Enantioselective addition of arylboronic acids to methyl 2-formylbenzoates by using a ruthenium/Me-BIPAM catalyst for synthesis of chiral 3-aryl-isobenzofuranones

Yohda, Masaaki; Yamamoto, Yasunori

Organic & biomolecular chemistry, 13(44): 10874-10880

2015-11-28

http://hdl.handle.net/2115/63683

article (author version)

OB-COM-08-2015-001661.pdf
Enantioselective Addition of Arylboronic Acids to Methyl 2-Formylbenzoates by using a Ruthenium/Me-BIPAM Catalyst for Synthesis of Chiral 3-Aryl-isobenzofuranones

Masaaki Yohda* and Yasunori Yamamoto

Abstract text goes here. The abstract should be a single paragraph that summarises the content of the article.

carbonyl compounds.11 Herein, we report the synthesis of optically active 3-aryl-isobenzofuranones by using enantioselective addition of arylboronic acids to methyl 2-formylbenzoates.

Our initial investigation began by screening catalysts to evaluate their ability to promote enantioselective arylation of methyl 2-formylbenzoate with phenylboronic acid. As shown in Table 1, when [RuCl2(p-cymene)]2, RuCl2(PPh3)3 or RuCl2[nbd](MeCN)2 with Me-BIPAM, which were used in our previous work,1-3 affording chiral 3-aryl-isobenzofuranones.

Table 1. Reaction Conditions

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Ligand</th>
<th>Base</th>
<th>Solvent</th>
<th>Yield (%)</th>
<th>ee (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>[RuCl2(p-cymene)]2</td>
<td>(R,R)-Me-BIPAM</td>
<td>K2CO3</td>
<td>toluene</td>
<td>96</td>
<td>94</td>
</tr>
<tr>
<td>2</td>
<td>[RuCl2(p-cymene)]2</td>
<td>(R,R)-Me-BIPAM</td>
<td>KOH</td>
<td>DCE</td>
<td>96</td>
<td>97</td>
</tr>
<tr>
<td>3</td>
<td>[RuCl2(p-cymene)]2</td>
<td>(R,R)-Me-BIPAM</td>
<td>K2CO3</td>
<td>toluene</td>
<td>99.9</td>
<td>97</td>
</tr>
<tr>
<td>4</td>
<td>[RuCl2(p-cymene)]2</td>
<td>(R,R)-Me-BIPAM</td>
<td>K2CO3</td>
<td>DCE</td>
<td>74</td>
<td>96</td>
</tr>
<tr>
<td>5</td>
<td>[RuCl2(p-cymene)]2</td>
<td>(R,R)-Me-BIPAM</td>
<td>K2CO3</td>
<td>DCE</td>
<td>96</td>
<td>93</td>
</tr>
<tr>
<td>6</td>
<td>RuCl2(PPh3)3</td>
<td>(R,R)-Me-BIPAM</td>
<td>K2CO3</td>
<td>DCE</td>
<td>98</td>
<td>96</td>
</tr>
<tr>
<td>7</td>
<td>RuCl2(PPh3)3</td>
<td>(R,R)-Me-BIPAM</td>
<td>K2CO3</td>
<td>toluene</td>
<td>96</td>
<td>93</td>
</tr>
<tr>
<td>8</td>
<td>RuCl2<a href="MeCN">nbd</a>2</td>
<td>(R,R)-Me-BIPAM</td>
<td>K2CO3</td>
<td>toluene</td>
<td>96</td>
<td>93</td>
</tr>
<tr>
<td>9</td>
<td>RuCl2(PPh3)3</td>
<td>(R,R)-Me-BIPAM</td>
<td>K2CO3</td>
<td>toluene</td>
<td>67</td>
<td>91</td>
</tr>
<tr>
<td>10</td>
<td>[RuCl2(p-cymene)]2</td>
<td>(R,R)-Me-BIPAM</td>
<td>K2CO3</td>
<td>toluene</td>
<td>26</td>
<td>-12</td>
</tr>
<tr>
<td>11</td>
<td>[RuCl2(p-cymene)]2</td>
<td>(R)-Monophos</td>
<td>K2CO3</td>
<td>toluene</td>
<td>70</td>
<td>78</td>
</tr>
</tbody>
</table>

*Reactions were carried out at 50-80 °C for 18 h by using methyl 2-formylbenzoates 1a (0.5 mmol), 2a (0.75 mmol), Ru catalyst (0.01 mmol), ligand (0.011 mmol), K2CO3 (0.5 mmol) and toluene/H2O (5/1, 3.0 mL).
†Isolated yield. The ee value of 3 was determined by chiral HPLC analysis. a
‡ 50 °C, 18 h. b MeCN (20 mol %) was added

Ruthenium/Me-BIPAM-catalyzed asymmetric addition of arylboronic acids to methyl 2-formylbenzoates afforded chiral 3-aryl-isobenzofuranones. [RuCl2(p-cymene)]2/Me-BIPAM and RuCl2(PPh3)3/Me-BIPAM catalyst systems tolerate a variety of functional groups and give high yields with high enantioselectivities.

Optically active 3-substituted isobenzofuranones are important structures in medicinal chemistry as well as in synthetic chemistry.1,2 Recently, various methods for the synthesis of these chiral compounds have been developed.1 Reported methods include lactonization followed by the hydrogenation of the corresponding ketones,3 intramolecular ketone hydroacylation,4 aldehyde reactions,5 addition reaction,6 and cyclization reaction.7 Over the past decade, transition metal-catalyzed addition reactions of arylboronic acids with 2-formylbenzoates have become useful tools for accessing 3-aryl-isobenzofuranones.8 However, to our knowledge, there have been only a few reports on the synthesis of optically active 3-aryl-isobenzofuranones using this strategy.10

We have already developed a bidentate chiral phosphoramidite (Me-BIPAM) and have used it in ruthenium-catalyzed asymmetric addition of arylboronic acids to various carbonyl compounds.11 Herein, we report the synthesis of optically active 3-aryl-isobenzofuranones by using enantioselective addition of arylboronic acids to methyl 2-formylbenzoates.

Our initial investigation began by screening catalysts to evaluate their ability to promote enantioselective arylation of methyl 2-formylbenzoate with phenylboronic acid. As shown in Table 1, when [RuCl2(p-cymene)]2, RuCl2(PPh3)3 or RuCl2[nbd](MeCN)2 with Me-BIPAM, which were used in our previous work,1-3 affording chiral 3-aryl-isobenzofuranones.
previous works, were used for this reaction, addition products were obtained in high yields with high enantioselectivities (entries 2, 7 and 8). Use of KOH and DCE resulted in lower yields (entries 4 and 5). Among the chiral ligands screened, the use of (R)-BINAP (entry 10) and monodentate phosphoramidite, (R)-MonoPhos (entry 11) resulted in lower enantioselectivities, -12% ee and 78% ee, respectively. \(^1\)

We then studied the substrate scope for various arylboronic acids with [RuCl\(_2(p\text{-cymene})\)]\(_2\) or RuCl\(_2(\text{PPh}_3)_3\)-Me-BIPAM catalyst (Table 1). Arylboronic acids with electron-donating and -withdrawing groups at para- and meta-positions afforded 3-aryl-isobenzofuranones in high yields with high enantioselectivities in the range of 91–97% ee. The addition of para-biphenylboronic acid and 3-thienylboronic acid resulted in a high yield with high enantioselectivities when the temperature was increased and the solvent ratio of toluene/H\(_2\)O was changed (entries 5 and 12). The structure of 3a\(_h\) was confirmed unequivocally by its X-ray crystal structure (entry 12). The absolute configuration of the product was assigned as S enantiomer from X-ray crystallographic analysis of the compound of 3a\(_h\) (Figure 1). \(^1\)

From the above results, [RuCl\(_2(p\text{-cymene})\)]\(_2\) with (R,R)-Me-BIPAM catalyst gave higher enantioselectivities for the electron-donating arylboronic acids, but RuCl\(_2(\text{PPh}_3)_3\) with (R,R)-Me-BIPAM catalyst gave higher yields and enantioselectivities for the electron-withdrawing arylboronic acids. The structure of [RuCl\(_2(p\text{-cymene})\)]\(_2\) with (R,R)-Me-BIPAM showed cationic complex, \(^1\)\(^4\) but the structure of RuCl\(_2(\text{PPh}_3)_3\) with (R,R)-Me-BIPAM complex showed neutral complex. \(^1\)\(^3\)\(^c\) The difference in reactivity between [RuCl\(_2(p\text{-}

cymene})\)]\(_2\) and RuCl\(_2(\text{PPh}_3)_3\) catalyst is correlated with the electronic effect of the arylruthenium intermediates.

Next, we investigated the substrate scope with focus on substituents on the aromatic ring of methyl 2-formylbenzoates (Table 3). Arylation of methyl 2-formylbenzoates gave the corresponding products in high yields (84–99%) with excellent enantioselectivities (87–97% ee). The arylation product of 5,6-desmethylenedioxy-5-methoxy-aglalactone (3b\(_f\)) which was isolated from the CH\(_3\)Cl soluble extract of the leaves and twigs of Aglaia ponapensis exhibit the NF-kB inhibitory activity. \(^1\)\(^2\)

Table 3. Substrate Scope for the methyl 2-formylbenzoates\(^a\)\(^b\)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ar = (Ar-B(OH))(_2) catalyst</th>
<th>Yield (%)</th>
<th>ee (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>C(_6)H(_5)</td>
<td>[RuCl(_2(p\text{-cymene}))]</td>
<td>96 (3a(_a))</td>
</tr>
<tr>
<td>2(^b)</td>
<td>4-MeOC(_6)H(_5)</td>
<td>[RuCl(_2(p\text{-cymene}))]</td>
<td>80 (3a(_b))</td>
</tr>
<tr>
<td>3(^b)</td>
<td>4-MeC(_6)H(_4)</td>
<td>[RuCl(_2(p\text{-cymene}))]</td>
<td>99 (3a(_c))</td>
</tr>
<tr>
<td>4</td>
<td>4-CH(_2\text{CHC}_6)H(_4)</td>
<td>[RuCl(_2(p\text{-cymene}))]</td>
<td>93 (3a(_d))</td>
</tr>
<tr>
<td>5(^b)</td>
<td>4-PhC(_6)H(_4)</td>
<td>RuCl(_2(\text{PPh}_3)_3)</td>
<td>87 (3a(_e))</td>
</tr>
<tr>
<td>6</td>
<td>4-FC(_6)H(_4)</td>
<td>RuCl(_2(\text{PPh}_3)_3)</td>
<td>98 (3a(_f))</td>
</tr>
<tr>
<td>7</td>
<td>4-ClC(_6)H(_4)</td>
<td>RuCl(_2(\text{PPh}_3)_3)</td>
<td>97 (3a(_g))</td>
</tr>
<tr>
<td>8</td>
<td>4-FC(_6)C(_6)H(_4)</td>
<td>RuCl(_2(\text{PPh}_3)_3)</td>
<td>74 (3a(_h))</td>
</tr>
<tr>
<td>9</td>
<td>2-naphthyl</td>
<td>RuCl(_2(\text{PPh}_3)_3)</td>
<td>92 (3a(_i))</td>
</tr>
<tr>
<td>10</td>
<td>3, 5-MeC(_6)H(_4)</td>
<td>RuCl(_2(\text{PPh}_3)_3)</td>
<td>99 (3a(_j))</td>
</tr>
<tr>
<td>11</td>
<td>3-ClC(_6)H(_4)</td>
<td>RuCl(_2(\text{PPh}_3)_3)</td>
<td>84 (3a(_k))</td>
</tr>
<tr>
<td>12(^b)</td>
<td>3-thienyl</td>
<td>RuCl(_2(\text{PPh}_3)_3)</td>
<td>92 (3a(_l))</td>
</tr>
</tbody>
</table>

\(^a\)Reactions were carried out at 50–80 °C for 18 h by using methyl 2-formylbenzoates 1a (0.5 mmol), 2 (0.75 mmol), Ru catalyst (0.01 mmol), ligand (0.011 mmol), K\(_2\)CO\(_3\) (0.5 mmol) and toluene/H\(_2\)O (5/1, 3.0 mL).

\(^b\)Isolated yield. The ee value of 3 was determined by chiral HPLC analysis. * 6 h. ° 80 °C, toluene/H\(_2\)O (20/1, 3 mL). † 80 °C, toluene/H\(_2\)O (10/1, 3 mL).

We propose a possible catalytic cycle of this reaction. The reaction may proceed through transmetalation of an arylboronic acid to a Ru/Me-BIPAM complex giving an Ar{[Ru]}. Insertion of the C=O bond of methyl 2-formyl benzoates into the Ar–Ru bond gave the Ru–O intermediate, and then provided 3-aryl-isobenzofuranones by hydrolysis and lactonization (Figure 2). The enantioselectivity is determined at the step of insertion of the C=O bond into an aryl ruthenium intermediate. Thus, the S configuration in Tables 1–3 caused by (R,R)-Me-BIPAM is rationalized by the coordination of an methyl 2-formyl benzoate with its si-face. The si-coordination of the substrate is preferred without significant steric interaction to give the experimentally observed S enantiomer by parallel coordination of the C=O bond to the Ar-Ru bond for the subsequent insertion step (Figure 3).

![Figure 1. ORTEP diagram of 3a\(_l\) (ORTEP drawing at 50% ellipsoid probability) (Please do not adjust margins)](image)
Conclusions

In summary, we have developed a ruthenium/Me-BIPAM-catalyzed addition of arylboronic acids to methyl 2-formylbenzoates for enantioselective synthesis of 3-aryl-isobenzofuranones. Various substituted chiral 3-aryl-isobenzofuranones were obtained with excellent enantioselectivities (87-97 % ee).

Experimental

Genetal methods

1H–NMR spectra were recorded on a JEOL ECX-400 (400 MHz) or JEOL ECS-400 (400 MHz) in CDCl₃, with tetramethylsilane (δ = 0.00) as internal standard. Chemical shifts are reported in part per million (ppm). HPLC analysis was directly performed with chiral stationary phase column, Chiralpak AD-H or Chiralcel OD-H purchased from DAICEL Co., Ltd. High resolution mass spectra (HRMS) were recorded on a JEOl JMS 700TZ mass spectrometer at the Center for Instrumental Analysis, Hokkaido University. Optical rotations were measured on a HORIBA SEPA-300 digital polarimeter. Kanto Chemical silica gel 60N (particle size 0.063–0.210 mm) was used for flash column chromatography.

Preparation of 2-formylbenzoates

To a solution of phthalides (2.0 mmol) in 10 mL dry benzene was added NBS (0.41g, 2.2 mmol) and AIBN (10.4 mg, 0.1 mmol) was added at room temperature. Then the mixture was refluxed at 85 °C overnight. It was cooled to room temperature and purified by flash chromatograph (silica gel, petroleum ether and ethyl acetate as eluent). The product was then suspended in 20 mL of H₂O and heated to 100 °C. After 1 h, the mixture was cooled to room temperature and then extracted with EtOAc (3×30 mL). The combined extracts were dried over MgSO₄, filtered and washed with acetone (3×15 mL). The combined filtrates were concentrated in vacuo and the residue was purified by flash chromatography (silica gel, eluent: petroleum/ethyl acetate = 20:1) to afford pure 3-aryl-ahydroxy-benzofuran-2-one.

General Procedure for Ruthenium/Me-BIPAM catalyzed Asymmetric Arylation of 2-formylbenzoic Acids

A flask was charged with Ruthenium catalyst (0.01 mmol, 2 mol%) and Me-BIPAM (0.01 mmol, 2.2 mol%) under nitrogen atmosphere. Toluene (2.5 mL) was added and the mixture was stirred at room temperature for 30 min. Phenylboronic acid (0.75 mmol), 2-formylbenzoate (0.5 mmol), K₂CO₃ (0.5 mmol) and H₂O (0.5 mL) were then added to this catalyst solution. The reaction mixture was then heated at 50 °C for 18 h. The mixture was quenched with aqueous saturated NH₄Cl, extracted with AcOEt, dried over MgSO₄, filtered off, and the solvents were evaporated. The crude product was purified by flash column chromatography (Hexane/AcOEt = 90/10, flow = 0.5 mL/min, wavelength = 230 nm, tᵣ = 23.4 min (major) and 30.9 min (minor)); [H' NMR (400 MHz, CDCl₃): δ = 7.96 (d, J = 7.8 Hz, 1H), 7.64 (t, J = 7.3 Hz 7.8 Hz, 1H), 7.55 (t, J = 7.3 Hz 7.8 Hz, 1H), 7.36 (m, 2H), 7.33 (d, J = 7.3 Hz, 1H, 7.28 (m, 2H), 6.40 (s, 1H); 13C NMR (100 MHz, CDCl₃): δ = 170.42, 149.53, 136.25, 134.23, 129.23, 129.14, 128.82, 128.61, 128.41, 125.34, 122.76, 82.57; MS (EI) m/z 136.25, 134.23, 129.23, 128.82, 126.11, 125.03 (100), 133.02 (12), 152.06 (12), 152.06 (12), 165.07 (34), 181.06 (16), 210.06 (78); HRMS (EI) m/z calcd for C₂₀H₁₆O₂ [M⁺]: 210.06980, found: 210.06768.

This journal is © The Royal Society of Chemistry 20xx

J. Name., 2013, 00, 1-3 | 3

Wako Pure Chemical Industries, Ltd. Phthalide was purchased from commercial source and substituted phthalides were synthesized according to known literature.¹-nine

Figure 2. Proposed catalytic cycle

Figure 3. Proposed coordination model

[Figure 2 and Figure 3 are not included in this text as they are not necessary for the natural text representation.]

Please do not adjust margins
$\text{(S)}$)-(3-methylphenyl)-1,3-dihydro-2-benzofuran-1-one (3af). $^{21}$ White solid; mp $121–124 ^\circ$C; 99% yield (112 mg); $[\alpha]_{25}^D = +31.0$ (c 0.50, CHCl$_3$), 94% ee [HPLC condition: Chiralpak AD-H column, hexane/2-propanol = 90/10, flow = 0.5 mL/min, wavelength = 230 nm, $\delta = 21.1$ (major) and 25.9 (minor)]; $^1$H NMR (400 MHz, CDCl$_3$); $\delta = 7.97$ (d, $J = 7.3$ Hz, 1H), 7.68 (t, $J = 7.3$ Hz 7.8 Hz, 1H), 7.58 (t, $J = 7.3$ Hz 7.8 Hz, 1H), 7.32 (d, $J = 7.8$ Hz 7.9 Hz, 1H), 6.84 (s, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$); $\delta = 170.19, 163.02$ (d, $J_{C-F} = 247.5$ Hz), 149.25, 134.36, 132.17, 129.40, 128.96 (d, $J_{C-F} = 8.8$ Hz), 125.50, 124.51, 122.76, 115.85 (d, $J_{C-F} = 21.3$ Hz), 81.87; MS (EI) m/z 77.04 (10), 105.03 (100), 123.02 (26), 133.03 (11), 170.05 (11), 183.06 (54), 199.05 (6), 228.06 (57); HRMS (EI) m/z calculated for C$_9$H$_8$O$_2$: [M$^+$] 286.0998, found: 286.09876.

$\text{(S)}$)-(3-fluorophenyl)-1,3-dihydro-2-benzofuran-1-one (3af). $^{21}$ White solid; mp $118–121 ^\circ$C; 84% yield (107 mg); $[\alpha]_{25}^D = +54.0$ (c 0.50, CHCl$_3$), 93% ee [HPLC condition: Chiralpak OD-H column, hexane/2-propanol = 90/10, flow = 0.5 mL/min, wavelength = 230 nm, $\delta = 22.6$ (major) and 31.5 (minor)]; $^1$H NMR (400 MHz, CDCl$_3$); $\delta = 7.96$ (d, $J = 7.8$ Hz, 1H), 7.67 (t, $J = 7.3$ Hz 7.8 Hz, 1H), 7.58 (t, $J = 7.3$ Hz 7.8 Hz, 1H), 7.37–7.31 (m, 3H), 7.24–7.21 (m, 2H), 6.38 (s, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$); $\delta = 170.19, 161.19, 135.14, 134.85, 134.42, 129.49, 129.10, 128.28, 125.63, 125.33, 122.70, 81.74; MS (EI) m/z 43.99 (28), 77.04 (32), 105.03 (100), 133.05 (13), 138.99 (21), 165.07 (60), 199.05 (3), 209.06 (90), 244.03 (29); HRMS (EI) m/z calculated for C$_7$H$_8$FO$_2$: [M$^+$] 244.0291, found: 244.02859.

$\text{(S)}$)-[(trifluoromethyl)phenyl]-1,3-dihydro-2-benzofuran-1-one (3af). $^{21}$ White solid; mp $118–121 ^\circ$C; 74% yield (103 mg); $[\alpha]_{25}^D = +34.0$ (c 0.50, CHCl$_3$), 91% ee [HPLC condition: Chiralpak OD-H column, hexane/2-propanol = 90/10, flow = 0.5 mL/min, wavelength = 230 nm, $\delta = 30.2$ (major) and 39.9 (minor)]; $^1$H NMR (400 MHz, CDCl$_3$); $\delta = 7.96$ (d, $J = 7.8$ Hz, 1H), 7.66 (t, $J = 7.3$ Hz 7.8 Hz, 1H), 7.58 (t, $J = 7.3$ Hz 7.8 Hz, 1H), 7.37–7.31 (m, 3H), 7.24–7.21 (m, 2H), 6.38 (s, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$); $\delta = 170.19, 161.19, 135.14, 134.85, 134.42, 129.49, 129.10, 128.28, 125.63, 125.33, 122.70, 81.74; MS (EI) m/z 43.99 (28), 77.04 (32), 105.03 (100), 133.05 (13), 138.99 (21), 165.07 (60), 199.05 (3), 209.06 (90), 244.03 (29); HRMS (EI) m/z calculated for C$_7$H$_8$FO$_2$: [M$^+$] 244.0291, found: 244.02859.
MHz, CDCl3; δ = 7.76 (d, J = 7.3 Hz, 1H), 7.69 (t, J = 7.3 Hz, 1H), 7.58 (t, J = 7.5 Hz, 1H), 7.43 (d, J = 7.8 Hz, 1H), 7.36–7.33 (m, 2H), 6.96–6.34 (m, 1H), 6.52 (s, 1H); 13C NMR (100 MHz, CDCl3; δ = 170.15, 148.89, 137.06, 134.23, 129.37, 129.13, 125.79, 125.61, 125.57, 124.41, 122.77, 78.34; MS (EI) m/z 77.04 (20), 82.99 (2), 105.03 (59), 110.99 (37), 133.03 (7), 171.02 (59), 187.01 (10), 216.02 (100); HRMS (EI) m/z caled for C16H11OS [M]+: 216.02450, found: 216.02450.

(-)-3-phenyl-5-(trifluoromethyl)-1,3-dihydro-2-benzofuran-1-one (3ba). White solid; mp 125–125.5 °C; 91% yield (127 mg); [α]D25 = +29.0 (c 0.5, CHCl3), 99% ee [HPLC condition: Chiralcel OD-H column, hexane/2-propanol = 90/10, flow = 0.5 mL/min, wavelength = 230 nm, tr = 19.5 min (major) and 26.3 min (minor)]; 1H NMR (400 MHz, CDCl3; δ = 7.75 (s, 1H), 7.46 (d, J = 7.8 Hz, 1H), 7.38–7.36 (m, 3H), 7.28–7.26 (m, 2H), 7.21 (d, J = 7.8 Hz, 1H), 6.37 (s, 1H), 2.47 (s, 3H); 13C NMR (100 MHz, CDCl3; δ = 170.61, 147.01, 139.55, 136.54, 135.42, 129.10, 128.81, 126.84, 125.59, 125.40, 122.47, 82.52, 21.16; MS (EI) m/z 41.04 (16), 91.05 (16), 105.02 (13), 119.04 (100), 147.03 (13), 165.05 (25), 178.06 (9), 224.06 (52); HRMS (EI) m/z caled for C16H10F2O2 [M]+: 224.08373, found: 224.08364.

(+)-3-phenyl-5-(trifluoromethyl)-1,3-dihydro-2-benzofuran-1-one (3ca). White solid; mp 110–111 °C; 95% yield (110 mg); [α]D25 = +25.0 (c 0.5, CHCl3), 95% ee [HPLC condition: Chiralcel OD-H column, hexane/2-propanol = 90/10, flow = 0.5 mL/min, wavelength = 230 nm, tr = 19.7 min (major) and 24.4 min (minor)]; 1H NMR (400 MHz, CDCl3; δ = 7.84 (d, J = 7.8 Hz, 1H), 7.41–7.34 (m, 4H), 7.29–7.26 (m, 2H), 7.11 (s, 1H), 6.35 (s, 1H), 2.44 (s, 3H); 13C NMR (100 MHz, CDCl3; δ = 170.54, 158.19, 154.38, 136.62, 130.45, 129.11, 128.84, 126.82, 125.23, 123.01, 122.80, 82.35, 21.96; MS (EI) m/z 43.99 (16), 77.03 (14), 91.05 (20), 119.04 (100), 147.03 (12), 165.05 (26), 178.06 (9), 195.06 (6), 224.06 (45); HRMS (EI) m/z caled for C16H10F2O2 [M]+: 224.08373, found: 224.08364.

(-)-6-bromo-3-phenyl-1,3-dihydro-2-benzofuran-1-one (3da). White solid; mp 102–106 °C; 87% yield (106 mg); [α]D25 = +17.0 (c 0.5, CHCl3), 95% ee [HPLC condition: Chiralcel OD-H column, hexane/2-propanol = 90/10, flow = 0.5 mL/min, wavelength = 230 nm, tr = 25.5 (major) and 43.5 min (minor)]; 1H NMR (400 MHz, CDCl3; δ = 7.92 (d, J = 1.8 Hz, 1H), 7.61 (dd, J = 1.8 Hz 7.9 Hz, 1H), 7.39 (t, J = 3.1 Hz, 3H), 7.29–7.23 (m, 3H), 6.39 (s, 1H); 13C NMR (100 MHz, CDCl3; δ = 170.54, 158.19, 154.38, 136.62, 130.45, 129.11, 128.84, 126.82, 125.23, 123.01, 122.80, 82.35, 21.96; MS (EI) m/z 77.04 (25), 103.05 (100), 138.99 (27), 165.07 (31), 181.06 (7), 199.03 (5), 209.06 (5), 244.03 (67); HRMS (EI) m/z caled for C16H10BrO2 [M]+: 244.02911, found: 244.02842.

Notes and references


13 CCDC 1420832 (3ai) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.