REGIOSELECTIVITY OF THE PALLADIUM-MEDIATED INTRAMOLECULAR COUPLING REACTION OF HIGHLY OXYGENATED PHENYL BENZOATE DERIVATIVES AND APPLICATION TO THE SYNTHESIS OF ALTERTENUOL

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Abstract – The regioselectivity of the intramolecular biaryl coupling reaction of 3',4'-dialkoxyphenyl 2,4-dimethoxybenzoates was investigated using a palladium reagent, and transition state models of the reaction are proposed. As an application of this study, a short-step synthesis of altertenuol is also performed.

INTRODUCTION

A palladium-mediated intramolecular biaryl coupling reaction of phenyl benzoate derivatives is a useful transformation for the preparation of the 6*H*-dibenzo[*b,d*]pyran-6-one skeleton.[1] There have been many studies of the total syntheses of natural products possessing this type of heterocyclic system, using the intramolecular biaryl coupling reaction.[2] In some cases, regioselectivity is a crucial concern in the inrtamolecular biaryl coupling, thus we recently reported several types of reactions involving the issue of regioselectivity.[3] In this report, as a series of our study, regioselectivity is examined in the Pd-mediated intramolecular biaryl coupling reaction of 3',4'-dialkoxyphenyl 2,4-dimethoxybenzoates, and the synthesis of a natural polyphenolic compound, altertenuol,[4] is also described.
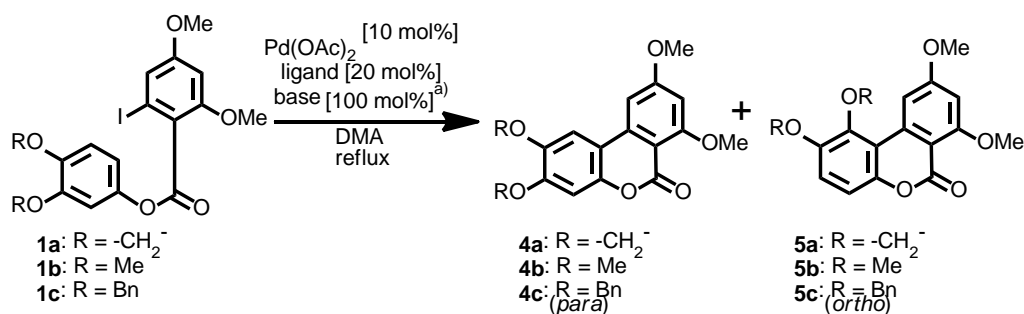
RESULTS AND DISCUSSION

As the substrates for the investigation, we prepared three kinds of phenyl benzoate derivatives **1a**-**1c**, which were easily obtained by a simple esterification between the corresponding phenols **2a**-**2c** and benzoic acid **3**. Initially, the regioselectivity was investigated using Ag_2CO_3 as the base (Table 1). For the ester **1a**, when Ph_3P was employed as the ligand, the *ortho*-product **5a** mainly generated. However, a poor regioselectivity for *para*- and *ortho*-products, **4a** and **5a,** was observed under no ligand condition (entries

1 and 2). On the contrary, for the substrates **1b** and **1c**, a dramatic change was observed in the product ratio. Namely, when using Ph_3P, the regioselectivity exhibited 1.4-0.7:1, although when using no ligand, the *para*-isomers **4b** and **4c** were predominantly generated (7.9-8.8:1, entries 3-6).

1a

1b: R = Me
1c: R = Bn

2a

2b: R = Me
2c: R = Bn

3
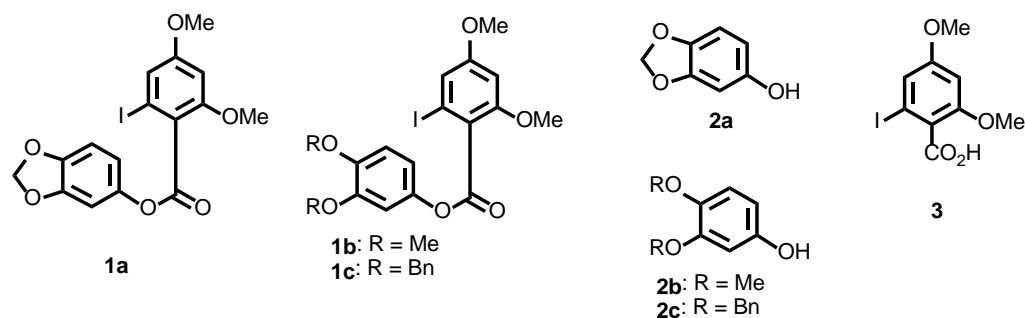
In contrast to the results above, employing K_2CO_3 as the base led to a different outcome for the product ratio. When several phosphine ligands[5] were attempted with the ester **1a**, the regioselectivity was almost identical to the result in entry 1 (entries 7-9). On the other hand, a slightly increased ratio was observed when using no phosphine ligand (entry 10). In the case of both **1b** and **1c**, a moderate selectivity was observed in the range of 1.2-3.6:1 under the condition that the phosphine ligand was employed (entries 11, 13, 14, and 15). When no ligand was used for **1b** and **1c**, the reaction proceeded with the product ratio of 4.4-4.5:1 (entries 12 and 16).

Table 1. Reaction of Phenyl Benzoate Derivatives **1a**-**1c**

1a: R = -CH₂-
1b: R = Me
1c: R = Bn

4a: R = -CH₂-
4b: R = Me
4c: R = Bn
(*para*)

5a: R = -CH₂-
5b: R = Me
5c: R = Bn
(*ortho*)

entry	substrate	ligand	yield (%) 4 + 5	ratio[b] 4 : 5	entry	substrate	ligand	yield (%) 4 + 5	ratio[b] 4 : 5
1	**1a**	Ph_3P	77	0.2 : 1	7	**1a**	XPhos[c]	89	0.3 : 1
2	**1a**	none	79	1.8 : 1	8	**1a**	Ph_3P	81	0.2 : 1
3	**1b**	Ph_3P	92	1.4 : 1	9	**1a**	$^nBu_3P$	77	0.2 : 1
4	**1b**	none	89	8.8 : 1	10	**1a**	none	96	0.5 : 1
5	**1c**	Ph_3P	99	0.7 : 1	11	**1b**	Ph_3P	81	2.5 : 1
6	**1c**	none	80	7.9 : 1	12	**1b**	none	84	4.4 : 1
					13	**1c**	XPhos[c]	79	3.6 : 1
					14	**1c**	Ph_3P	89	1.7 : 1
					15	**1c**	$^nBu_3P$	81	1.2 : 1
					16	**1c**	none	77	4.5 : 1

a) Ag_2CO_3 was used as the base in entries 1-6. K_2CO_3 was used as the base in entries 7-16.
b) Determined by ^{1}H-NMR analysis.
c) Ref. 5

For the mechanistic aspect, we would be able to explain the regioselectivity by considering the transition state models.[3i] Based on Echavarren's intermolecular-assisted mechanism,[6] the transition state of substrate **1a** can be illustrated as Figure 1. *A1* and *A2* describe the models in the case of using Ag_2CO_3 as the base. Strong affinity between the silver and the iodo atom causes a partial cationic character on the palladium. Therefore, the alkoxy oxygen can coordinate to the palladium atom (*A2*) leading to providing the *ortho*-products **5a**-**5c**, whereas the steric hindrance, which was generated between the alkoxy group and the ligand on the palladium atom, is also significant (*A2*; L = phosphine). Consequently, the product ratios are controlled by the balance of both the coordinating power and the steric factor. However, when using no phosphine ligand, the tight solvation of the DMA takes place to make the surrounding of the palladium to be bulkier (*A1* and *A2*; L = DMA). Thus, no phosphine ligand condition leads to the severe steric repulsion between the alkoxy group and DMA, as shown in *A2*, so that the ratio of the *para*-products **4a**-**4c** is increased.

**Figure 1.** Transition State Models under Ag_2CO_3 Condition
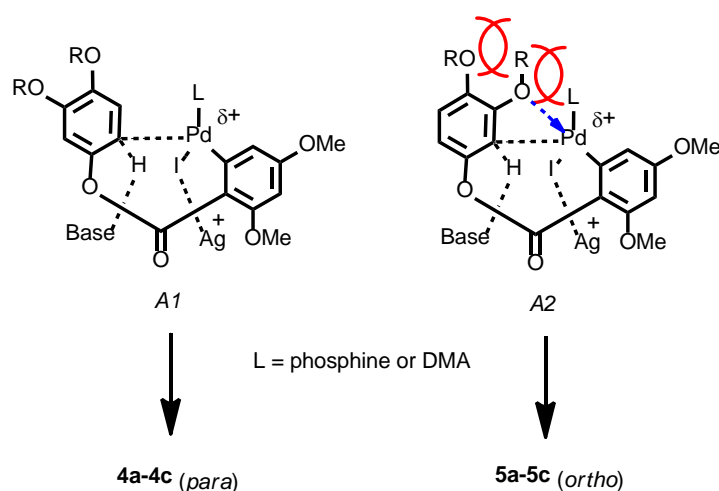
Contrary to the above, *B1*-*B3* illustrate the transition state models under the condition using K_2CO_3 as the base (Figure 2). In these cases, the cationic property of the palladium atom may not be considered because of the hard character of the potassium ion. The coordinating effect of the alkoxy group to the palladium is not an important factor for the substrates **1b** and **1c**, thus the *para*-isomers **4b** and **4c** are slightly predominant (*B1* and *B2*). Since the coordinating ability of the methylenedioxy group of the substrate **1a** is stronger than **1b** and **1c**, the attractive interaction between the oxygen and the palladium can control and mainly produce the *ortho*-isomer **5a** (*B3*).

Figure 2. Transition State Models under K_2CO_3 Condition

L = phosphine or DMA

4b-4c (*para*)　　　**5b-5c** (*ortho*)　　　**5a** (*ortho*)
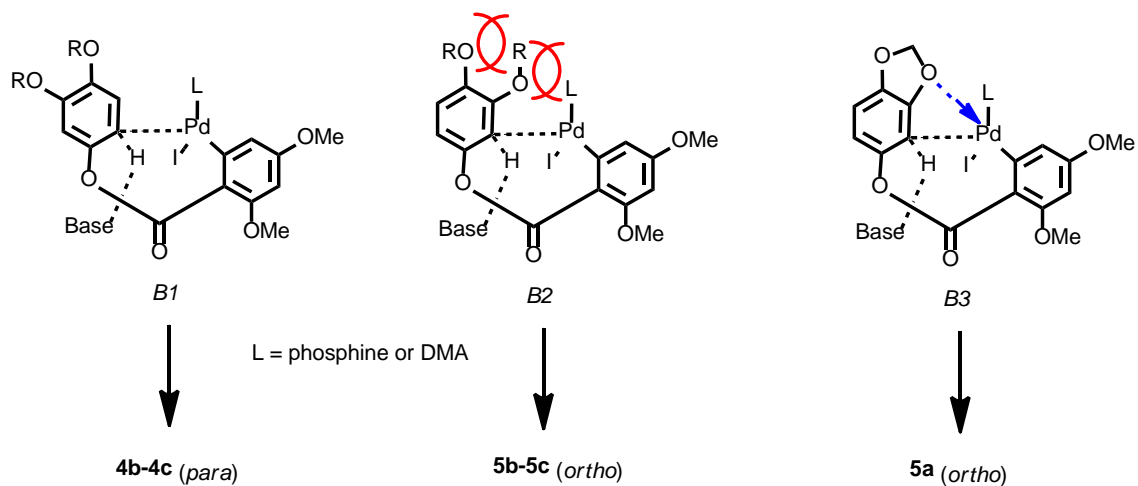
Since the coupling product **4c** was regioselectively obtained with the conditions of entry 6 in Table 1, we attempted a further transformation toward the natural product, alternenuol **6**, which was found from *Alternaria tenuis* in 1957.[7] The selective demethylation of **4c** by the Node's method[8] was successful to afford **7**, which was debenzylated by the conventional hydrogenolysis reaction leading to **6**. As an alternative way, partial dealkylation with BBr_3 proceeded effectively to produce **6** in a single step. The spectral data of synthetic **6** were in accordance with the reported data.[4]

Scheme 1. Transformation of **4c** into Altertenuol (**6**)
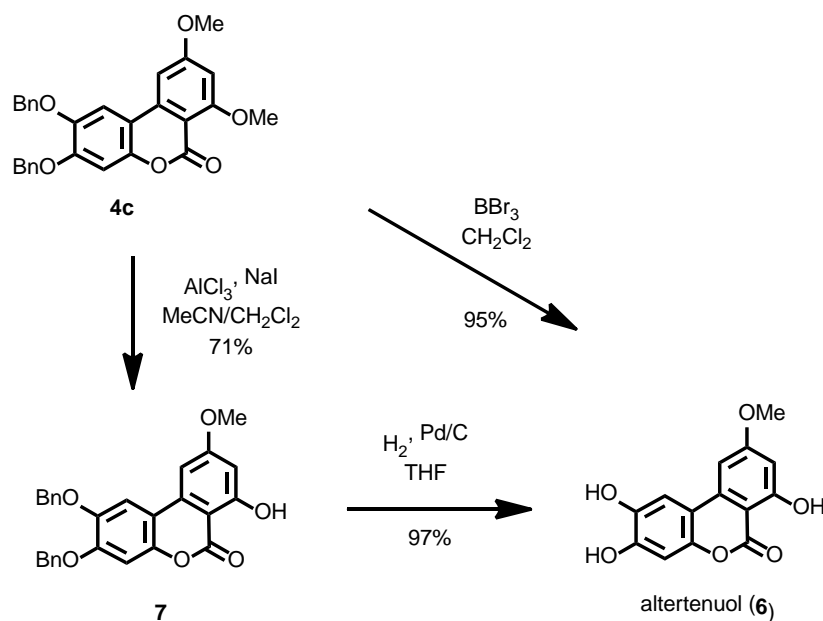
CONCLUSION

The regioselectivity of the Pd-mediated biaryl coupling reaction of 3',4'-dialkoxyphenyl 2,4-dimethoxybenzoates was intensively investigated. It was found that the combination of the ligand and the base influences the regioselectivity of the reaction. We also demonstrated the synthesis of alterenulol using the regioselective condition. This method would be utilized for further application to other syntheses of biaryl-type natural products.

EXPERIMENTAL

General Information

Melting points were measured using a Yanagimoto micro melting point hot-plate and are uncorrected. The IR spectra were recorded using a SHIMADZU FTIR-8400 spectrophotometer. The NMR spectra were obtained using a JEOL α-400 (400 MHz) instrument. The chemical shifts are given in δ ppm with TMS as an internal standard. The elemental analyses were performed using a Thermo Scientific FlashEA1112 analyzer. Silica gel column chromatography was carried out using a wakogel® C-200 or C-400HG (Wako).

3,4-Dimethoxyphenol (2b)[9]

A mixture of THF (2 mL), 31% H_2O_2 (0.13 mL), H_3BO_3 (189 mg, 3.05 mmol), and conc. H_2SO_4 (0.06 mL) was stirred for 30 min at rt. To the mixture was added a solution of 3,4-dimethoxybenzaldehyde (101 mg, 0.607 mmol) in THF (1 mL). The mixture was stirred for 19 h at rt, then a saturated $NaHCO_3$ aqueous solution was added. The mixture was extracted with $CHCl_3$ and the organic layer was washed with brine. After drying with $MgSO_4$ and evaporation, a residue was subjected to silica gel column chromatography with hexane-AcOEt (4:1) to give **2b** (73.1 mg, 78%) as colorless prisms, mp 83.9-85.2 °C (hexane-CHCl$_3$) [lit.[9] mp 79 °C]. ^{1}H-NMR (400 MHz, CDCl$_3$) δ: 6.72 (1H, d, J = 8.8 Hz, ArH), 6.47 (1H, d, J = 2.7 Hz, ArH), 6.35 (1H, dd, J = 8.6, 2.7 Hz, ArH), 5.39 (1H, s, ArOH), 3.81 (3H, s, ArOMe), 3.79 (3H, s, ArOMe).

3,4-Dibenzyloxyphenol (2c)

A mixture of THF (2 mL), 31% H_2O_2 (0.07 mL), H_3BO_3 (100 mg, 1.62 mmol), and conc. H_2SO_4 (0.032 mL) was stirred for 30 min at rt. To the mixture was added a solution of 3,4-dibenzyloxybenzaldehyde (102 mg, 0.320 mmol) in THF (1.5 mL). The mixture was stirred for 19 h at rt, then a saturated $NaHCO_3$ aqueous solution was added. The mixture was extracted with $CHCl_3$ and the organic layer was washed with brine. After drying with $MgSO_4$ and evaporation, a residue was subjected to silica gel column chromatography with hexane-AcOEt (7:3) to give **2c** (86.8 mg, 88%) as a colorless solid, mp 117.4-118.8

^{o}C (hexane-CHCl$_3$). ^{1}H-NMR (400 MHz, CDCl$_3$) δ: 7.44-7.28 (10H, m, ArH), 6.79 (1H, d, J = 8.6 Hz, ArH), 6.49 (1H, d, J = 3.0 Hz, ArH), 6.29 (1H, dd, J = 8.7, 2.8 Hz, ArH), 5.09 (2H, s, ArOCH$_2$), 5.07 (2H, s, ArOCH$_2$), 4.83 (1H, s, ArOH).

3,4-Methylenedioxyphenyl 2-iodo-4,6-dimethoxybenzoate (1a)

Under an N$_2$ atmosphere, a solution of 2-iodo-4,6-dimethoxybenzoic acid[3d] (104 mg, 0.337 mmol), sesamol (50.7 mg, 0.367 mmol), EDC (90.9 mg, 0.474 mmol), and DMAP (40.7mg, 0.333 mmol) in dry CH$_2$Cl$_2$ (3 mL) was stirred for 1 h at rt. The mixture was washed with water and brine, then the organic layer was dried over MgSO$_4$. After evaporation, the resulting residue was subjected to silica gel column chromatography with chloroform to give **1** (90.2 mg, 63%). Colorless prisms, mp 110.2-110.9 ^{o}C (hexane-CH$_2$Cl$_2$). IR (KBr) cm^{-1}: 1742, 1593, 1562, 1503, 1478, 1459, 1438, 1408, 1309, 1287, 1243, 1220, 1188, 1169, 1144, 1114, 1097, 1068, 1023, 938, 926, 881, 841, 828, 807, 791, 597. ^{1}H-NMR (400 MHz, CDCl$_3$) δ: 6.95 (1H, d, J = 2.2 Hz, ArH), 6.84-6.81 (2H, t, ArH), 6.75 (1H, dd, J = 8.4, 2.3 Hz, ArH), 6.48 (1H, d, J = 1.9 Hz, ArH) 6.00 (2H, s, ArOCH$_2$OAr), 3.85 (3H, s, ArOMe), 3.82 (3H, s, ArOMe). ^{13}C-NMR (100 MHz, CDCl$_3$) δ: 166.3, 162.0, 158.2, 148.1, 145.7, 145.2, 122.4, 115.4, 114.2, 108.1, 103.9, 101.8, 99.1, 92.9, 56.2, 55.9. *Anal*. Calcd for C$_{16}$H$_{13}$IO$_6$: C, 44.88; H, 3.06. Found: C, 44.74; H, 2.94.

3,4-Dimethoxyphenyl 2-iodo-4,6-dimethoxybenzoate (1b)

In the same procedure mentioned above using **2b** (52.8 mg, 0.343 mmol), **1b** (63.4 mg, 44%) was obtained. Colorless prisms, mp 80.2-80.5 ^{o}C (hexane-CH$_2$Cl$_2$). IR (KBr) cm^{-1}: 1749, 1598, 1562, 1510, 1455, 1255, 1228, 1182, 1151, 1124, 1076, 1030. ^{1}H-NMR (400 MHz, CDCl$_3$) δ: 6.95 (1H, d, J = 2.2 Hz, ArH), 6.87 (2H, d, J = 1.5 Hz,   ArH), 6.84 (1H, t, J = 1.5 Hz), 6.47 (1H, d, J = 2.2 Hz, ArH) 3.88 (3H, s, ArOMe), 3.87 (3H, s, ArOMe), 3.83 (3H, s, ArOMe), 3.80 (3H, s, ArOMe). ^{13}C-NMR (100 MHz, CDCl$_3$) δ: 166.3, 161.9, 158.1, 149.5, 147.2, 144.6, 122.5, 115.4, 113.0, 111.3, 105.9, 99.0, 92.9, 56.3, 56.2, 56.1, 55.8. *Anal*. Calcd for C$_{17}$H$_{17}$IO$_6$: C, 45.96; H, 3.86. Found: C, 45.84; H, 3.72.

3,4-Dibenzyloxyphenyl 2-iodo-4,6-dimethoxybenzoate (1c)

In the same procedure mentioned above using **2c** (4.04 g, 13.2 mmol), **1c** (4.87 g, 63%) was obtained. Colorless solid, mp 101.4-102.0 ^{o}C (Et$_2$O-CH$_2$Cl$_2$). IR (KBr) cm^{-1}: 1751, 1603, 1560, 1510, 1454, 1435, 1421, 1400, 1387, 1331, 1315, 1277, 1250, 1236, 1215, 1184, 1153, 1119, 1074, 1030, 1001, 989, 922, 883, 818, 804, 787, 770, 750, 731, 702, 594. ^{1}H-NMR (400 MHz, CDCl$_3$) δ: 7.47-7.29 (10H, m, ArH), 6.97-6.93 (3H, m, ArH), 6.84 (1H, dd, J = 8.7, 2.6 Hz, ArH), 6.47 (1H, d, J = 2.2 Hz, ArH), 5.18 (2H, s, ArOCH$_2$), 5.16 (2H, s, ArOCH$_2$), 3.82 (3H, s, ArOMe), 3.81 (3H, s, ArOMe). ^{13}C-NMR (100 MHz,

CDCl$_3$) δ: 166.1, 161.9, 158.2, 149.6, 147.0, 145.1, 137.3, 137.0, 128.6, 128.6, 128.0, 127.9, 127.5, 127.5, 122.5, 115.6, 115.4, 114.0, 109.1, 99.1, 93.0, 72.0, 71.5, 56.2, 55.8. *Anal*. Calcd for C$_{29}$H$_{25}$IO$_6$: C, 58.40; H, 4.23. Found: C, 58.62; H, 4.15.

Typical Procedure for the Coupling Reaction (Table 1)

Under an N$_2$ atmosphere, a mixture of **1a** (100 mg, 0.234 mmol), Pd(OAc)$_2$ (0.023 mmol), ligand (0.047 mmol), base (0.023 mmol), and DMA (7 mL) was heated under reflux for 1 h with stirring. Unsolved materials were filtered off, then water was added to the filtrate. After extraction with CH$_2$Cl$_2$, the organic layer was washed with brine and dried over MgSO$_4$. Evaporation of the solvent gave a residue which was subjected to silica gel column chromatography with hexane-AcOEt-CH$_2$Cl$_2$ (1:1:3).

2,3-Methylenedioxy-7,9-dimethoxy-6*H*-benzo[*c*]chromen-6-one (4a)

Colorless needles, mp 240.5-241.0 °C (hexane-CH$_2$Cl$_2$). ^{1}H-NMR (400 MHz, CDCl$_3$) δ: 7.25 (1H, s, ArH), 6.83 (1H, d, *J* = 2.2 Hz, ArH), 6.75 (1H, s, ArH), 6.48 (1H, d, *J* = 2.2 Hz, ArH), 6.04 (2H, s, ArOCH$_2$OAr), 3.98 (3H, s, ArOMe), 3.96 (3H, s, ArOMe). ^{13}C-NMR (100 MHz, CDCl$_3$) δ: 165.5, 164.2, 158.1, 150.0, 148.1, 145.0, 139.7, 111.1, 102.9, 102.2, 101.2, 98.6, 98.3, 96.8, 56.5, 55.8. IR (KBr) cm^{-1}: 1719, 1603, 1574, 1504, 1472, 1454, 1433, 1381, 1344, 1254, 1211, 1180, 1146, 1092, 1063, 1030, 1005, 827. *Anal*. Calcd for C$_{16}$H$_{12}$O$_6$: C, 64.00; H, 4.03. Found: C, 63.85; H, 3.84.

1,2-Methylenedioxy-7,9-dimethoxy-6*H*-benzo[*c*]chromen-6-one (5a)

Colorless needles, mp 254.8-256.5 °C (hexane-CH$_2$Cl$_2$). ^{1}H-NMR (400 MHz, CDCl$_3$) δ : 7.58 (1H, d, *J* = 2.2 Hz, ArH), 6.91 (1H, d, *J* = 8.6 Hz, ArH), 6.80 (1H, d, *J* = 8.8 Hz, ArH), 6.56 (1H, d, *J* = 2.4 Hz, ArH), 6.16 (2H, s, ArOCH$_2$OAr), 4.00 (3H, s, ArOMe), 3.95 (3H, s, ArOMe). ^{13}C-NMR (100 MHz, CDCl$_3$) δ: 165.5, 163.8, 157.9, 146.8, 144.0, 143.7, 137.2, 109.8, 109.0, 105.3, 103.4, 102.3, 101.8, 99.4, 56.5, 55.8. IR (KBr) cm^{-1}: 1722, 1641, 1612, 1597, 1574, 1504, 1489, 1456, 1445, 1418, 1346, 1265, 1246, 1205, 1165, 1080, 1057, 1043, 1007, 986, 920, 839, 916. *Anal*. Calcd for C$_{16}$H$_{12}$O$_6$: C, 64.00; H, 4.03. Found: C, 63.92; H, 3.96.

2,3,7,9- Tetramethoxy-6*H*-benzo[*c*]chromen-6-one (4b)

Colorless solid, mp 180.8-181.7 °C (hexane-CH$_2$Cl$_2$). ^{1}H-NMR (400 MHz, CDCl$_3$) δ: 7.21 (1H, s, ArH), 6.87 (1H, d, *J* = 2.2 Hz, ArH), 6.77 (1H, s, ArH), 6.46 (1H, d, *J* = 2.2 Hz, ArH), 3.98 (3H, s, ArOMe), 3.98 (3H, s, ArOMe), 3.97 (3H, s, ArOMe), 3.91 (3H, s, ArOMe). ^{13}C-NMR (100 MHz, CDCl$_3$) δ: 165.1, 163.8, 157.9, 151.4, 146.5, 145.7, 139.0, 109.3, 104.0, 102.5, 99.8, 97.5, 96.2, 56.3, 56.0, 56.0, 55.5. IR (KBr) cm^{-1}: 3576, 1686, 1618, 1597, 1570, 1520, 1458, 1439, 1425, 1408, 1273, 1238, 1211, 1198, 1173, 1159, 1123, 1070, 995, 824. *Anal*. Calcd for C$_{17}$H$_{16}$O$_6$: C, 64.55; H, 5.10. Found: C, 64.33; H, 4.98.

1,2,7,9- Tetramethoxy-6*H*-benzo[*c*]chromen-6-one (5b)

Colorless solid, mp 202.2-203.5 $^{\circ}$C (hexane-CH$_2$Cl$_2$). ^{1}H-NMR (400 MHz, CDCl$_3$) δ: 8.33 (1H, d, J = 2.2 Hz, ArH), 7.07 (2H, s, ArH), 6.61 (1H, d, J = 2.4 Hz, ArH), 3.99 (3H, s, ArOMe), 3.96 (3H, s, ArOMe), 3.92 (3H, s, ArOMe), 3.91 (3H, s, ArOMe). ^{13}C-NMR (100 MHz, CDCl$_3$) δ: 165.4, 163.7, 157.9, 149.5, 147.3, 146.4, 138.5, 114.7, 112.7, 112.4, 104.1, 102.3, 99.6, 60.4, 56.7, 56.5, 55.6. IR (KBr) cm^{-1}: 1724, 1601, 1587, 1570, 1497, 1474, 1456, 1443, 1414, 1337, 1298, 1267, 1246, 1229, 1213, 1204, 1163, 1090, 1072, 1059, 1024, 962, 837, 804. *Anal*. Calcd for C$_{17}$H$_{16}$O$_6$: C, 64.55; H, 5.10. Found: C, 64.45 ; H, 5.05.

2,3-Dibenzyloxy-7,9-dimethoxy-6H-benzo[c]chromen-6-one (4c)

Colorless solid, mp 166.5-167.3 $^{\circ}$C (hexane-CH$_2$Cl$_2$). ^{1}H-NMR (400 MHz, CDCl$_3$) δ: 7.49-7.30 (11H, m, ArH), 6.81 (1H, s, ArH), 6.72 (1H, d, J = 2.2 Hz, ArH), 6.42 (1H, d, J = 2.2 Hz, ArH), 5.20 (2H, s, ArOCH$_2$), 5.18 (2H, s, ArOCH$_2$), 3.95 (3H, s, ArOMe), 3.92 (3H, s, ArOMe). ^{13}C-NMR (100 MHz, CDCl$_3$) δ: 165.4, 164.2, 158.2, 152.0, 147.4, 145.4, 139.4, 137.2, 136.2, 128.8, 128.7, 128.3, 128.1, 127.6, 127.3, 110.2, 109.9, 103.0, 102.5, 98.1, 96.6, 72.8, 71.0, 56.4, 55.7. IR (KBr) cm^{-1}: 1738, 1614, 1593, 1568, 1518, 1499, 1448, 1431, 1391, 1333, 1244, 1211, 1196, 1159, 1126, 1061, 1020, 1003, 924, 839, 824, 733, 694. *Anal*. Calcd for C$_{29}$H$_{24}$O$_6$: C, 74.35; H, 5.16. Found: C, 74.47; H, 5.22.

1,2-Dibenzyloxy-7,9-dimethoxy-6H-benzo[c]chromen-6-one (5c)

Colorless solid, mp 184.4-186.1 $^{\circ}$C (hexane-CH$_2$Cl$_2$). ^{1}H-NMR (400 MHz, CDCl$_3$) δ: 8.29 (1H, d, J = 2.4 Hz, ArH), 7.47-7.31 (10H, m, ArH), 7.14 (1H, d, J = 9.0 Hz, ArH), 7.06 (1H, d, J = 9.0 Hz, ArH), 6.55 (1H, d, J = 2.2 Hz, ArH), 5.16 (2H, s, ArOCH$_2$), 5.08 (2H, s, ArOCH$_2$), 3.96 (3H, s, ArOMe), 3.43 (3H, s, ArOMe). ^{13}C-NMR (100 MHz, CDCl$_3$) δ: 165.4, 163.5, 157.9, 148.7, 146.8, 138.7, 137.0, 136.7, 128.7, 128.6, 128.5, 128.4, 128.3, 127.8, 117.0, 113.2, 112.6, 104.1, 102.2, 100.2, 75.2, 72.1, 56.4, 55.3. IR (KBr) cm^{-1}: 1742, 1601, 1572, 1501, 1474, 1456, 1443, 1427, 1371, 1337, 1290, 1261, 1252, 1215, 1196, 1167, 1049, 1022, 959, 800, 752, 731, 696. *Anal*. Calcd for C$_{29}$H$_{24}$O$_6$: C, 74.35; H, 5.16. Found: C, 74.26; H, 5.13.

Altertenuol (2,3,7-Trihydroxy-9-methoxy-6H-benzo[c]chromen-6-one) (6)

Under N$_2$ atmosphere, to a solution of **4c** (50.1 mg, 0.107 mmol) in CH$_2$Cl$_2$ (3.5 mL) was added BBr$_3$ (1M CH$_2$Cl$_2$ solution, 0.320 mL, 0.320 mmol) at 0 $^{\circ}$C. The mixture was stirred for 1 h at rt, and quenched with water. After extraction with AcOEt, the organic layer was washed with brine and dried over MgSO$_4$ to give a residue which was subjected to silica gel column chromatography with AcOEt. A colorless solid of **1** (27.9 mg, 95%) was obtained, mp 283.9-285.8 $^{\circ}$C (acetone) [lit.[7] mp 284-285 $^{\circ}$C]. ^{1}H-NMR (400 MHz, CD$_3$OD) δ: 7.38 (1H, s, ArH), 6.94 (1H, d, J = 2.4 Hz, ArH), 6.74 (1H, s, ArH), 6.50 (1H, d, J = 2.2 Hz, ArH), 3.93 (3H, s, ArOMe). ^{13}C-NMR (100 MHz, DMSO-d$_6$) δ: 166.8, 165.1, 163.8, 149.3, 144.4, 143.8, 137.6, 109.1, 109.0, 103.5, 100.0, 98.6. 98.0, 56.1. IR (KBr) cm^{-1}: 3535, 3285, 3105, 1647, 1607, 1568, 1528, 1510, 1456, 1431, 1279, 1227, 1202, 1165. *Anal*. Calcd for C$_{14}$H$_{10}$O$_6$: C, 61.32; H, 3.68.

Found: C, 61.26; H, 3.69.

2,3-Dibenzyloxy-7-hydroxy-9-methoxy-6*H*-benzo[*c*]chromen-6-one (7)[4a]

Under N_2 atmosphere, to a solution of **4c** (102 mg, 0.218 mmol) in a mixed solvent of CH_2Cl_2 (4.7 mL) and CH_3CN (1.4 mL) was added $AlCl_3$ (69.6 mg, 0.522 mmol) and NaI (83.3 mg, 0.556 mmol) at 0 °C. The mixture was stirred for 4.5 h at rt, and quenched with water. After extraction with CH_2Cl_2, the organic layer was washed with brine and dried over $MgSO_4$ to give a residue which was subjected to silica gel column chromatography with hexane-AcOEt (4:3). Colorless solid of **7** (69.9 mg, 71%) was obtained, mp 211.3-212.5 °C (AcOEt) [lit.[4a] mp 199-200 °C]. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 11.5 (1H, s, ArOH), 7.49-7.32 (11H, m, ArH), 6.88 (1H, s, ArH), 6.75 (1H, d, *J* = 2.2 Hz, ArH), 6.50 (1H, d, *J* = 2.2 Hz, ArH), 5.22 (4H, s, $ArOCH_2$), 3.91 (3H, s, ArOMe).

Conversion of 7 into 6

Under H_2 atmosphere, a mixture of **7** (53.6 mg, 0.118 mmol), 10% Pd/C (12.1 mg), and THF (4 mL) was vigorously stirred for 19 h at rt. After filtration and washing the filter paper with $CHCl_3$-MeOH (10:1), the filtrate was concentrated. An obtained residue was purified by silica gel column chromatography with AcOEt to give **6** (31.6 mg, 97%).

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