Palladium-Catalysed Coupling and Acid-Mediated Cyclisation: Synthesis of Fluorenones and Fluorenes

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Abstract Palladium-catalysed sequential one-pot synthesis of fluorenones is described. The reaction comprises intermolecular Suzuki coupling and intramolecular acid-mediated cyclisation in a one-pot procedure. The protocol is also applied to the synthesis of fluorenes using a single column purification.

Key words Friedel–Crafts, cyclocarbonylation, fluorenone, fluorine

One-pot or sequential one-pot strategies enhance synthetic efficiency and enable access to diversified molecules. Fluorenones comprise fused tricyclic frameworks of biological and pharmaceutical significance, through scavenging of redundant radicals in the body. Significantly, the fluorenone core constitutes a complete carbon skeleton in certain natural products. As a result of interest in developing new synthetic strategies for the preparation of fluorenones, some interesting approaches have been established. Conventional synthetic paths for the preparation of fluorenones involve Friedel–Crafts ring closure of biarylcaboxyclic acids and the oxidation of fluorenes, which usually involves several synthetic steps. Other methods for the synthesis of fluorenones include radical cyclisation, transition-metal catalysed ring closure of benzophenones and biphenyl-2-carbonitrile, and cyclocarbonylation of 2-halobiphenyls. In particular, Hilt and co-workers have synthesised fluorenes by using an intramolecular Friedel–Crafts acylation of biphenyl 2-carboxylic acid esters. Functionalised fluorenes are useful materials for optical brightening agents, dyes and ligands in organometallic chemistry. Similar to fluorenones, conventional approaches for the synthesis of fluorenes are also mostly based on multistep approaches. For example, Jana et al. prepared fluorenes from 2-phenylbenzyl alcohols by using a Lewis acid mediated Friedel–Crafts reaction as the key reaction. Wang et al. accomplished the synthesis of fluorenes from N-tosylhydrazones by a carbene aromatic substitution reaction. The research group of Sarkar has described the preparation of fluorenes from ortho-bromobenzaldehydes in a two-step process. Although the established methodologies that are used to synthesise fluorenones are effective, they are stepwise and require advanced synthetic precursors. Therefore, there is scope for the development new protocols, particularly one-pot versions. To our knowledge, there are no reports on the synthesis of fluorenones using a one-pot process and simple starting materials. Based on our interest in the development of one-pot or sequential one-pot processes, we have recently presented a synthesis of fluorenones from benzylamines and iodoarenes, under palladium-catalysed functional group-directing triple ortho-C–H activation. More recently, we described the synthesis of fluorenes via Suzuki coupling and subsequent oxidative cyclisation in a sequential one-pot manner. Herein, we present a one-pot approach to the synthesis of fluorenes through palladium-catalysed coupling of ortho-bromobenzonic acid esters and arylboronic acids and subsequent intramolecular Friedel–Crafts acylation. Furthermore, the strategy was applied to the synthesis of fluorenes by using the same strategy, with a single column purification.

To begin with, it was anticipated that fluorenone 4aa could be obtained in a sequential one-pot operation by employing an intramolecular Friedel–Crafts acylation of the Suzuki product biphenyl ester 3aa generated in situ. Based on our earlier achievements in the synthesis of indanones and dihydrocoumarins, it was conceived that Friedel–Crafts acylation of benzylamines and iodoarenes, under palladium-catalysed functional group-directing triple ortho-C–H activation. More recently, we described the synthesis of fluorenones via Suzuki coupling and subsequent oxidative cyclisation in a sequential one-pot manner. Herein, we present a one-pot approach to the synthesis of fluorenes through palladium-catalysed coupling of ortho-bromobenzonic acid esters and arylboronic acids and subsequent intramolecular Friedel–Crafts acylation. Furthermore, the strategy was applied to the synthesis of fluorenes by using the same strategy, with a single column purification.

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sufficiently strong acid. Furthermore, to promote in situ acylation in a one-pot protocol, some acid will be sacrificed to quench the base used for the initial Suzuki coupling step.

Thus, the screening study was initiated with 2-bromomethyl benzoate 1a and phenylboronic acid 2a. Suzuki coupling was performed in the presence of Pd(OAc)$_2$ (5 mol%) and K$_2$CO$_3$ (2 equiv) in various solvents, at 80 °C for 15 to 24 h (Table 1, entries 1–15). After confirming the formation of Suzuki product 3aa, by TLC, the subsequent Friedel–Crafts acylation to give the desired fluorenone 4aa was carried out by the addition of different acids to the reaction mixture at room temperature and the resultant reaction mixture was again heated (80 °C or 100 °C). Thus, treatment with conc. sulfuric acid at 100 °C for 5 h, gave fluorenone 4aa in trace amounts (entry 1) and TfOH at 100 °C gave a similar result (entry 2). A slight improvement was observed when conc. sulfuric acid was added to the Suzuki product in N,N-dimethylformamide (DMF) (entries 3 and 4); whereas fluorenone 4aa was obtained in moderate yield when 3aa in DMF was reacted with TfOH (entry 5). The reaction was inferior when TfOH was added to 3aa in a 1:1 mixture of DMF and H$_2$O (entry 6) and there was no reaction with TfOH in CH$_2$CN or DMSO (entries 7 and 8). Since most of such acid mediated reactions have been carried out in halogenated solvents, we decided to carry out both reactions in 1,2-dichloroethane (DCE). Therefore, to the biaryl Suzuki product 3aa formed in DCE, TfOH was added and the mixture was heated at 80 °C, giving the desired fluorenone 4aa in 58% yield (entry 9). Acylation with conc. sulfuric acid in DCE gave 4aa in 54% yield (entry 10). On the other hand, acylation with the addition of TfOH in CH$_2$Cl$_2$ furnished 4aa in moderate yield (entry 11). Gratifyingly, treatment of 3aa in DCE with 10 equiv of TfOH raised the yield to 68% (entry 12). On the contrary, when the amount of TfOH was further increased to 15 equiv, the yield of 4aa decreased to 40% (entry 13). Finally, reaction in DCE, with BF$_3$-OEt$_2$ or AlCl$_3$ furnished 4aa in inferior yields (entries 14 and 15).

With the above optimized conditions established for the formation of 4aa (Table 1, entry 12), the one-pot process was examined with other 2-bromobenzoic acid esters 1a–e and phenylboronic acids 2a–g. Gratifyingly, the process proved to be generally applicable and delivered fluorenes 4aa–ff (Scheme 1). In addition to ethyl 2-bromobenzoate, the protocol occurred smoothly with ortho-bromobenzoic acid esters bearing Me (1b), OMe (1c and 1d) and even electron deactivating F (1e) on the aromatic ring (Scheme 1). The reaction was also compatible with different arylboronic acids 2a–g. Thus, the strategy was successful with para-methyl and para-ethylphenylboronic acids 2d and 2e (4ae, 4be, 4cd, 4ce, 4dd, 4de and 4ed, Scheme 1) and with electron-rich arylboronic acids such as 2f and 2g (4af, 4bg, 4cf, 4cg, 4df and 4ef, Scheme 1). Significantly, the protocol was also successful with an arylboronic acid (2c) bearing an electron-deactivating functional group (4dc, Scheme 1).

After the successful synthesis of fluorenes, we turned our attention to the synthesis of fluorenones. For this purpose, it was conceived that biaryl secondary alcohols would serve as ideal precursors for fluorenones. Since a polar solvent is required for smooth reduction of the carbonyl group, a sequential one-pot Suzuki protocols of palladium-catalysed Heck reaction and subsequent reduction of the carbonyl group, a sequential one-pot Suzuki coupling and reduction sequence in a one-pot strategy was considered. Thus, intramolecular Friedel–Crafts alkylation reaction of biaryl secondary alcohols would generate the desired fluorenones. Since a polar solvent is required for smooth reduction of the carbonyl group of the Suzuki product, in this case the reaction between ortho-bromoacetophenone 5a and para-tolylboronic acid 2a

**Table 1** Optimisation Study for the Formation of Fluorenone 4aa

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent (2 mL)</th>
<th>Acid$^b$</th>
<th>Temp (°C)</th>
<th>Time (h)</th>
<th>Yield 4aa (%)$^c$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>H$_2$O</td>
<td>H$_2$SO$_4$</td>
<td>100</td>
<td>5</td>
<td>trace$^d$</td>
</tr>
<tr>
<td>2</td>
<td>H$_2$O</td>
<td>TfOH</td>
<td>100</td>
<td>5</td>
<td>trace$^d$</td>
</tr>
<tr>
<td>3</td>
<td>DMF</td>
<td>H$_2$SO$_4$</td>
<td>100</td>
<td>5</td>
<td>20</td>
</tr>
<tr>
<td>4</td>
<td>DMF</td>
<td>H$_2$SO$_4$</td>
<td>100</td>
<td>10</td>
<td>23</td>
</tr>
<tr>
<td>5</td>
<td>DMF</td>
<td>TfOH</td>
<td>100</td>
<td>10</td>
<td>40</td>
</tr>
<tr>
<td>6</td>
<td>DMF + H$_2$O (1:1)</td>
<td>TfOH</td>
<td>100</td>
<td>10</td>
<td>trace$^d$</td>
</tr>
<tr>
<td>7</td>
<td>CH$_2$CN</td>
<td>TfOH</td>
<td>100</td>
<td></td>
<td>trace$^d$</td>
</tr>
<tr>
<td>8</td>
<td>DMSO</td>
<td>TfOH</td>
<td>100</td>
<td>10</td>
<td>trace$^d$</td>
</tr>
<tr>
<td>9</td>
<td>DCE</td>
<td>TfOH</td>
<td>80</td>
<td>10</td>
<td>58</td>
</tr>
<tr>
<td>10</td>
<td>DCE</td>
<td>H$_2$SO$_4$</td>
<td>80</td>
<td>10</td>
<td>54</td>
</tr>
<tr>
<td>11</td>
<td>CH$_2$Cl$_2$</td>
<td>TfOH</td>
<td>100</td>
<td>10</td>
<td>43</td>
</tr>
<tr>
<td>12</td>
<td>DCE</td>
<td>TfOH</td>
<td>80</td>
<td>10</td>
<td>68$^e$</td>
</tr>
<tr>
<td>13</td>
<td>DCE</td>
<td>TfOH</td>
<td>80</td>
<td>10</td>
<td>40$^f$</td>
</tr>
<tr>
<td>14</td>
<td>DCE</td>
<td>BF$_3$-OEt$_2$</td>
<td>80</td>
<td>10</td>
<td>trace$^d$</td>
</tr>
<tr>
<td>15</td>
<td>DCE</td>
<td>AlCl$_3$</td>
<td>80</td>
<td>10</td>
<td>trace$^d$</td>
</tr>
</tbody>
</table>

$^a$ Unless otherwise mentioned, all the reactions were carried out using 2-bromomethyl benzoate 1a (0.50 mmol), phenylboronic acid 2a (0.55 mmol), K$_2$CO$_3$ (1.0 mmol), acid (5 mmol), Pd(OAc)$_2$ (5 mol%), TBAI (16 mg, 10 mol%) in a screw-cap vial.

$^b$ Acid (5 equiv) was used.

$^c$ Isolated yields of chromatographically pure products.

$^d$ Only a trace amount of product was formed.

$^e$ TfOH (10 equiv) was used.

$^f$ TfOH (15 equiv) has been used.
was conducted in DNF in the presence of Pd(OAc)₂ (5 mol%) and K₂CO₃ (2 equiv) at 80 °C for 24 h. After confirming formation of the Suzuki product 6aa, by TLC, the cooled reaction mixture was then subjected to reduction with NaBH₄ in situ, at 0 °C to r.t., for 30 min. After work-up, the crude biaryl secondary alcohol 7aa was then treated with mild Lewis acid BF₃·OEt₂ in DCE, 0 °C to r.t., and fluorene 8aa was isolated in 77% overall yield after column chromatography (Scheme 2). With these established conditions, the procedure was extended to the synthesis of a range of fluorenes derived from ortho-bromoacetophenones 5a–f and arylboronic acids 2a–g, furnishing fluorenes 8ad–eg (Scheme 2).

In conclusion, we have established a sequential one-pot strategy for the synthesis of fluorenones. Palladium-catalysed Suzuki coupling and acid-mediated intramolecular Friedel–Crafts acylation were employed in the one-pot protocol. In addition, Suzuki coupling, followed by reduction and intramolecular Friedel–Crafts alklylation in a one-pot protocol has been developed for the synthesis of fluorenes.
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Synthesis of Fluorenones 4; General Procedure

In an oven-dried Schlenk tube, were added ethyl 2-bromobenzoate 1 (114–145 mg, 0.5 mmol), phenylboronic acid 2 (122–182 mg, 0.55 mmol), palladium acetate (5.6 mg, 5 mol%), potassium carbonate (138 mg, 1.0 mmol) and TBAI (16 mg, 10 mol%), followed by DCE (2 mL) at r.t. and the reaction mixture was stirred for 15 h. Progress of the reaction for the formation of the Suzuki product, NaBH₄ (37.8 mg, 1.0 mmol) was added at 0 °C then the reaction mixture was stirred at room temperature for 0.5 h. After confirming formation of the corresponding alcohol, BF₃·OEt₂ was added to the worked up reaction mixture. Yields in the parentheses are isolated yields of chromatographically pure products.

Synthesis of Fluorenes 8; General Procedure

In an oven-dried Schlenk tube, were added 2-bromophenylketone 5 (100–137 mg, 0.5 mmol), phenylboronic acid 2 (122–182 mg, 0.55 mmol), palladium acetate (5.6 mg, 5 mol%) and potassium carbonate (138 mg, 1.0 mmol), followed by DMF (2.0 mL) at r.t. and the reaction mixture was stirred at room temperature for 15 h. Progress of the reaction for the formation of the Suzuki product, NaBH₄ (375 mg, 10 mmol) was added and the mixture was stirred at 80 °C, 15 h, after confirming formation of the Suzuki product, NaBH₄ (37.8 mg, 1.0 mmol) was added at 0 °C then the reaction mixture was stirred at room temperature for 0.5 h. After confirming formation of the corresponding alcohol, BF₃·OEt₂ was added to the worked up reaction mixture. Yields in the parentheses are isolated yields of chromatographically pure products.

S = broad singlet. The assignment of signals was confirmed by ¹H, ¹³C carbon-proton decoupling and DEPT spectroscopy. High-resolution mass spectra (HRMS) were recorded with an Agilent 6538 UHD Q-TOF under electrospray ionisation (ESI) mode and atmospheric pressure chemical ionisation (APCI) mode. All small-scale anhydrous reactions were carried out using Schlenk tubes under an inert atmosphere. Reactions were monitored by TLC on silica gel using a combination of hexane and EtOAc as eluent. Reactions were generally run under argon or nitrogen atmosphere. Solvents were distilled prior to use; petroleum ether with a boiling range of 60 to 80 °C was used. Palladium acetate, potassium carbonate, TBAI, TfOH, NaBH₄ and BF₃·OEt₂ were purchased from Sigma–Aldrich and used as received. 2-Bromoethyl benzoates were used as received. 2-Bromoaryl ketones were prepared from 2-bromobenzaldehydes by using standard Grignard and oxidation protocol. Acme silica gel (60–120 mesh) was used for column chromatography (ca. 20 g per gram of crude material).
mixture was stirred at 80 °C for 20 h. Progress of formation of the Suzuki product was monitored by TLC, then the mixture was cooled to r.t. To the reaction mixture was added NaBH₄ (76 mg, 2 mmol) at 0 °C and stirring was continued at r.t. for 0.5 h. The reaction mixture was quenched with aq. NH₄Cl and extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with saturated aq. NaCl, dried (Na₂SO₄), and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/EtOAc) furnished fluorenes 8 (67 to 88%), as semi-solid/solid products. Several of the fluorenes are already reported in the literature.²⁵⁻²⁷

2-Ethyl-7-methyl-9H-fluoren-9-one (4be)
In an oven-dried Schlenk tube, were added 2-ethyl 2-bromobenzoate 1b (121.5 mg, 0.5 mmol), arylboronic acid 2e (83 mg, 0.55 mmol), Pd(OAc)₂ (5.6 mg, 5 mol%), K₂CO₃ (138 mg, 1.0 mmol) and TBAI (16 mg, 10 mol%) followed by DCE (2 mL) at r.t. and the reaction mixture was stirred at 80 °C for 20 h. To the cooled reaction mixture at r.t., was added Ti(OH)₃ (755 mg, 5.0 mmol) and stirring was continued at 80 °C for 15 h. Purification of the crude material by silica gel column chromatography (petroleum ether/EtOAc, 99:1 to 95:5) furnished 4be.

Yield: 87.0 mg (82%); yellow solid; TLC (petroleum ether/EtOAc, 95:05; UV detection): Rₛ = 0.1 (1b), 0.6 (4be).

1H NMR (CDCl₃, 400 MHz): δ = 7.39 (s, 1 H, Ar-H), 7.26–7.16 (m, 2 H, Ar-H), 7.15 (s, 1 H, Ar-H), 6.94 (s, 1 H, Ar-H), 3.98 (s, 3 H, ArOCH₃), 3.89 (s, 3 H, ArOCH₃), 2.62 (q, J = 7.5 Hz, 2 H, CH₂CH₃), 1.22 (t, J = 7.5 Hz, 3 H, ArCH₃).


2-Fluoro-7-methyl-9H-fluoren-9-one (4ed)
In an oven-dried Schlenk tube, were added ethyl 2-bromobenzoate 1e (123.5 mg, 0.5 mmol), arylboronic acid 2d (75 mg, 0.55 mmol), Pd(OAc)₂ (5.6 mg, 5 mol%), K₂CO₃ (138 mg, 1.0 mmol), and TBAI (16 mg, 10 mol%) followed by DCE (2.0 mL) at r.t. and the reaction mixture was stirred at 80 °C for 20 h. To the cooled reaction mixture at r.t., was added Ti(OH)₃ (755 mg, 5.0 mmol) and stirring was continued at 80 °C for 15 h. Purification of the crude material by silica gel column chromatography (petroleum ether/EtOAc, 99:1 to 95:5) furnished 4ed.

Yield: 87.0 mg (82%); yellow solid; TLC (petroleum ether/EtOAc, 95:05; UV detection): Rₛ = 0.1 (1e), 0.6 (4ed).

1H NMR (CDCl₃, 400 MHz): δ = 7.43 (s, 1 H, Ar-H), 7.42–7.36 (m, 1 H, Ar-H), 7.32 (d, J = 7.8 Hz, 1 H, Ar-H), 7.32–7.23 (m, 2 H, Ar-H), 7.11 (dd, J = 8.8, 8.3, 2.4 Hz, 1 H, Ar-H), 2.35 (s, 3 H, ArCH₃).


2,3-Dimethoxy-9-methyl-9H-fluorene (8ag)
In an oven-dried Schlenk tube, were added 2-bromomethylketone 5a (100 mg, 0.5 mmol), arylboronic acid 2g (100 mg, 0.55 mmol), Pd(OAc)₂ (5.6 mg, 5 mol%), and K₂CO₃ (138 mg, 1.0 mmol) followed by DMF at r.t. and the reaction mixture was stirred at 80 °C for 20 h. Then, to the cooled reaction mixture at ice temperature, was added NaBH₄ (76 mg, 2 mmol) and stirring was continued at the same temperature for 0.5 h. After work-up, the crude reaction mixture at ice temperature, was added DCE and BF₃·OEt₂ (710 mg, 5 mmol) and stirring was continued for 1 h. Progress of the reaction for the formation of 2,3-dimethoxy-9-methyl-9H-fluorene 8ag was monitored by THIEME OPEN ACCESS

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TLC. The reaction mixture was then quenched withaq. NaHCO₃, and the mixture was diluted withaq. NH₄Cl and extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with saturatedaq. NaCl, dried (Na₂SO₄) and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/EtOAc, 99:1 to 95:5) furnished the product **8ag**.

Yield: 100 mg (82%); white solid; TLC (petroleum ether/EtOAc, 93:07; UV detection): Rₜ = 0.8 (5a), 0.6 (8ag).  

1H NMR (CDCl₃, 400 MHz): δ = 7.26 (d, J = 7.4 Hz, 1 H, Ar-H), 7.44 (d, J = 7.3 Hz, 1 H, Ar-H), 7.32 (dd, J = 7.3, 7.3 Hz, 1 H, Ar-H), 7.24 (s, 1 H, Ar-H), 7.29 (dd, J = 7.4, 7.3, 1 Hz, 1 H, Ar-H), 7.02 (s, 1 H, Ar-H), 3.97 (s, 3 H, ArOCH₃), 3.94 (s, 3 H, ArOCH₃), 3.83 (q, J = 7.4 Hz, CH₃), 1.48 (d, J = 7.4 Hz, 3 H, CH₃).

13C NMR (CDCl₃, 100 MHz): δ = 149.0 (s, Ar-C), 148.9 (s, Ar-C), 148.7 (s, Ar-C), 141.5 (s, Ar-C), 140.8 (s, Ar-C), 132.8 (s, Ar-C), 126.8 (d, Ar-CH), 125.6 (d, Ar-CH), 123.7 (d, Ar-CH), 118.8 (d, Ar-CH), 107.3 (d, Ar-CH), 103.0 (d, Ar-CH), 56.1 (q, ArOCH₃), 56.0 (q, ArOCH₃), 42.2 (d, CH), 18.3 (q, CH₃).


9-Ethyl-2,3,7-trimethoxy-9H-fluorene (8bf)

In an oven-dried Schlenk tube, were added 2-bromophenylketone **5b** (115 mg, 0.55 mmol), arylboronic acid **2f** (84 mg, 0.55 mmol), Pd(OAc)₂ (5.6 mg, 5 mol%) and K₂CO₃ (138 mg, 1.0 mmol) followed by DMF at r.t. and the reaction mixture was stirred for 1 h. Progress of the reaction for the formation of 2,3,7-trimethoxy-9-fluorene **8bf** was monitored by TLC. The reaction was then quenched withaq. NaHCO₃, and the mixture was diluted withaq. NH₄Cl and extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with saturatedaq. NaCl, dried (Na₂SO₄) and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/EtOAc, 99:1 to 92:8) furnished **8bg**.

Yield: 116 mg (85%); colourless solid; TLC (petroleum ether/EtOAc, 92:08; UV detection): Rₜ = 0.7 (5b), 0.4 (8bg).

1H NMR (CDCl₃, 400 MHz): δ = 7.50 (d, J = 8.3 Hz, 1 H, Ar-H), 7.17 (s, 1 H, Ar-H), 7.02 (d, J = 2.2 Hz, 1 H, Ar-H), 7.00 (s, 1 H, Ar-H), 6.87 (dd, J = 13.3, 2.3 Hz, 1 H, Ar-H), 3.96 (s, 3 H, ArOCH₃), 3.93 (s, 3 H, ArOCH₃), 3.85 (s, 3 H, ArOCH₃), 3.82 (q, J = 7.4 Hz, 1 H, CH₃), 1.48 (d, J = 7.4 Hz, 3 H, CH₃).

13C NMR (CDCl₃, 100 MHz): δ = 158.6 (s, Ar-C), 150.9 (s, Ar-C), 148.7 (s, Ar-C), 148.1 (s, Ar-C), 140.8 (s, Ar-C), 133.8 (s, Ar-C), 131.9 (d, Ar-CH), 112.3 (d, Ar-CH), 110.0 (d, Ar-CH), 107.5 (d, Ar-CH), 102.6 (d, Ar-CH), 56.1 (q, ArOCH₃), 56.1 (q, ArOCH₃), 55.4 (q, ArOCH₃), 42.2 (d, CH), 18.4 (q, CH₃).


9-Ethyl,2,3,7-trimethoxy-9H-fluorene (8cf)

In an oven-dried Schlenk tube, were added 2-bromophenylketone **5c** (137 mg, 0.55 mmol), arylboronic acid **2f** (84 mg, 0.55 mmol), Pd(OAc)₂ (5.6 mg, 5 mol%) and K₂CO₃ (138 mg, 1.0 mmol) followed by DMF at r.t. and the reaction mixture was stirred at 80 °C for 20 h. Then, to the cooled reaction mixture at ice temperature, were added DCE and BF₃·OEt₂ (710 mg, 5 mmol) and stirring was continued for 1 h. Progress of the reaction for the formation of 2,3,7-trimethoxy-9H-fluorene **8cf** was monitored by TLC. The reaction was then quenched withaq. NaHCO₃, and the mixture was diluted withaq. NH₄Cl and extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with saturatedaq. NaCl, dried (Na₂SO₄) and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/EtOAc, 99:1 to 92:8) furnished **8cg**.

Yield: 103 mg (72%); colourless solid; TLC (petroleum ether/EtOAc, 95:05; UV detection): Rₜ = 0.6 (5c), 0.8 (8cf).

1H NMR (CDCl₃, 400 MHz): δ = 7.51 (d, J = 8.2 Hz, 1 H, Ar-H), 7.16 (s, 1 H, Ar-H), 7.02 (d, J = 2.5 Hz, 1 H, Ar-H), 7.00 (s, 1 H, Ar-H), 6.88 (dd, J = 8.2, 2.8 Hz, 1 H, Ar-H), 3.96 (s, 3 H, ArOCH₃), 3.93 (s, 3 H, ArOCH₃), 3.91–3.84 (m, 1 H, CH), 3.85 (s, 3 H, ArOCH₃), 2.10–1.99 (m, 2 H, CH₂CH₃), 0.68 (t, J = 7.4 Hz, 3 H, CH₂CH₃).

13C NMR (CDCl₃, 100 MHz): δ = 158.5 (s, Ar-C), 149.1 (s, Ar-C), 148.7 (s, Ar-C), 148.0 (s, Ar-C), 139.0 (s, Ar-C), 134.7 (s, Ar-C), 133.9 (s, Ar-C), 119.2 (d, Ar-CH), 112.3 (d, Ar-CH), 110.4 (d, Ar-CH), 107.8 (d, Ar-CH), 102.4 (d, Ar-CH), 56.2 (q, ArOCH₃), 56.1 (q, ArOCH₃), 55.6 (q, ArOCH₃), 48.3 (d, CH), 25.8 (t, CH₂CH₃), 9.4 (q, CH₂CH₃).

In an oven-dried Schlenk tube, were added 2-bromophenylketone (131 mg, 0.5 mmol), aryloboric acid (2g (100 mg, 0.55 mmol), Pd(OAc)2 (5.6 mg, 5 mol%) and K2CO3 (138 mg, 1.0 mmol) followed by DMF at r.t. and the reaction mixture was stirred at 80 °C for 20 h. Then, to the cooled reaction mixture at ice temperature, was added NaBH4 (76 mg, 2 mmol) and stirring was continued at the same temperature for 0.5 h. After work-up, to the crude reaction mixture at ice temperature, were added DCE and BF3·OEt2 (710 mg, 5 mmol) and stirring was continued for 1 h. Progress of the reaction for the formation of 2,3-dimethoxy-9-phenyl-9H-fluorene 8ee was monitored by TLC. The reaction was then quenched with aq. NaHCO3, and the mixture was diluted with aq. NH4Cl and extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with saturated aq. NaCl, dried (Na2SO4), and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/EtOAc, 99:1 to 95:5) furnished 8ee.

Yield: 91 mg (67%); colourless solid; TLC (petroleum ether/EtOAc, 95:05; UV detection): Rf = 0.5 (5e), 0.7 (8ee).

1H NMR (CDCl3, 400 MHz): δ = 7.74 (d, J = 7.3 Hz, 1 H, Ar-H), 7.69 (d, J = 7.8 Hz, 1 H, Ar-H), 7.34 (dd, J = 7.3, 7.3 Hz, 1 H, Ar-H), 7.30–7.16 (m, 6 H, Ar-H), 7.14 (s, 1 H, Ar-H), 7.16–7.03 (m, 2 H, Ar-H), 4.99 (s, 1 H, CH2), 2.63 (q, J = 7.8 Hz, 2 H, CH2CH3), 1.20 (t, J = 7.8 Hz, 3 H, CH2CH3).

13C NMR (CDCl3, 100 MHz): δ = 148.2 (s, Ar-C), 147.9 (s, Ar-C), 143.8 (s, Ar-C), 141.9 (s, Ar-C), 141.1 (s, Ar-C), 138.7 (s, Ar-C), 128.7 (d, 2C, 2 × Ar-CH), 128.4 (d, 2C, 2 × Ar-CH), 127.3 (d, Ar-CH), 127.1 (d, Ar-C), 126.9 (d, Ar-CH), 126.8 (d, Ar-CH), 125.3 (3 C, Ar-CH), 124.9 (d, Ar-CH), 119.7 (d, Ar-CH), 119.6 (d, Ar-CH), 54.4 (d, CH), 29.1 (t, C2 × Ar-CH), 128.4 (d, 2C, 2 × Ar-CH), 128.2 (d, 2C, 2 × Ar-CH), 127.2 (d, Ar-C), 126.8 (d, Ar-CH), 126.0 (d, Ar-CH), 125.0 (d, Ar-CH), 118.7 (d, Ar-CH), 108.3 (d, Ar-CH), 102.8 (d, Ar-CH), 56.1 (s, ArOCH3), 56.0 (s, ArOCH3), 54.3 (d, CH).

HRMS (APCI+): m/z [M + H]+ calculated for [C28H18O3]: 393.1380; found: 393.1361.

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References