) in the presence of DCC (740 mg, 3.58 mmol), DMAP (100 mg, 8.18 mmol) and DCM (12 mL) as for **1a**.

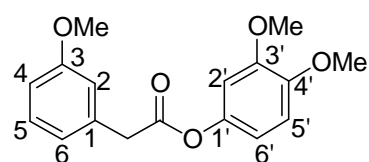
m.p. 54-56 °C

$^1\text{H}$  NMR:  $\delta$  6.97 (d, 2H,  $J = 9.3$  Hz,  $\text{Ar}-\text{H}-2', 6'$ ), 6.93 (d, 1H,  $J = 9.3$  Hz,  $\text{Ar}-\text{H}-5$ ), 6.90 (dd, 1H,  $J = 9.3, 3.0$  Hz,  $\text{Ar}-\text{H}-6$ ), 6.87 (d, 2H,  $J = 9.3$  Hz,  $\text{Ar}-\text{H}-3', 5'$ ), 6.86 (d, 1H,  $J = 3.0$  Hz,  $\text{Ar}-\text{H}-2$ ), 3.89 (s, 3H,  $\text{OCH}_3$ )\*, 3.88 (s, 3H,  $\text{OCH}_3$ )\*, 3.78 (s, 3H,  $\text{OCH}_3$ )\*, 3.77 (s, 2H,  $\text{Ar}-\text{CH}_2$ ).

$^{13}\text{C}$  NMR:  $\delta$  170.7 ( $\text{C}=\text{O}$ ), 157.1 ( $\text{Ar}-\text{C}-\text{OCH}_3-4'$ ), 148.8 ( $\text{Ar}-\text{C}-\text{OCH}_3-3$ ), 148.1 ( $\text{Ar}-\text{C}-\text{OCH}_3-4$ ), 144.1 ( $\text{Ar}-\text{C}-1'$ ), 125.8 ( $\text{Ar}-\text{C}-1$ ), 122.1 (2 x  $\text{Ar}-\text{C}-\text{H}-2', 6'$ ), 121.4 ( $\text{Ar}-\text{C}-\text{H}-6$ ), 114.3 (2 x  $\text{Ar}-\text{C}-\text{H}-3', 5'$ ), 112.2 ( $\text{Ar}-\text{C}-\text{H}-5$ ), 111.1 ( $\text{Ar}-\text{C}-\text{H}-2$ ), 56.6 ( $\text{Ar}-\text{OCH}_3$ )\*, 55.7 ( $\text{Ar}-\text{OCH}_3$ )\*, 55.4 ( $\text{Ar}-\text{OCH}_3$ )\*, 40.7 ( $\text{Ar}-\text{CH}_2$ ).

MS (EI+):  $m/z$  302 ( $\text{M}^+$ , 14 %), 151 (100 %), HRMS (EI+): Calcd for  $\text{C}_{17}\text{H}_{18}\text{O}_5 = 302.1154$  ( $\text{M}^+$ ), found 302.1155.

### 3,4-Dimethoxyphenyl 3-methoxyphenylacetate **1e**



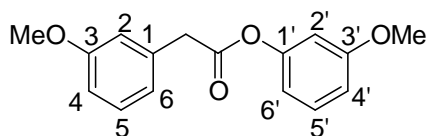
The title compound was prepared in 97 % yield (waxy cream solid, 712 mg) from 3-methoxyphenylacetic acid (400 mg, 2.40 mmol) and 3,4-dimethoxyphenol (352 mg, 2.28 mmol) in the presence of DCC (546 mg, 2.64 mmol), DMAP (73 mg, 0.61 mmol) and DCM (10 mL) as for

**1a.**

$^1\text{H}$  NMR:  $\delta$  7.24 (t, 1H,  $J = 7.8$  Hz, Ar-H-5), 6.93 (d, 1H,  $J = 7.8$  Hz, Ar-H-6), 6.92 (d, 1H,  $J = 2.4$  Hz, Ar-H-2), 6.82 (dd, 1H,  $J = 7.8, 2.4$  Hz, Ar-H-4), 6.77 (dd, 1H,  $J = 6.9, 2.1$  Hz, Ar-H-6'), 6.61 (d, 1H,  $J = 2.1$  Hz, Ar-H-2'), 6.60 (d, 1H,  $J = 6.9$  Hz, Ar-H-5'), 3.79 (s, 3H, OCH<sub>3</sub>-3'), 3.78 (s, 6H, OCH<sub>3</sub>-3, 4'), 3.75 (s, 2H, Ar-CH<sub>2</sub>-CO).

$^{13}\text{C}$  NMR:  $\delta$  169.8 (C=O), 159.5 (Ar-C-OCH<sub>3</sub>-3), 149.0 (Ar-C-OCH<sub>3</sub>-3'), 146.5 (Ar-C-OCH<sub>3</sub>-4'), 144.0 (Ar-C-1'), 134.6 (Ar-C-1), 129.3 (Ar-C-H-5), 121.3 (Ar-C-H-6), 114.7 (Ar-C-H-2), 112.5 (Ar-C-H-4), 112.4 (Ar-C-H-5'), 110.8 (Ar-C-H-6'), 105.3 (Ar-C-H-2'), 55.7 (Ar-OCH<sub>3</sub>-3'), 55.6 (Ar-OCH<sub>3</sub>-4'), 54.8 (Ar-OCH<sub>3</sub>-3), 40.9 (Ar-CH<sub>2</sub>-CO).

MS (CI<sup>+</sup>):  $m/z$  303 (M+H, 100 %), HRMS (EI<sup>+</sup>): Calcd for C<sub>17</sub>H<sub>18</sub>O<sub>5</sub> = 302.1154 (M<sup>+</sup>), found 302.1158.

**3-Methoxyphenyl 3-methoxyphenylacetate 1f**

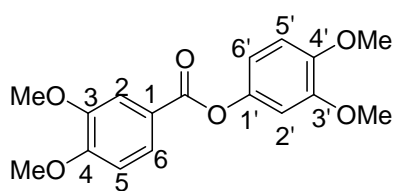
The title compound was prepared in 91 % yield (pale oil, 702 mg) from 3-methoxyphenylacetic acid (515 mg, 3.10 mmol) and 3-methoxyphenol (350 mg, 2.92 mmol) in the presence of DCC (703 mg, 3.41 mmol), DMAP (95 mg, 0.77 mmol) and DCM (10 mL) as for **1a**.

$^1\text{H}$  NMR:  $\delta$  7.28-7.19 (m, 2H, Ar-H-5, 5'), 6.96-6.91 (m, 2H, Ar-H-2,6), 6.83 (dd, 1H,  $J = 8.4, 2.7$  Hz, Ar-H-4'), 6.74 (dd, 1H,  $J = 8.1, 2.1$  Hz, Ar-H-6'), 6.65 (dd, 1H,  $J = 8.1, 2.1$  Hz, Ar-H-4), 6.61 (t, 1H,  $J = 2.1$  Hz, Ar-H-2'), 3.79 (s, 2H, Ar-CH<sub>2</sub>), 3.77 (s, 3H, OCH<sub>3</sub>-3'), 3.73 (s, 3H, OCH<sub>3</sub>-3).

$^{13}\text{C}$  NMR:  $\delta$  169.7 (C=O), 160.3 (Ar-C-OCH<sub>3</sub>-3), 159.6 (Ar-C-OCH<sub>3</sub>-3'), 151.5 (Ar-C-1'), 134.6 (Ar-C-1), 129.5 (Ar-C-H-5'), 121.5 (Ar-C-H-6), 114.8 (Ar-C-H-2), 113.5 (Ar-C-H-4), 112.7 (Ar-C-H-4'), 111.5 (Ar-C-H-6'), 107.3 (Ar-C-H-2), 55.2 (Ar-OCH<sub>3</sub>-3), 55.0 (Ar-OCH<sub>3</sub>-3'), 41.2 (Ar-CH<sub>2</sub>).

MS (EI<sup>+</sup>):  $m/z$  272 (M<sup>+</sup>, 6 %), 148 (100%), HRMS (EI<sup>+</sup>): Calcd for C<sub>16</sub>H<sub>16</sub>O<sub>4</sub> = 272.1048 (M<sup>+</sup>), found 272.1052.

**3,4-Dimethoxy 3,4-dimethoxyphenylbenzoate 11a**



The title compound was prepared in 91 % yield (white solid, 1.31 g) from 3,4-dimethoxybenzoic acid (910 mg, 5.00 mmol) and 3,4-dimethoxyphenol (700 mg 4.54 mmol) in the presence of DCC (1.10 g, 5.33 mmol), DMAP (150 mg, 1.27 mmol) and DCM (20 mL) as for

### 1a.

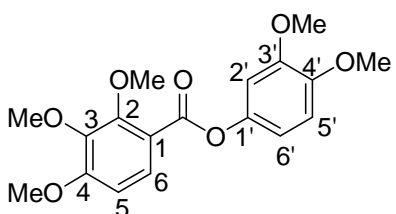
m.p. 142-144 °C

$^1\text{H NMR}$ :  $\delta$  7.86 (dd, 1H,  $J = 8.6, 2.0$  Hz, Ar-H-6), 7.67 (d, 1H,  $J = 2.0$  Hz, Ar-H-2), 6.95 (d, 1H,  $J = 8.6$  Hz, Ar-H-5), 6.89 (d, 1H,  $J = 9.3$  Hz, Ar-H-2'), 6.77 (d, 1H,  $J = 2.6$  Hz, Ar-H-5'), 6.76 (dd, 1H,  $J = 9.3, 2.6$  Hz, Ar-H-6'), 3.98 (s, 3H,  $\text{OCH}_3$ )\*, 3.97 (s, 3H,  $\text{OCH}_3$ )\*, 3.90 (s, 3H,  $\text{OCH}_3$ )\*, 3.88 (s, 3H,  $\text{OCH}_3$ )\*.

$^{13}\text{C NMR}$ :  $\delta$  164.8 ( $\text{C}=\text{O}$ ), 153.1 (Ar-C-OCH<sub>3</sub>-4), 149.0 (Ar-C-OCH<sub>3</sub>-3'), 148.3 (Ar-C-OCH<sub>3</sub>-3), 146.4 (Ar-C-OCH<sub>3</sub>-4), 144.3 (Ar-C-1'), 123.9 (Ar-C-H-6), 121.5 (Ar-C-1), 112.7 (Ar-C-H-6'), 111.9 (Ar-C-H-2), 110.9 (Ar-C-H-5'), 110.0 (Ar-C-H-5), 105.6 (Ar-C-H-2'), 55.7 (Ar-OCH<sub>3</sub>)\*, 55.66 (Ar-OCH<sub>3</sub>)\*, 55.64 (Ar-OCH<sub>3</sub>)\*, 55.5 (Ar-OCH<sub>3</sub>)\*.

MS (EI<sup>+</sup>):  $m/z$  331 ( $\text{M}^+$ , 9 %), HRMS (EI<sup>+</sup>): Calcd for  $\text{C}_{17}\text{H}_{18}\text{O}_6 = 318.1103$  ( $\text{M}^+$ ), found 318.1099.

### 3,4-Dimethoxyphenyl 2,3,4-trimethoxybenzoate 11b



The title compound was prepared in 93 % yield (cream solid, 840 mg) from 2,3,4-trimethoxybenzoic acid (549 mg, 2.58 mmol) and 3,4-dimethoxyphenol (400 mg, 2.59 mmol) in the presence of DCC (600 mg, 2.90 mmol), DMAP (72 mg, 0.59 mmol) and DCM (10 mL) as for **1a**.

m.p. 85-86 °C

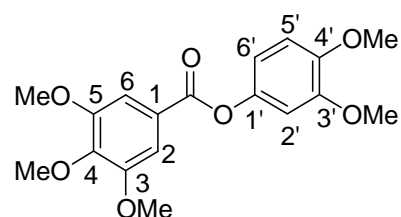
$^1\text{H NMR}$ :  $\delta$  7.79 (d, 1H,  $J = 9.0$  Hz, Ar-H-6), 6.88 (dd, 1H,  $J = 6.7, 2.2$  Hz, Ar-H-6'), 6.76 (d, 1H,  $J = 2.2$  Hz, Ar-H-2'), 6.75 (d, 1H,  $J = 6.7$  Hz, Ar-H-5'), 6.74 (d, 1H,  $J = 9.0$  Hz, Ar-H-5), 3.98 (s, 3H, Ar-OCH<sub>3</sub>-2), 3.94 (s, 3H, Ar-OCH<sub>3</sub>-3), 3.90 (s, 3H, Ar-OCH<sub>3</sub>-4), 3.88 (s, 3H, Ar-OCH<sub>3</sub>-4'), 3.87 (s, 3H, Ar-OCH<sub>3</sub>-3').

$^{13}\text{C NMR}$ :  $\delta$  163.9 ( $\text{C}=\text{O}$ ), 157.6 (Ar-C-OCH<sub>3</sub>-4), 155.1 (Ar-C-OCH<sub>3</sub>-2), 149.2 (Ar-C-OCH<sub>3</sub>-3'), 146.6 (Ar-C-OCH<sub>3</sub>-4'), 144.4 (Ar-C-1'), 142.9 (Ar-C-OCH<sub>3</sub>-3), 127.2 (Ar-C-H-6), 116.7 (Ar-C-1), 112.8

(Ar-C-H-5), 111.0 (Ar-C-H-6'), 106.8 (Ar-C-H-5'), 105.8 (Ar-C-H-2'), 61.6 (Ar-OCH<sub>3</sub>-2), 60.8 (Ar-OCH<sub>3</sub>-4), 56.0 (Ar-OCH<sub>3</sub>-4'), 55.9 (Ar-OCH<sub>3</sub>-3'), 55.7 (Ar-OCH<sub>3</sub>-3).

MS (EI<sup>+</sup>): *m/z* 348 (M<sup>+</sup>, 10 %), 151 (100 %) HRMS (EI<sup>+</sup>): Calcd for C<sub>18</sub>H<sub>20</sub>O<sub>7</sub> = 348.1209 (M<sup>+</sup>), found 348.1213.

### 3,4-Dimethoxyphenyl 3,4,5-trimethoxybenzoate 11c



The title compound was prepared in 97 % yield (cream solid, 877 mg) from 3,4,5-trimethoxybenzoic acid (549 mg, 2.58 mmol) and 3,4-dimethoxyphenol (400 mg, 2.59 mmol) in the presence of DCC (600 mg, 2.90 mmol), DMAP (72 mg, 0.59 mmol) and DCM (10 mL) as for **1a**.

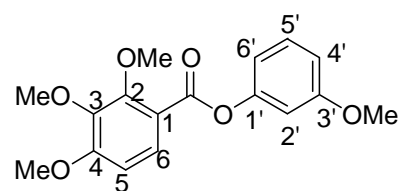
m.p. 136-138 °C

<sup>1</sup>H NMR: δ 7.38 (s, 2H, Ar-H-2, 6), 6.83 (dd, 1H, *J* = 7.8, 1.2 Hz, Ar-H-6'), 6.71 (d, 1H, *J* = 1.2 Hz, Ar-H-2'), 6.70 (d, 1H, *J* = 7.8 Hz, Ar-H-5'), 3.88 (s, 3H, OCH<sub>3</sub>-4), 3.87 (s, 6H, OCH<sub>3</sub>-3, 5), 3.83 (s, 3H, OCH<sub>3</sub>-4'), 3.81 (s, 3H, OCH<sub>3</sub>-3').

<sup>13</sup>C NMR: δ 164.8 (C=O), 152.7 (2 x Ar-C-OCH<sub>3</sub>-3, 5), 149.2 (Ar-C-OCH<sub>3</sub>-4'), 146.6 (Ar-C-OCH<sub>3</sub>-3'), 144.3 (Ar-C-1'), 142.4 (Ar-C-OCH<sub>3</sub>-4), 124.1 (Ar-C-1), 112.7 (Ar-C-H-5'), 111.0 (Ar-C-H-6'), 107.0 (2 x Ar-C-H-2,6), 105.6 (Ar-C-H-2'), 60.6 (Ar-OCH<sub>3</sub>-4), 56.0 (2 x Ar-OCH<sub>3</sub>-3,5), 55.9 (Ar-OCH<sub>3</sub>-3'), 55.7 (Ar-OCH<sub>3</sub>-4').

MS (EI<sup>+</sup>): *m/z* 348 (M<sup>+</sup>, 30 %), 195 (100 %), HRMS (EI<sup>+</sup>): Calcd for C<sub>18</sub>H<sub>21</sub>O<sub>7</sub> = 349.1287 (M<sup>+</sup>), found 349.1281.

### 3-Methoxyphenyl 2,3,4-trimethoxybenzoate 11d



The title compound was prepared in 98 % yield (white solid, 735 mg) from 2,3,4-trimethoxybenzoic acid (500 mg, 2.35 mmol) and 3-methoxyphenol (321 mg, 2.59 mmol) in the presence of DCC (534 mg, 2.59 mmol), DMAP (79 mg, 6.47 mmol) and DCM (10 mL) as

for **1a**.

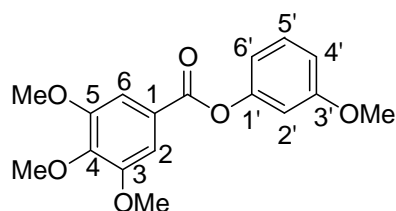
m.p. 50-52 °C

$^1\text{H}$  NMR:  $\delta$  7.80 (d, 1H,  $J = 8.7$  Hz, Ar-H-6), 7.31 (d, 1H,  $J = 8.2$  Hz, Ar-H-5'), 6.81 (dd, 2H,  $J = 8.2, 2.2$  Hz, Ar-H-4', 6'), 6.77 (t, 1H,  $J = 2.2$  Hz, Ar-H-2'), 6.76 (d, 1H,  $J = 8.7$  Hz, Ar-H-5), 3.98 (s, 3H, OCH<sub>3</sub>-4), 3.94 (s, 3H, OCH<sub>3</sub>-2), 3.90 (s, 3H, OCH<sub>3</sub>-3), 3.81 (s, 3H, OCH<sub>3</sub>-3').

$^{13}\text{C}$  NMR:  $\delta$  163.6 (C=O), 160.4 (Ar-C-OCH<sub>3</sub>-3), 157.7 (Ar-C-OCH<sub>3</sub>-2), 155.3 (Ar-C-OCH<sub>3</sub>-4), 151.9 (Ar-C-OCH<sub>3</sub>-3'), 143.1 (Ar-C-1'), 129.7 (Ar-C-H-5), 127.5 (Ar-C-OCH<sub>3</sub>-6), 116.9 (Ar-C-1), 114.4 (Ar-C-H-6'), 111.6 (Ar-C-H-4'), 107.7 (Ar-C-H-2'), 106.9 (Ar-C-H-5'), 61.8 (Ar-OCH<sub>3</sub>-4), 61.0 (Ar-OCH<sub>3</sub>-3), 56.1 (Ar-OCH<sub>3</sub>-2), 55.3 (Ar-OCH<sub>3</sub>-3').

MS (EI<sup>+</sup>):  $m/z$  318 (M<sup>+</sup>, 6 %), 195 (100 %), HRMS (EI<sup>+</sup>): Calcd for C<sub>17</sub>H<sub>18</sub>O<sub>6</sub> = 318.1103 (M<sup>+</sup>), found 318.1105.

### 3-Methoxyphenyl 3,4,5-trimethoxybenzoate 11e<sup>1</sup>



The title compound was prepared in 98 % yield (white solid, 740 mg) from 3,4,5-trimethoxybenzoic acid (500 mg, 2.35 mmol) and 3-methoxyphenol (321 mg, 2.59 mmol) in the presence of DCC (534 mg, 2.59 mmol), DMAP (79 mg, 6.47 mmol) and DCM (10 mL) as

for 1a. NMR data not reported.<sup>1</sup>

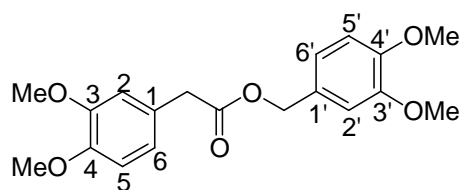
m.p. 92-94 °C (lit.<sup>1</sup> m.p. not reported)

$^1\text{H}$  NMR:  $\delta$  7.45 (s, 2H, Ar-H-2, 6), 7.33 (t, 1H,  $J = 8.0$  Hz, Ar-H-5'), 6.83 (dd, 1H,  $J = 8.0, 2.4$  Hz, Ar-H-4'), 6.80 (dd, 1H,  $J = 8.0, 2.4$  Hz, Ar-H-6'), 6.76 (t, 1H,  $J = 2.1$  Hz, Ar-H-2'), 3.95 (s, 3H, OCH<sub>3</sub>-4), 3.94 (s, 6H, OCH<sub>3</sub>-3, 5), 3.82 (s, 3H, OCH<sub>3</sub>-3').

$^{13}\text{C}$  NMR:  $\delta$  164.7 (C=O), 160.5 (Ar-C-OCH<sub>3</sub>-3'), 152.9 (2 x Ar-C-OCH<sub>3</sub>-3,5), 151.8 (Ar-C-OCH<sub>3</sub>-4), 142.6 (Ar-C-1'), 129.8 (Ar-C-H-5'), 124.3 (Ar-C-1), 113.9 (Ar-C-OCH<sub>3</sub>-6'), 111.8 (Ar-C-OCH<sub>3</sub>-4'), 107.6 (Ar-C-H-2'), 107.3 (2 x Ar-C-H-2, 6), 60.9 (Ar-OCH<sub>3</sub>-4), 56.2 (2 x Ar-OCH<sub>3</sub>-3, 5), 55.3 (Ar-OCH<sub>3</sub>-3').

MS (EI<sup>+</sup>):  $m/z$  318 (M<sup>+</sup>, 31 %), 195 (100 %), HRMS (EI<sup>+</sup>): Calcd for C<sub>17</sub>H<sub>18</sub>O<sub>6</sub> = 318.1103 (M<sup>+</sup>), found 318.1106.

### 3,4-Dimethoxybenzyl 3,4-dimethoxyphenylacetate 17a<sup>2</sup>



The title compound was prepared in 78 % yield (cream solid, 689 mg) from 3,4-dimethoxyphenylacetic acid (500 mg, 2.55 mmol) and 3,4-dimethoxybenzyl alcohol (0.44 mL, 3.05 mmol) in the presence of DCC (578 mg, 2.80 mmol), DMAP (62 mg, 0.509 mmol) and DCM (10 mL) as for **1a**. NMR data not recorded.<sup>2</sup>

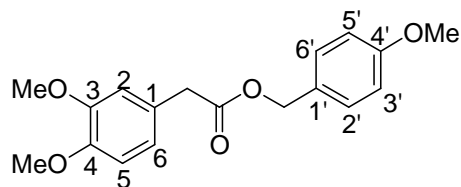
m.p. 104-106 °C (lit.<sup>2</sup> m.p. not reported)

<sup>1</sup>H NMR:  $\delta$  6.88 (dd, 1H,  $J$  = 8.1, 1.8 Hz, Ar-H-6), 6.82 (bs, 2H, Ar-H-2, 5), 6.79 (bs, 3H, Ar-H-2', 5', 6'), 5.06 (s, 2H, Ar-CH<sub>2</sub>-O), 3.84 (s, 3H, OCH<sub>3</sub>-3), 3.83 (s, 3H, OCH<sub>3</sub>-4), 3.81 (s, 6H, -OCH<sub>3</sub>-3', 4'), 3.58 (s, 2H, Ar-CH<sub>2</sub>-CO).

<sup>13</sup>C NMR:  $\delta$  171.2 (C=O), 148.6 (Ar-C-OCH<sub>3</sub>-4'), 148.5 (Ar-C-OCH<sub>3</sub>-3), 148.4 (Ar-C-OCH<sub>3</sub>-3'), 147.7 (Ar-C-OCH<sub>3</sub>-4), 128.0 (Ar-C-1), 126.0 (Ar-C-1'), 121.0 (Ar-C-H-6'), 120.7 (Ar-C-H-6), 111.9 (Ar-C-H-5), 111.1 (Ar-C-H-2), 110.7 (Ar-C-H-5'), 110.5 (Ar-C-H-2'), 66.2 (Ar-CH<sub>2</sub>-O), 55.5 (Ar-OCH<sub>3</sub>-3), 55.4 (Ar-OCH<sub>3</sub>-4), 55.3 (Ar-OCH<sub>3</sub>-3'), 55.2 (Ar-OCH<sub>3</sub>-4'), 40.5 (Ar-CH<sub>2</sub>-CO).

MS (EI+):  $m/z$  346 (M<sup>+</sup>, 9 %), 151 (100 %), HRMS (EI+): Calcd for C<sub>19</sub>H<sub>22</sub>O<sub>6</sub> = 346.1416 (M<sup>+</sup>), found 346.1415.

#### 4-Methoxybenzyl 3,4-dimethoxyphenylacetate **17b**



The title compound was prepared in 81 % yield (white film, 735 mg) from 3,4-dimethoxyphenylacetic acid (400 mg, 2.03 mmol) and 4-methoxybenzyl alcohol (267 mg, 1.93 mmol) in the presence of DCC (462 mg, 2.24 mmol), DMAP (62 mg, 0.509

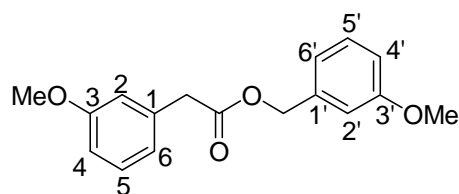
mmol) and DCM (10 mL) as for **1a**.

<sup>1</sup>H NMR:  $\delta$  7.24 (d, 2H,  $J$  = 8.8 Hz, Ar-H-2', 6'), 6.84 (d, 2H,  $J$  = 8.8 Hz, Ar-H-3', 5'), 6.77 (s, 3H, Ar-H-2, 5, 6), 5.04 (s, 2H, Ar-CH<sub>2</sub>-O), 3.81 (s, 3H, OCH<sub>3</sub>-3), 3.79 (s, 3H, OCH<sub>3</sub>-4), 3.75 (s, 3H, OCH<sub>3</sub>-4'), 3.55 (s, 2H, Ar-CH<sub>2</sub>-CO).

<sup>13</sup>C NMR:  $\delta$  171.3 (C=O), 159.3 (Ar-C-OCH<sub>3</sub>-4'), 148.6 (Ar-C-OCH<sub>3</sub>-3), 147.8 (Ar-C-OCH<sub>3</sub>-4), 129.7 (2 x Ar-C-H-2' 6'), 127.7 (Ar-C-1'), 126.1 (Ar-C-1), 121.1 (Ar-C-H-6), 113.6 (2 x Ar-C-H-3', 5'), 112.1 (Ar-C-H-5), 110.9 (Ar-C-H-2), 66.0 (Ar-CH<sub>2</sub>-O), 55.5 (Ar-OCH<sub>3</sub>-3), 55.4 (Ar-OCH<sub>3</sub>-4), 54.9 (Ar-OCH<sub>3</sub>-4'), 40.5 (Ar-CH<sub>2</sub>-CO).

MS (EI+):  $m/z$  316 ( $M^+$ , 19 %), 121 (100 %), HRMS (EI+): Calcd for  $C_{18}H_{20}O_5 = 316.1311$  ( $M^+$ ), found 316.1309.

### 3-Methoxybenzyl 3-methoxyphenylacetate 17c



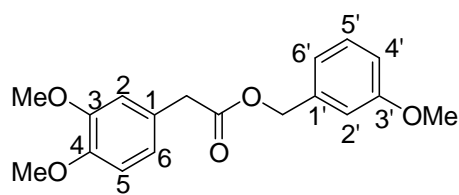
The title compound was prepared in 80 % yield (waxy cream solid, 580 mg) from 3-methoxyphenylacetic acid (463 mg, 2.78 mmol) and 3-methoxybenzyl alcohol (350 mg, 2.53 mmol) in the presence of DCC (632 mg, 3.06 mmol), DMAP (85 mg, 0.69 mmol) and DCM (10 mL) as for **1a**.

$^1H$  NMR:  $\delta$  7.28-7.20 (m, 2H Ar-H-5, 5'), 6.90 (bs, 1H Ar-H-2), 6.89-6.82 (m, 4H Ar-H-4, 4', 6, 6'), 6.79 (d, 1H,  $J = 2.1$  Hz, Ar-H-2'), 5.11 (s, 2H, Ar-CH<sub>2</sub>-O), 3.78 (s, 3H, OCH<sub>3</sub>-3), 3.77 (s, 3H, OCH<sub>3</sub>-3'), 3.65 (s, 2H, Ar-CH<sub>2</sub>-CO).

$^{13}C$  NMR:  $\delta$  171.0 (C=O), 159.6 (2 x Ar-C-OCH<sub>3</sub>-3, 3'), 137.2 (Ar-C-1'), 135.1 (Ar-C-1), 129.4 (Ar-C-H-5), 129.3 (Ar-C-H-5'), 121.5 (Ar-C-H-6), 120.0 (Ar-C-H-6'), 114.6 (Ar-C-H-2), 113.6 (Ar-C-H-4'), 113.1 (Ar-C-H-4), 112.6 (Ar-C-H-2'), 66.2 (Ar-CH<sub>2</sub>-O), 55.0 (Ar-OCH<sub>3</sub>-3), 54.9 (Ar-OCH<sub>3</sub>-3'), 41.2 (Ar-CH<sub>2</sub>-CO).

MS (EI+):  $m/z$  286 ( $M^+$ , 25 %), 121 (100 %), HRMS (EI+): Calcd for  $C_{17}H_{18}O_4 = 286.1205$  ( $M^+$ ), found 286.1201.

### 3-Methoxybenzyl 3,4-dimethoxyphenylacetate 17d



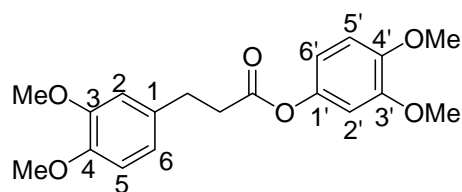
The title compound was prepared in 84 % yield (waxy cream solid, 678 mg) from 3,4-dimethoxyphenylacetic acid (546 mg, 2.78 mmol) and 3-methoxybenzyl alcohol (350 mg, 2.53 mmol) in the presence of DCC (632 mg, 3.06 mmol), DMAP (85 mg, 0.69 mmol) and DCM (10 mL) as for **1a**.

$^1H$  NMR:  $\delta$  7.22 (t, 1H,  $J = 8.2$  Hz, Ar-H-5'), 6.86 (d, 1H,  $J = 8.2$  Hz, Ar-H-6'), 6.84-6.77 (m, 2H Ar-H-2, 2'), 6.81 (dd, 1H,  $J = 8.0, 2.4$  Hz, Ar-H-6), 6.78 (d, 1H,  $J = 8.0$  Hz, Ar-H-5), 6.23 (d, 1H,  $J = 8.2$  Hz, Ar-H-4'), 5.08 (s, 2H, Ar-CH<sub>2</sub>-O), 3.81 (s, 3H, OCH<sub>3</sub>-4), 3.80 (s, 3H, OCH<sub>3</sub>-3'), 3.72 (s, 3H, OCH<sub>3</sub>-3), 3.59 (s, 2H, Ar-CH<sub>2</sub>-CO).

$^{13}\text{C}$  NMR:  $\delta$  171.1 ( $\text{C}=\text{O}$ ), 159.4 ( $\text{Ar}-\text{C}-\text{OCH}_3-3'$ ), 148.6 ( $\text{Ar}-\text{C}-\text{OCH}_3-4$ ), 147.8 ( $\text{Ar}-\text{C}-\text{OCH}_3-3$ ), 137.1 ( $\text{Ar}-\text{C}-1'$ ), 129.2 ( $\text{Ar}-\text{C}-\text{H}-5'$ ), 126.0 ( $\text{Ar}-\text{C}-1$ ), 121.1 ( $\text{Ar}-\text{C}-\text{H}-6$ ), 119.8 ( $\text{Ar}-\text{C}-\text{H}-2'$ ), 113.4 ( $\text{Ar}-\text{C}-\text{H}-4'$ ), 113.1 ( $\text{Ar}-\text{C}-\text{H}-6'$ ), 112.1 ( $\text{Ar}-\text{C}-\text{H}-5$ ), 110.9 ( $\text{Ar}-\text{C}-\text{H}-2$ ), 66.0 ( $\text{Ar}-\text{CH}_2-\text{O}$ ), 55.5 ( $\text{Ar}-\text{OCH}_3-4$ ), 55.4 ( $\text{Ar}-\text{OCH}_3-3$ ), 54.8 ( $\text{Ar}-\text{OCH}_3-3'$ ), 40.5 ( $\text{Ar}-\text{CH}_2-\text{CO}$ ).

MS (EI<sup>+</sup>):  $m/z$  316 ( $\text{M}^+$ , 23 %), 151 (100 %), HRMS (EI<sup>+</sup>): Calcd for  $\text{C}_{18}\text{H}_{20}\text{O}_5 = 316.1311$  ( $\text{M}^+$ ), found 316.1316.

### 3,4-Dimethoxyphenyl 3,4-dimethoxyphenylpropanoate 19



The title compound was prepared in 82 % yield (waxy solid, 648 mg) from 3-(3,4-dimethoxyphenyl)propanoic acid (524 mg, 2.5 mmol) and 3,4-dimethoxyphenol (350 mg 2.70 mmol) in the presence of DCC (566 mg, 2.74 mmol), DMAP (76 mg, 0.62

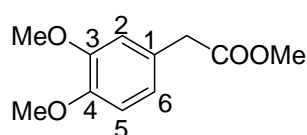
mmol) and DCM (10 mL) as for **1a**.

$^1\text{H}$  NMR:  $\delta$  6.83 (d, 1H,  $J = 8.7$  Hz,  $\text{Ar}-\text{H}-5'$ ), 6.82 (d, 1H,  $J = 1.5$  Hz,  $\text{Ar}-\text{H}-2$ ), 6.81 (dd, 1H,  $J = 8.7$ , 1.5 Hz,  $\text{Ar}-\text{H}-6$ ), 6.80 (d, 1H,  $J = 8.8$  Hz,  $\text{Ar}-\text{H}-5$ ), 6.57 (dd, 1H,  $J = 8.8$ , 2.7 Hz,  $\text{Ar}-\text{H}-6'$ ), 6.51 (d, 1H,  $J = 2.7$  Hz,  $\text{Ar}-\text{H}-2'$ ), 3.88 (s, 3H,  $\text{OCH}_3$ )\*, 3.87 (s, 3H,  $\text{OCH}_3$ )\*, 3.86 (s, 3H,  $\text{OCH}_3$ )\*, 3.83 (s, 3H,  $\text{OCH}_3$ )\*, 3.02 (t, 2H,  $J = 7.2$  Hz,  $\text{Ar}-\text{CH}_2$ ), 2.85 (t, 2H,  $J = 7.2$  Hz,  $\text{Ar}-\text{CH}_2-\text{CH}_2$ ).

$^{13}\text{C}$  NMR:  $\delta$  171.4 ( $\text{C}=\text{O}$ ), 148.9 ( $\text{Ar}-\text{C}-\text{OCH}_3-3'$ ), 148.5 ( $\text{Ar}-\text{C}-\text{OCH}_3-3$ ), 147.2 ( $\text{Ar}-\text{C}-\text{OCH}_3-4$ ), 146.4 ( $\text{Ar}-\text{C}-\text{OCH}_3-4'$ ), 143.9 ( $\text{Ar}-\text{C}-1'$ ), 132.3 ( $\text{Ar}-\text{C}-1$ ), 119.9 ( $\text{Ar}-\text{C}-\text{H}-6$ ), 112.4 ( $\text{Ar}-\text{C}-\text{H}-6'$ ), 111.4 ( $\text{Ar}-\text{C}-\text{H}-5$ ), 110.9 ( $\text{Ar}-\text{C}-\text{H}-5'$ ), 110.7 ( $\text{Ar}-\text{C}-\text{H}-2$ ), 105.2 ( $\text{Ar}-\text{C}-\text{H}-2'$ ), 55.7 ( $\text{Ar}-\text{OCH}_3$ )\*, 55.5 (2 x  $\text{Ar}-\text{OCH}_3$ )\*, 55.4 ( $\text{Ar}-\text{OCH}_3$ )\*, 35.8 ( $\text{Ar}-\text{CH}_2-\text{CH}_2$ ), 30.2 ( $\text{Ar}-\text{CH}_2$ ).

MS (EI<sup>+</sup>):  $m/z$  346 ( $\text{M}^+$ , 8 %), HRMS (EI<sup>+</sup>): Calcd for  $\text{C}_{19}\text{H}_{22}\text{O}_6 = 346.1416$  ( $\text{M}^+$ ), found 346.1424.

### 3,4-Dimethoxyphenyl acetate 5<sup>3</sup>



Thionyl chloride (5.6 mL, 76.46 mmol) was added under  $\text{N}_2$  to an ice-cold solution of 3,4-dimethoxyphenylacetic acid (5.0 g, 25.48 mmol) in dry MeOH (30 mL). The reaction was stirred for 18 h with warming to RT. The

volatiles were evaporated and the residue dissolved in DCM (20 mL). The solution was washed with sat. aqueous  $\text{Na}_2\text{CO}_3$  solution (20 mL), dried over  $\text{MgSO}_4$ , filtered, evaporated and chromatographed



using EtOAc:PS (2:1) as the mobile phase to yield the title compound as a clear oil (5.31 g, 99 %).

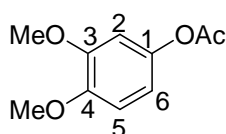
NMR data was not reported.<sup>3</sup>

<sup>1</sup>H NMR:  $\delta$  6.82 (s, 3H, Ar-H-2, 5, 6), 3.88 (s, 3H, OCH<sub>3</sub>-4), 3.86 (s, 3H, OCH<sub>3</sub>-3), 3.69 (s, 2H, Ar-CH<sub>2</sub>), 3.57 (s, 3H, CO<sub>2</sub>CH<sub>3</sub>).

<sup>13</sup>C NMR:  $\delta$  171.9 (C=O), 148.6 (Ar-C-OCH<sub>3</sub>-3), 147.9 (Ar-C-OCH<sub>3</sub>-4), 126.2 (Ar-C-1), 121.1 (Ar-C-H-6), 112.1 (Ar-C-H-5), 111.0 (Ar-C-H-2), 55.76 (Ar-OCH<sub>3</sub>)\*, 55.73 (Ar-OCH<sub>3</sub>)\*, 51.8 (CO<sub>2</sub>CH<sub>3</sub>), 40.6 (Ar-CH<sub>2</sub>).

MS (EI+): *m/z* 210 (M<sup>+</sup>, 23) 197 (100 %), HRMS (EI+): Calcd for C<sub>11</sub>H<sub>14</sub>O<sub>4</sub> = 210.0892 (M<sup>+</sup>), found 210.0886.

### 3,4-Dimethoxyphenyl acetate 7<sup>4</sup>



3,4-Dimethoxyphenol (400 mg, 2.59 mmol) was dissolved in dry pyridine (3 mL) and acetic anhydride (3 mL) was added. The solution was stirred for 18 h at RT.

The mixture was diluted and stirred with 1M HCl solution (30 mL) for 30 min, then extracted with DCM (2 x 20 mL). The extracts were washed with sat. aqueous NaHCO<sub>3</sub> solution (2 x 20 mL), dried over MgSO<sub>4</sub>, filtered and evaporated. Purification by flash silica gel chromatography with EtOAc : PS (1 : 1) as mobile phase yielded the title compound as a clear oil (474 mg, 93 %). NMR data was not reported.<sup>4</sup>

<sup>1</sup>H NMR:  $\delta$  6.83 (d, 1H, *J* = 8.5 Hz, Ar-H-5), 6.637 (d, 1H, *J* = 2.4 Hz, Ar-H-2), 6.635 (dd, 1H, *J* = 8.5, 2.4 Hz, Ar-H-6), 3.85 (s, 3H, OCH<sub>3</sub>-4), 3.84 (s, 3H, OCH<sub>3</sub>-3), 2.27 (s, 3H, COCH<sub>3</sub>).

<sup>13</sup>C NMR:  $\delta$  169.6 (C=O), 149.0 (Ar-C-OCH<sub>3</sub>-3), 146.5 (Ar-C-OCH<sub>3</sub>-4), 144.0 (Ar-C-1), 112.5 (Ar-C-H-6), 110.8 (Ar-C-H-5), 105.4 (Ar-C-H-2), 55.8 (Ar-OCH<sub>3</sub>)\*, 55.6 (Ar-OCH<sub>3</sub>)\*, 20.8 (COCH<sub>3</sub>).

MS (CI+): *m/z* 197 (M+H<sup>+</sup>, 100 %), HRMS (EI+): Calcd for C<sub>10</sub>H<sub>12</sub>O<sub>4</sub> = 196.0735 (M<sup>+</sup>), found 196.0735.

### References

Arnone, A., Camarda, L., Merlini, L., Nasini, G. *J. Chem. Soc. Perkin Trans. 1* **1975**, 186-194.

Sainsbury, M., Wyatt, J. *J. Chem. Soc. Perkin Trans. 1* **1977**, 1750-1753.

Gardiner, J. M., Bryce, M. R. *J. Org. Chem.* **1990**, 55, 1261-1266.

Yoshida, K., Shigi, M., Kanbe, T., Fueno, T. *J. Org. Chem.* **1975**, *40*, 3805-3806.