A Synthetic Pathway to the 1,4-Dihydro-2*H*-3-benzoxocine System from Morita–Baylis–Hillman Cinnamyl Alcohols with 2,5-Dimethoxy-2,5-dihydrofuran via the Heck Reaction

Sang-Hyun Ahn, Young Keun Kim, Jina Hyun, Kee-Jung Lee*

Organic Synthesis Laboratory, Department of Chemical Engineering, Hanyang University, Seoul 133-791, South Korea
Fax +82(2)22984101; E-mail: leekj@hanyang.ac.kr

Received: 10.08.2012; Accepted after revision: 24.09.2012

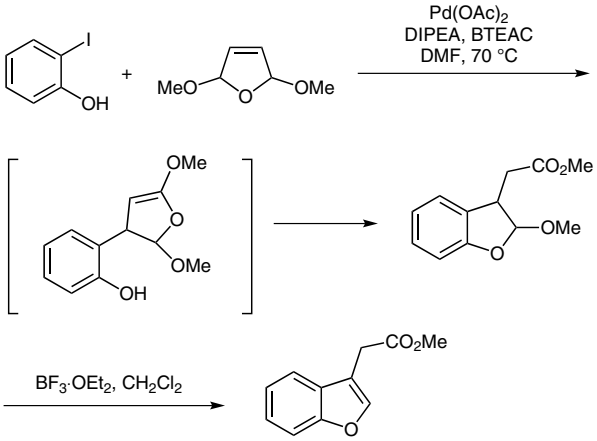
Abstract: A new synthetic method for methyl 2-methoxy-1-(methoxycarbonylmethyl)-1,4-dihydro-2*H*-3-benzoxocine-5-carboxylates was developed using the Heck reaction between 2,5-dimethoxy-2,5-dihydrofuran and methyl 2-(hydroxymethyl)-3-(2-iodophenyl)propenoates as a key step. The latter were readily obtained from the Morita–Baylis–Hillman reaction of iodobenzaldehydes with methyl acrylate through acetylation, rearrangement, and hydrolysis. The methyl 2-methoxy-1-(methoxycarbonylmethyl)-1,4-dihydro-2*H*-3-benzoxocine-5-carboxylates were converted into methyl 2-oxo-1,2,5,11b-tetrahydro-3a*H*-furo[3,2-*a*][3]benzoxocine-6-carboxylates on exposure to excess trifluoroacetic acid.

Key words: Morita–Baylis–Hillman, Heck reaction, 1,4-dihydro-2*H*-3-benzoxocines, iodobenzaldehydes, 2,5-dimethoxy-2,5-dihydrofuran

Medium-sized oxacycles, oxocines, are an important structural unit present in numerous biologically active molecules.[1] Among them, 3-benzoxocines are devoid of any biological profile and only a few synthetic procedures have been implemented. 3-Benzoxocines have been prepared from 2-phenylethanol bearing bromoallenes in the presence of a palladium(0) catalyst and alcohol,[2] by flash vacuum pyrolysis of 8-oxabenzo[*c*]tricyclo[5.1.0.0^{2,6}]octanes via ring expansion,[3] and by a platinum-catalyzed skeletal rearrangement of 2-epoxy-1-(siloxyalk-2-ynyl)benzenes.[4]

Ogasawara and co-workers have reported the expedient synthesis of methyl benzofuran-3-acetate[5] and indole-3-acetic acid[6] by employing the Heck reaction between 2-iodophenol or 2-iodoaniline derivatives and 2,5-dimethoxy-2,5-dihydrofuran as the key step (Scheme 1).

The Morita–Baylis–Hillman (MBH) reaction[7] has attracted the attention of organic chemists in recent years. This reaction provides synthetically useful, multifunctional molecules that have been successfully employed in various heterocycle syntheses. In efforts to expand MBH chemistry,[8] we have developed a method to synthesize the 3-benzoxocine derivatives **10** using the Heck reaction between the MBH cinnamyl alcohols **5** and 2,5-dimethoxy-2,5-dihydrofuran (**6**), as shown in Scheme 2.

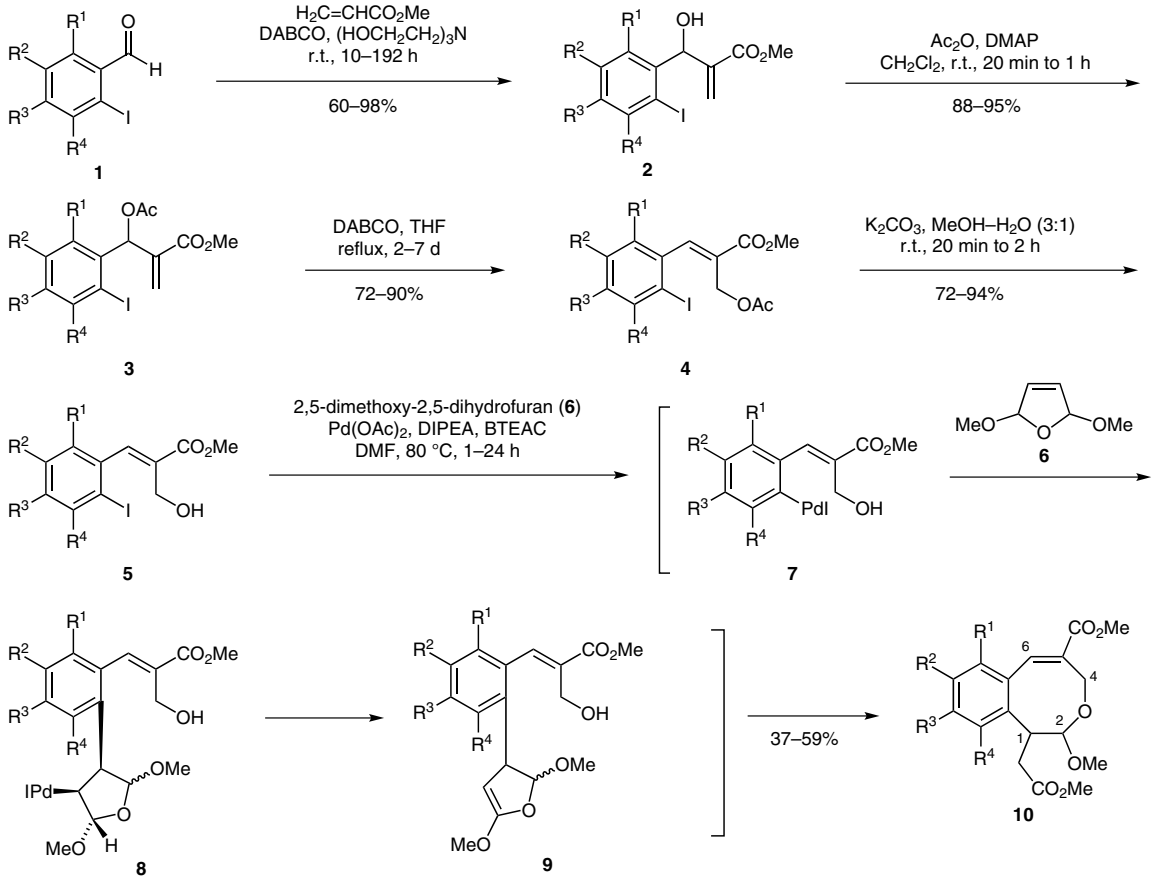


Scheme 1

Our synthesis began with the generation of methyl 2-(hydroxymethyl)-3-(2-iodophenyl)propenoates **5** as the starting material following a previously reported procedure. In the MBH reaction of iodobenzaldehydes **1** with methyl acrylate, 1,4-diazabicyclo[2.2.2]octane (DABCO), and triethanolamine without solvent, the MBH adducts **2** were produced in 60–98% yield. Acetylation of the adducts **2** with acetic anhydride in the presence of a catalytic amount of 4-(dimethylamino)pyridine in dichloromethane at room temperature gave the MBH acetates **3** in 88–95% yield.[9] In a DABCO-catalyzed rearrangement of allylic esters **3** in tetrahydrofuran at reflux temperature,[10] methyl 2-(acetoxymethyl)-3-(2-iodophenyl)propenoates **4** were obtained in 72–90% yield. Hydrolysis of the latter with potassium carbonate in aqueous methanol[11] at room temperature gave the desired iodocinnamyl alcohols **5** (72–94% yield).

In the Heck reaction of the MBH cinnamyl alcohols **5** with 2,5-dimethoxy-2,5-dihydrofuran (**6**) in *N*,*N*-dimethylformamide containing *N*,*N*-diisopropylethylamine (DIPEA) and benzyltriethylammonium chloride (BTEAC), in the presence of a catalytic amount of palladium(II) acetate at 80 °C for 1–24 hours, methyl 2-methoxy-1-(methoxycarbonylmethyl)-1,4-dihydro-2*H*-3-benzoxocine-5-carboxylates **10a**–**f** were produced in 37–59% yield as single diastereomers (Scheme 2 and Table 1); however, the dimethoxy-substituted cinnamyl alcohol **5g** did not react, and unchanged **5g** was recovered. The substituent group at the 3-position seems to be important for the reactivity

SYNTHESIS 2012, 44, 3613–3622
Advanced online publication: 17.10.2012
DOI: 10.1055/s-0032-1317471; Art ID: SS-2012-F0656-OP



1, 2, 3, 4, 5, 10	R^1	R^2	R^3	R^4
a	H	H	H	H
b	F	H	H	H
c	H	Br	H	H
d	H	H	Cl	H
e	H	Me	H	H
f	H	OMe	H	H
g	H	H	OMe	OMe

Scheme 2

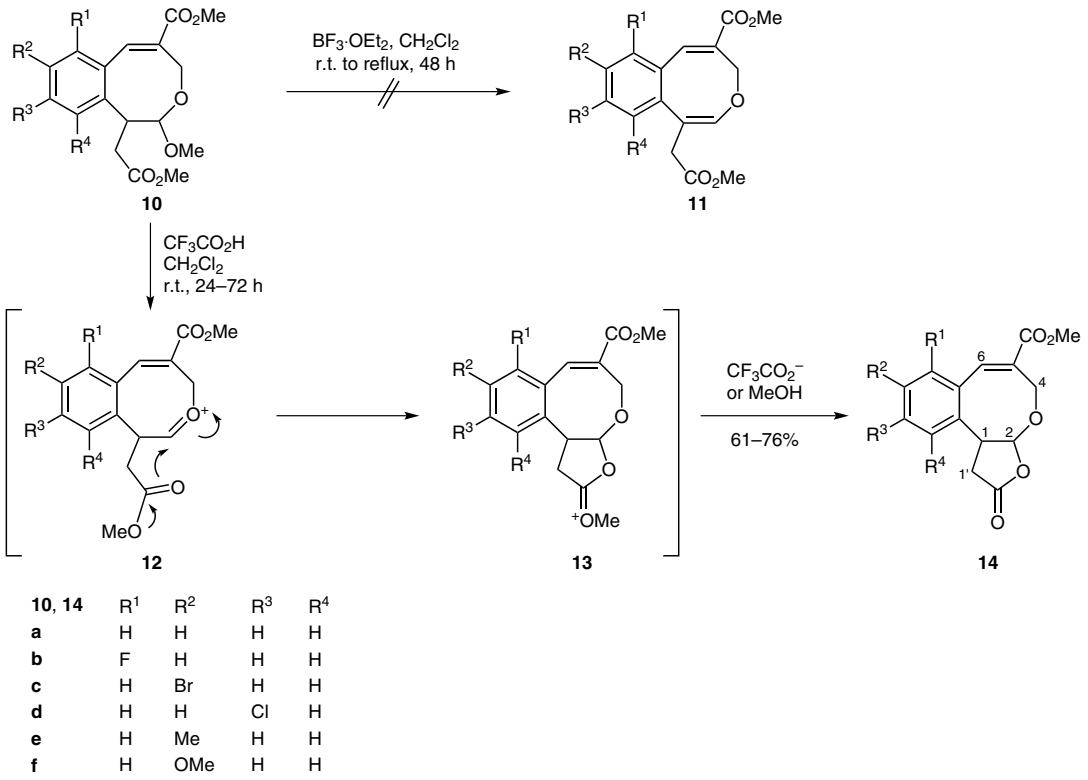
of the substrate due to steric factors. The formation of 3-benzoxocines **10** might be explained by a typical Heck reaction mechanism involving the oxidative addition of the aryl iodide to give the arylpalladium iodide **7**, then carbometalation of the dihydrofuran **6** to give the 3-aryl-2,5-dimethoxytetrahydrofuran-4-palladium iodide **8**,[12] and a subsequent β-hydride *syn* elimination to give the dihydrofuran **9**. Then, acid-catalyzed (DIPEA·HI) transacetalization and concomitant ring opening of **9** would produce the 3-benzoxocine **10**.

Next, we examined the feasibility of 3-benzoxocines **10** as a factor in the elimination of methanol for the preparation of methyl 1-(methoxycarbonylmethyl)-4*H*-3-benzoxocine-5-carboxylates **11** (Scheme 3). When 3-benzoxocine **10a** was treated with boron trifluoride–diethyl ether complex in dichloromethane,[5] the elimination reaction did not occur and unchanged starting material **10a** was recovered. On exposure to excess trifluoroacetic acid, the 3-benzoxocines **10** were converted into methyl 2-oxo-1,2,5,11b-tetrahydro-3a*H*-furo[3,2-*a*][3]benzoxocine-6-carboxylates **14** as single products in 61–76% yield (Scheme 3 and Table 1). The expected compounds **11** were not produced.

Table 1 Preparation of 3-Benzoxocine Derivatives **10** and **14**

10	Time (h)	Yield (%)	14	Time (h)	Yield (%)
10a	3	41	**14a**	24	69
10b	6	59	**14b**	72	68
10c	23	37	**14c**	24	70
10d	24	43	**14d**	48	76
10e	2	43	**14e**	24	63
10f	1	42	**14f**	24	61
10g	24	0[a]			

[a] Starting material **5g** was recovered.



10, 14	R^1	R^2	R^3	R^4
a	H	H	H	H
b	F	H	H	H
c	H	Br	H	H
d	H	H	Cl	H
e	H	Me	H	H
f	H	OMe	H	H

Scheme 3

The pathway is presumed to be initiated by the acid-mediated elimination of methanol generating the oxonium ion **12**, followed by attack of the ester carbonyl oxygen to give **13**, and subsequent demethylation by nucleophilic attack of a trifluoroacetate ion or methanol to give the lactone **14**.

The structures of the 3-benzoxocine derivatives **10** and **14** were elucidated by ^{1}H and ^{13}C NMR spectroscopy.[13] In the ^{1}H NMR spectrum of **10a**, the characteristic chemical shift of the methine proton at C_1 was at δ = 3.71–3.76 as a multiplet, and the methine proton at C_2 was observed at δ = 4.21 as a doublet (*J* = 9.4 Hz). The methine proton at C_6 was found at δ = 7.76 as a singlet. The methylene protons at C_4 were observed at δ = 4.41 as a doublet (*J* = 19.0 Hz) and 4.90 as a doublet of a doublet (*J* = 19.0, 1.8 Hz), and the methylene protons of the acetate at C_1 appeared at δ = 2.75 and 2.92, each as a doublet of a doublet (*J* = 15.9, 7.6 Hz). The proton signals for the three methoxy groups appeared as three singlets at δ = 3.35, 3.61, and 3.82. The ^{13}C NMR spectrum of **10a** showed two ester carbonyl carbon signals at δ = 166.6 and 172.4, and three methoxy carbon signals at δ = 51.7, 52.0, and 55.5. The structure of **10a** was confirmed by HMQC and DEPT experiments. Methylene protons correlated with carbon atoms at δ = 34.6 for acetate at C_1 and with carbon atoms at δ = 59.4 for C_4. The three methine protons at C_1, C_2, and C_6 were correlated with carbon atoms at δ = 41.2, 104.6, and 137.4, respectively.

In contrast, in the ^{1}H NMR spectrum of **14a**, the methine proton at C_1 was observed at δ = 3.69–3.75 as a multiplet, the methine proton at C_2 at δ = 5.24 as a doublet (*J* = 7.4 Hz), and the methine proton at C_6 at δ = 8.00 as a singlet. The methylene protons at C_4 were found at δ = 3.77–3.82 as a multiplet and 4.90 as a doublet (*J* = 14.4 Hz), each for a single proton. The methylene protons of the lactone were observed at δ = 2.84 (*J* = 17.3, 8.4 Hz) and 3.21 (*J* = 17.3, 13.2 Hz), each as a doublet of a doublet. Only a single methyl signal was found at δ = 3.88, as a singlet. The structure of **14a** was also confirmed by HMQC and DEPT experiments. The two methylene protons of the lactone correlated with carbon atoms at δ = 33.2 and the C_4 methylene protons correlated with carbon atoms at δ = 60.7. The three methine protons at C_1, C_2, and C_6 were correlated with carbon atoms at δ = 45.0, 106.0, and 141.3, respectively.

Next, in order to determine the stereochemistry of **10** and **14**, NOE experiments were conducted on **10a** and **14a**. Irradiation of the signal for C_1H (δ = 3.71–3.76) in **10a** led to NOE enhancement of the signal for C_2H (0.58%) and irradiation of the signal for C_2H (δ = 4.21) led to NOE enhancement of the signal for C_1H (0.41%). Small NOE enhancements might suggest that **10a** is a *trans*-compound, but the stereochemistry is uncertain.[14] In the case of **14a**, as shown in Figure 1, irradiation of the signal for C_1H (δ = 3.69–3.75) led to NOE enhancement of the signals for $C_{1'}H_a$ (δ = 2.84, 2.03%) and C_2H (0.58%), and no enhancement of the signal for $C_{1'}H_b$ (δ = 3.21, 0%). Irradiation of the signal for C_2H (δ = 5.24) led to NOE enhancement of the signals for $C_{1'}H_b$ (0.70%) and C_1H (0.86%), and no enhancement of the signal for $C_{1'}H_a$ (0%).

These results suggest that **14a** is presumably a *trans*-compound.[14]

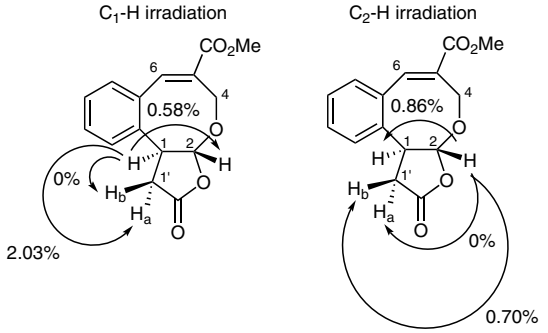


Figure 1

To introduce more diversity in the products, we tested our strategy by investigating the Heck reaction of the bromo-substituted MBH cinnamyl alcohol **15** (Figure 2), instead of the iodocinnamyl alcohol **5a**, and found that the reaction did not occur. In addition, we examined the Heck reaction of the MBH iodocinnamyl alcohol **16** derived from methyl vinyl ketone; however, the reaction yielded a very complex mixture of products that could not be purified, indicating a limitation of the method. Other typical Heck reaction conditions were also unsuccessful.

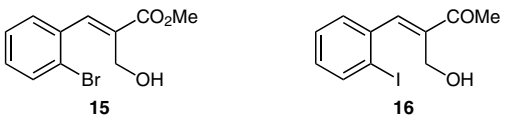


Figure 2

In summary, a new method for the synthesis of methyl 2-methoxy-1-(methoxycarbonylmethyl)-1,4-dihydro-2*H*-3-benzoxocine-5-carboxylates from the MBH adducts of iodobenzaldehydes was developed through a process of acetylation, rearrangement, hydrolysis, and palladium-catalyzed Heck reaction with 2,5-dimethoxy-2,5-dihydrofuran. Lactonization of the 2-methoxy-1-(methoxycarbonylmethyl)-1,4-dihydro-2*H*-3-benzoxocine derivatives occurred to yield methyl 2-oxo-1,2,5,11b-tetrahydro-3a*H*-furo[3,2-*a*][3]benzoxocine-6-carboxylates on exposure to excess trifluoroacetic acid.

Silica gel 60 (70–230 mesh ASTM) used for column chromatography was supplied by E. Merck. Analytical TLC was carried out on Merck silica gel 60 F_{254} TLC plates. Melting points were determined using an electrothermal melting point apparatus and are uncorrected. Elemental analyses were obtained using a Thermo Electron Corporation Flash EA 1112 instrument. Low-resolution mass spectra were recorded on a PerkinElmer Clarus 600 mass spectrometer at 70 eV. IR spectra were recorded on a Nicolet Magna 550 FTIR spectrometer. ^{1}H and ^{13}C NMR spectra were measured on a Varian 300 spectrometer using $CDCl_3$. HMQC, DEPT, and NOE spectra were measured on a Varian 600 spectrometer. All chemical shifts are reported in ppm relative to TMS. Coupling constants (*J*) are expressed in Hz.

2-Iodobenzaldehyde (**1a**) and 2-fluoro-6-iodobenzaldehyde (**1b**) were purchased from Aldrich. The known iodobenzaldehydes **1c**,[15a] **1d–f**,[15b] and **1g**,[15c] MBH adduct **2a**,[9a] and MBH acetate **3a**[9b] were prepared according to the literature procedures. Petroleum ether (PE) refers to the fraction boiling at 30–60 °C.

Morita–Baylis–Hillman Adducts 2; General Procedure

A mixture of the iodobenzaldehyde **1** (10 mmol), methyl acrylate (2.70 mL, 30 mmol), DABCO (1.12 g, 10 mmol), and triethanolamine (1.19 g, 8 mmol) was stirred at r.t. for 10–192 h. Then, the mixture was diluted with H_2O (20 mL) and extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were dried ($MgSO_4$) and the solvent was evaporated under reduced pressure. The resulting mixture was chromatographed on silica gel (hexane–EtOAc, 3:1) to provide **2**.

Methyl 3-(2-Fluoro-6-iodophenyl)-3-hydroxy-2-methylenepropanoate (2b)

Reaction time: 10 h; yield: 3.29 g (98%); yellow oil.

IR (CH_2Cl_2): 3435, 1720, 1664, 1631, 1595, 1566, 1449 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 3.12 (dd, *J* = 6.7, 2.6 Hz, 1 H, OH), 3.76 (s, 3 H, OCH_3), 5.81 (s, 1 H, CH), 5.96 (dd, *J* = 6.7, 1.8 Hz, 1 H, CH), 6.40 (s, 1 H, CH), 6.94–7.09 (m, 2 H_{arom}), 7.67–7.70 (m, 1 H_{arom}).

^{13}C NMR ($CDCl_3$): δ = 52.1, 75.8, 100.0, 116.9 (d, *J* = 23.1 Hz), 126.2, 130.5 (d, *J* = 12.8 Hz), 130.9 (d, *J* = 9.4 Hz), 135.9 (d, *J* = 3.1 Hz), 139.5, 160.6 (d, *J* = 253.8 Hz), 166.4.

EIMS: *m*/*z* (%) = 336 (1) [M$^+$], 249 (36), 209 (100), 177 (60), 149 (16), 123 (47), 101 (20), 87 (62).

Anal. Calcd for $C_{11}H_{10}FIO_3$: C, 39.31; H, 3.00. Found: C, 39.14; H, 3.19.

Methyl 3-(5-Bromo-2-iodophenyl)-3-hydroxy-2-methylenepropanoate (2c)

Reaction time: 17 h; yield: 3.85 g (97%); colorless oil.

IR (CH_2Cl_2): 3436, 1720, 1630, 1439 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 3.24 (d, *J* = 4.1 Hz, 1 H, OH), 3.82 (s, 3 H, OCH_3), 5.53 (s, 1 H, CH), 5.73 (d, *J* = 4.1 Hz, 1 H, CH), 6.38 (s, 1 H, CH), 7.16 (dd, *J* = 8.5, 2.6 Hz, 1 H_{arom}), 7.66 (d, *J* = 2.6 Hz, 1 H_{arom}), 7.68 (d, *J* = 8.5 Hz, 1 H_{arom}).

^{13}C NMR ($CDCl_3$): δ = 52.3, 75.4, 96.7, 123.1, 127.7, 131.3, 132.7, 140.1, 140.6, 144.8, 166.8.

EIMS: *m*/*z* (%) = 397 (1), 395 (1) [M$^+$], 311 (13), 309 (11), 271 (91), 269 (100), 239 (14), 237 (14), 185 (33), 183 (37), 158 (51), 156 (33), 131 (27), 115 (26), 102 (43).

Anal. Calcd for $C_{11}H_{10}BrIO_3$: C, 33.28; H, 2.54. Found: C, 33.06; H, 2.38.

Methyl 3-(4-Chloro-2-iodophenyl)-3-hydroxy-2-methylenepropanoate (2d)

Reaction time: 17 h; yield: 3.25 g (92%); colorless oil.

IR (CH_2Cl_2): 3432, 1722, 1630, 1577, 1553, 1463, 1438 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 3.27 (d, *J* = 4.1 Hz, 1 H, OH), 3.79 (s, 3 H, OCH_3), 5.55 (s, 1 H, CH), 5.74 (d, *J* = 4.1 Hz, 1 H, CH), 6.36 (s, 1 H, CH), 7.37 (dd, *J* = 8.5, 2.1 Hz, 1 H_{arom}), 7.43 (d, *J* = 8.5 Hz, 1 H_{arom}), 7.84 (d, *J* = 2.1 Hz, 1 H_{arom}).

^{13}C NMR ($CDCl_3$): δ = 52.2, 75.3, 98.8, 127.4, 128.7, 128.8, 134.2, 138.6, 140.4, 141.4, 166.8.

EIMS: *m*/*z* (%) = 353 (2), 351 (5) [M$^+$], 267 (23), 265 (33), 227 (33), 225 (100), 195 (25), 193 (70), 167 (8), 165 (23), 141 (25), 139 (74), 131 (17), 115 (20), 112 (60), 102 (24).

Anal. Calcd for $C_{11}H_{10}ClIO_3$: C, 37.47; H, 2.86. Found: C, 37.18; H, 2.99.

Methyl 3-Hydroxy-3-(2-iodo-5-methylphenyl)-2-methylenepropanoate (2e)
Reaction time: 61 h; yield: 3.15 g (95%); colorless oil.

IR (CH_2Cl_2): 3434, 1723, 1630, 1464, 1438 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 2.31 (s, 3 H, CH_3), 3.14 (d, *J* = 4.1 Hz, 1 H, OH), 3.80 (s, 3 H, OCH_3), 5.55 (s, 1 H, CH), 5.77 (d, *J* = 4.1 Hz, 1 H, CH), 6.36 (s, 1 H, CH), 6.84 (dd, *J* = 7.9, 2.1 Hz, 1 H_{arom}), 7.31 (d, *J* = 2.1 Hz, 1 H_{arom}), 7.69 (d, *J* = 7.9 Hz, 1 H_{arom}).

^{13}C NMR ($CDCl_3$): δ = 21.1, 52.2, 75.8, 95.0, 127.3, 128.8, 130.7, 138.6, 139.2, 140.8, 142.3, 167.0.

EIMS: *m*/*z* (%) = 332 (1) [M^+], 245 (13), 205 (100), 173 (18), 145 (23), 119 (52), 105 (11).

Anal. Calcd for $C_{12}H_{13}IO_3$: C, 43.39; H, 3.95. Found: C, 43.06; H, 3.79.

Methyl 3-Hydroxy-3-(2-iodo-5-methoxyphenyl)-2-methylenepropanoate (2f)
Reaction time: 49 h; yield: 2.89 g (83%); colorless oil.

IR (CH_2Cl_2): 3445, 1720, 1630, 1589, 1568, 1466 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 3.30 (d, *J* = 4.1 Hz, 1 H, OH), 3.79 (s, 3 H, OCH_3), 3.80 (s, 3 H, OCH_3), 5.52 (s, 1 H, CH), 5.74 (d, *J* = 4.1 Hz, 1 H, CH), 6.35 (s, 1 H, CH), 6.62 (dd, *J* = 8.5, 3.2 Hz, 1 H_{arom}), 7.10 (d, *J* = 3.2 Hz, 1 H_{arom}), 7.68 (d, *J* = 8.5 Hz, 1 H_{arom}).

^{13}C NMR ($CDCl_3$): δ = 52.2, 55.4, 75.6, 87.2, 113.8, 115.9, 127.4, 139.8, 140.6, 143.7, 160.1, 167.0.

EIMS: *m*/*z* (%) = 348 (7) [M^+], 261 (5), 221 (100), 189 (10), 161 (34), 145 (12), 135 (51), 121 (25), 108 (19).

Anal. Calcd for $C_{12}H_{13}IO_4$: C, 41.40; H, 3.76. Found: C, 41.26; H, 3.52.

Methyl 3-Hydroxy-3-(2-iodo-3,4-dimethoxyphenyl)-2-methylenepropanoate (2g)
Reaction time: 192 h; yield: 2.27 g (60%); white solid; mp 114–115 °C (Et_2O–PE).

IR (KBr): 3461, 1720, 1630, 1586, 1480 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 3.07 (d, *J* = 4.4 Hz, 1 H, OH), 3.78 (s, 3 H, OCH_3), 3.84 (s, 3 H, OCH_3), 3.87 (s, 3 H, OCH_3), 5.61 (s, 1 H, CH), 5.84 (d, *J* = 4.4 Hz, 1 H, CH), 6.36 (s, 1 H, CH), 6.92 (d, *J* = 8.5 Hz, 1 H_{arom}), 7.20 (d, *J* = 8.5 Hz, 1 H_{arom}).

^{13}C NMR ($CDCl_3$): δ = 52.1, 56.0, 60.3, 75.6, 98.4, 112.3, 123.5, 127.0, 135.8, 141.1, 148.6, 152.2, 167.0.

EIMS: *m*/*z* (%) = 378 (10) [M^+], 291 (13), 251 (26), 219 (53), 191 (20), 175 (13), 165 (100), 151 (59), 138 (28), 113 (76).

Anal. Calcd for $C_{13}H_{15}IO_5$: C, 41.29; H, 4.00. Found: C, 41.45; H, 4.14.

Morita–Baylis–Hillman Acetates 3; General Procedure
Ac_2O (1.53 g, 15 mmol) was added to a stirred soln of the MBH adduct **2** (10 mmol) and DMAP (0.34 g, 3 mmol) in CH_2Cl_2 (20 mL) at r.t. The reaction mixture was stirred at r.t. for 20 min to 1 h, then diluted with H_2O (5 mL) and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were dried ($MgSO_4$) and the solvent was evaporated under reduced pressure. The resulting mixture was chromatographed on silica gel (hexane–EtOAc, 3:1) to provide **3**.

Methyl 3-Acetoxy-3-(2-fluoro-6-iodophenyl)-2-methylenepropanoate (3b)
Reaction time: 1 h; yield: 3.44 g (91%); yellow oil.

IR (CH_2Cl_2): 1751, 1728, 1636, 1596, 1567, 1451 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 2.13 (s, 3 H, CH_3), 3.75 (s, 3 H, OCH_3), 5.80 (s, 1 H, CH), 6.49 (s, 1 H, CH), 6.95–7.08 (m, CH and 2 H_{arom}), 7.68–7.71 (m, 1 H_{arom}).

^{13}C NMR ($CDCl_3$): δ = 20.7, 52.0, 75.4, 100.2 (d, *J* = 3.4 Hz), 116.7 (d, *J* = 22.8 Hz), 127.4, 127.5 (d, *J* = 12.8 Hz), 131.3 (d, *J* = 9.1 Hz), 136.0 (d, *J* = 3.4 Hz), 136.3, 160.9 (d, *J* = 256.4 Hz), 165.2, 169.2.

EIMS: *m*/*z* (%) = 378 (1) [M^+], 303 (11), 251 (68), 209 (38), 177 (73), 149 (15), 133 (42), 43 (100).

Anal. Calcd for $C_{13}H_{12}FIO_4$: C, 41.29; H, 3.20. Found: C, 41.42; H, 3.48.

Methyl 3-Acetoxy-3-(5-bromo-2-iodophenyl)-2-methylenepropanoate (3c)
Reaction time: 20 min; yield: 3.99 g (91%); white solid; mp 84–86 °C (Et_2O–PE).

IR (KBr): 1748, 1727, 1634, 1439, 1371 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 2.15 (s, 3 H, CH_3), 3.78 (s, 3 H, OCH_3), 5.64 (s, 1 H, CH), 6.52 (s, 1 H, CH), 6.76 (s, 1 H, CH), 7.17 (dd, *J* = 8.5, 2.4 Hz, 1 H_{arom}), 7.40 (d, *J* = 2.4 Hz, 1 H_{arom}), 7.72 (d, *J* = 8.5 Hz, 1 H_{arom}).

^{13}C NMR ($CDCl_3$): δ = 20.8, 52.3, 76.2, 97.4, 122.8, 128.5, 131.3, 133.1, 137.7, 141.1, 142.2, 165.1, 169.1.

EIMS: *m*/*z* (%) = 313 (14), 311 (20), 271 (11), 269 (11), 190 (40), 158 (17), 114 (13), 43 (100).

Anal. Calcd for $C_{13}H_{12}BrIO_4$: C, 35.56; H, 2.75. Found: C, 35.30; H, 2.98.

Methyl 3-Acetoxy-3-(4-chloro-2-iodophenyl)-2-methylenepropanoate (3d)
Reaction time: 30 min; yield: 3.74 g (95%); white solid; mp 67–69 °C (Et_2O–PE).

IR (KBr): 1748, 1726, 1636, 1578, 1464, 1438 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 2.13 (s, 3 H, CH_3), 3.76 (s, 3 H, OCH_3), 5.64 (s, 1 H, CH), 6.50 (s, 1 H, CH), 6.77 (s, 1 H, CH), 7.22 (d, *J* = 8.2 Hz, 1 H_{arom}), 7.34 (dd, *J* = 8.2, 2.1 Hz, 1 H_{arom}), 7.88 (d, *J* = 2.1 Hz, 1 H_{arom}).

^{13}C NMR ($CDCl_3$): δ = 20.8, 52.2, 76.0, 99.4, 128.1, 128.5, 128.9, 134.8, 137.9, 138.7, 139.2, 165.1, 169.0.

EIMS: *m*/*z* (%) = 394 (1) [M^+], 269 (11), 267 (38), 225 (22), 195 (11), 193 (32), 167 (6), 165 (16), 151 (6), 149 (20), 113 (33), 43 (100).

Anal. Calcd for $C_{13}H_{12}ClIO_4$: C, 39.57; H, 3.07. Found: C, 39.32; H, 2.95.

Methyl 3-Acetoxy-3-(2-iodo-5-methylphenyl)-2-methylenepropanoate (3e)
Reaction time: 30 min; yield: 3.48 g (93%); white solid; mp 65–67 °C (Et_2O–PE).

IR (KBr): 1746, 1726, 1633, 1466, 1437 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 2.13 (s, 3 H, CH_3), 2.30 (s, 3 H, CH_3), 3.76 (s, 3 H, OCH_3), 5.61 (s, 1 H, CH), 6.49 (s, 1 H, CH), 6.80 (s, 1 H, CH), 6.85 (dd, *J* = 8.0, 2.1 Hz, 1 H_{arom}), 7.09 (d, *J* = 2.1 Hz, 1 H_{arom}), 7.73 (d, *J* = 8.0 Hz, 1 H_{arom}).

^{13}C NMR ($CDCl_3$): δ = 20.9, 21.1, 52.2, 76.5, 95.5, 127.8, 129.0, 131.1, 138.3, 138.4, 139.5, 139.6, 165.4, 169.2.

EIMS: *m*/*z* (%) = 374 (1) [M^+], 247 (73), 245 (27), 205 (67), 173 (53), 145 (66), 129 (36), 119 (14), 115 (19), 43 (100).

Anal. Calcd for $C_{14}H_{15}IO_4$: C, 44.94; H, 4.04. Found: C, 44.76; H, 3.88.

Methyl 3-Acetoxy-3-(2-iodo-5-methoxyphenyl)-2-methylenepropanoate (3f)
Reaction time: 30 min; yield: 3.43 g (88%); white solid; mp 92–94 °C (Et_2O–PE).

IR (KBr): 1747, 1726, 1635, 1591, 1569, 1468 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 2.13 (s, 3 H, CH_3), 3.77 (s, 3 H, OCH_3), 3.78 (s, 3 H, OCH_3), 5.59 (s, 1 H, CH), 6.48 (s, 1 H, CH), 6.63 (dd,

J = 8.8, 2.9 Hz, 1 H_{arom}), 6.77 (s, 1 H, CH), 6.88 (d, J = 2.9 Hz, 1 H_{arom}), 7.73 (d, J = 8.8 Hz, 1 H_{arom}).

^{13}C NMR ($CDCl_3$): δ = 20.9, 52.2, 55.3, 76.5, 87.7, 115.0, 115.3, 128.2, 138.2, 140.3, 141.0, 159.9, 165.3, 169.1.

EIMS: m/z (%) = 390 (3) [M^+], 263 (58), 221 (67), 189 (34), 161 (100), 145 (30), 135 (15), 115 (17), 43 (93).

Anal. Calcd for $C_{14}H_{15}IO_5$: C, 43.10; H, 3.87. Found: C, 42.66; H, 4.18.

Methyl 3-Acetoxy-3-(2-iodo-3,4-dimethoxyphenyl)-2-methylenepropanoate (3g)
Reaction time: 40 min; yield: 3.99 g (95%); white solid; mp 88–90 °C (Et_2O–PE).

IR (KBr): 1746, 1725, 1635, 1586, 1481 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.12 (s, 3 H, CH_3), 3.75 (s, 3 H, OCH_3), 3.84 (s, 3 H, OCH_3), 3.87 (s, 3 H, OCH_3), 5.62 (s, 1 H, CH), 6.47 (s, 1 H, CH), 6.85 (s, 1 H, CH), 6.87 (d, J = 8.5 Hz, 1 H_{arom}), 7.02 (d, J = 8.5 Hz, 1 H_{arom}).

^{13}C NMR ($CDCl_3$): δ = 20.9, 52.1, 56.0, 60.3, 76.7, 98.9, 112.0, 123.9, 127.5, 132.8, 138.7, 149.0, 152.6, 165.4, 169.2.

EIMS: m/z (%) = 420 (5) [M^+], 293 (23), 251 (45), 233 (25), 219 (46), 205 (16), 191 (27), 175 (21), 165 (14), 131 (20), 113 (51), 43 (100).

Anal. Calcd for $C_{15}H_{17}IO_6$: C, 42.88; H, 4.08. Found: C, 42.50; H, 3.72.

Morita–Baylis–Hillman Cinnamyl Acetates 4; General Procedure
A mixture of the MBH acetate **3** (5 mmol) and DABCO (0.14 g, 1.25 mmol) in THF (20 mL) was stirred at reflux temperature for 2–7 d. Then, the mixture was diluted with H_2O (20 mL) and extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were dried ($MgSO_4$) and the solvent was evaporated under reduced pressure. The resulting mixture was chromatographed on silica gel (hexane–EtOAc, 3:1) to yield **4**.

Methyl (*E*)-2-(Acetoxymethyl)-3-(2-iodophenyl)propenoate (4a)[9b]
Reaction time: 2 d; yield: 1.62 g (90%); white solid; mp 65–66 °C (Et_2O–PE).

IR (KBr): 1743, 1704, 1638, 1580, 1557 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.06 (s, 3 H, CH_3), 3.88 (s, 3 H, OCH_3), 4.80 (s, 2 H, CH_2), 7.04–7.41 (m, 3 H_{arom}), 7.87 (s, 1 H, CH), 7.89–7.92 (m, 1 H_{arom}).

^{13}C NMR ($CDCl_3$): δ = 20.8, 52.4, 59.2, 99.1, 128.0, 128.2, 129.5, 130.4, 138.4, 139.2, 148.0, 166.6, 170.4.

Methyl (*E*)-2-(Acetoxymethyl)-3-(2-fluoro-6-iodophenyl)propenoate (4b)
Reaction time: 3 d; yield: 1.36 g (72%); yellow oil.

IR (CH_2Cl_2): 1724, 1651, 1594, 1560, 1452, 1437 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.93 (s, 3 H, CH_3), 3.89 (s, 3 H, OCH_3), 4.74 (s, 2 H, CH_2), 7.06–7.16 (m, 2 H_{arom}), 7.48 (s, 1 H, CH), 7.68–7.71 (m, 1 H_{arom}).

^{13}C NMR ($CDCl_3$): δ = 20.6, 52.5, 59.8, 98.8, 115.7 (d, J = 22.5 Hz), 127.0, 131.3 (d, J = 12.8 Hz), 131.5, 134.6, 139.5, 158.2 (d, J = 252.7 Hz), 165.9, 170.4.

EIMS: m/z (%) = 335 (2), 251 (57), 209 (22), 177 (60), 148 (24), 133 (25), 120 (15), 101 (12), 43 (100).

Anal. Calcd for $C_{13}H_{12}FIO_4$: C, 41.29; H, 3.20. Found: C, 41.14; H, 3.04.

Methyl (*E*)-2-(Acetoxymethyl)-3-(5-bromo-2-iodophenyl)propenoate (4c)
Reaction time: 7 d; yield: 1.94 g (88%); yellow oil.

IR (CH_2Cl_2): 1744, 1723, 1636, 1567, 1540, 1449, 1433 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.09 (s, 3 H, CH_3), 3.88 (s, 3 H, OCH_3), 4.77 (s, 2 H, CH_2), 7.20 (dd, J = 8.5, 2.4 Hz, 1 H_{arom}), 7.42 (d, J = 2.4 Hz, 1 H_{arom}), 7.74 (d, J = 8.5 Hz, 1 H_{arom}), 7.77 (s, 1 H, CH).

^{13}C NMR ($CDCl_3$): δ = 20.8, 52.5, 58.9, 96.7, 122.4, 128.9, 132.4, 133.4, 140.3, 140.4, 146.7, 166.2, 170.3.

EIMS: m/z (%) = 313 (24), 311 (27), 239 (9), 237 (10), 190 (50), 158 (18), 114 (15), 43 (100).

Anal. Calcd for $C_{13}H_{12}BrIO_4$: C, 35.56; H, 2.75. Found: C, 35.34; H, 2.59.

Methyl (*E*)-2-(Acetoxymethyl)-3-(4-chloro-2-iodophenyl)propenoate (4d)
Reaction time: 7 d; yield: 1.56 g (79%); yellow oil.

IR (CH_2Cl_2): 1738, 1723, 1638, 1574, 1545, 1460, 1436 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.07 (s, 3 H, CH_3), 3.88 (s, 3 H, OCH_3), 4.78 (s, 2 H, CH_2), 7.20 (d, J = 8.2 Hz, 1 H_{arom}), 7.38 (dd, J = 8.2, 2.1 Hz, 1 H_{arom}), 7.80 (s, 1 H, CH), 7.91 (d, J = 2.1 Hz, 1 H_{arom}).

^{13}C NMR ($CDCl_3$): δ = 20.9, 52.5, 59.0, 99.2, 128.4, 128.5, 130.1, 135.4, 136.8, 138.6, 146.9, 166.4, 170.4.

EIMS: m/z (%) = 269 (13), 267 (41), 227 (7), 225 (23), 195 (14), 193 (41), 167 (7), 165 (20), 149 (14), 43 (100).

Anal. Calcd for $C_{13}H_{12}ClIO_4$: C, 39.57; H, 3.07. Found: C, 39.38; H, 2.88.

Methyl (*E*)-2-(Acetoxymethyl)-3-(2-iodo-5-methylphenyl)propenoate (4e)
Reaction time: 7 d; yield: 1.66 g (89%); white solid; mp 79–80 °C (Et_2O–PE).

IR (KBr): 1741, 1720, 1635, 1459, 1435 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.07 (s, 3 H, CH_3), 2.30 (s, 3 H, CH_3), 3.88 (s, 3 H, OCH_3), 4.80 (s, 2 H, CH_2), 6.90 (dd, J = 8.2, 2.1 Hz, 1 H_{arom}), 7.06 (d, J = 2.1 Hz, 1 H_{arom}), 7.76 (d, J = 8.2 Hz, 1 H_{arom}), 7.85 (s, 1 H, CH).

^{13}C NMR ($CDCl_3$): δ = 20.9, 21.0, 52.4, 59.3, 94.9, 127.8, 130.4, 131.5, 138.1, 138.2, 138.9, 148.3, 166.7, 170.5.

EIMS: m/z (%) = 374 (1) [M^+], 299 (5), 247 (100), 205 (30), 173 (66), 145 (74), 128 (30), 115 (41), 43 (96).

Anal. Calcd for $C_{14}H_{15}IO_4$: C, 44.94; H, 4.04. Found: C, 44.78; H, 4.19.

Methyl (*E*)-2-(Acetoxymethyl)-3-(2-iodo-5-methoxyphenyl)propenoate (4f)
Reaction time: 4 d; yield: 1.62 g (83%); pale yellow solid; mp 97–99 °C (Et_2O–PE).

IR (KBr): 1738, 1720, 1636, 1585, 1563, 1462 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.07 (s, 3 H, CH_3), 3.78 (s, 3 H, OCH_3), 3.88 (s, 3 H, OCH_3), 4.82 (s, 2 H, CH_2), 6.67 (dd, J = 8.5, 2.9 Hz, 1 H_{arom}), 6.86 (d, J = 2.9 Hz, 1 H_{arom}), 7.74 (d, J = 8.5 Hz, 1 H_{arom}), 7.84 (s, 1 H, CH).

^{13}C NMR ($CDCl_3$): δ = 20.9, 52.5, 55.3, 59.3, 87.4, 115.5, 116.7, 128.0, 139.0, 139.7, 148.2, 159.7, 166.6, 170.4.

EIMS: m/z (%) = 390 (1) [M^+], 263 (91), 221 (20), 189 (44), 161 (100), 145 (16), 133 (11), 115 (14), 102 (22), 43 (84).

Anal. Calcd for $C_{14}H_{15}IO_5$: C, 43.10; H, 3.87. Found: C, 42.82; H, 3.68.

Methyl (*E*)-2-(Acetoxymethyl)-3-(2-iodo-3,4-dimethoxyphenyl)propenoate (4g)
Reaction time: 2 d; yield: 1.70 g (81%); white solid; mp 82–83 °C (Et_2O–PE).

IR (KBr): 1740, 1718, 1633, 1582, 1481, 1434 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.10 (s, 3 H, CH_3), 3.85 (s, 3 H, OCH_3), 3.87 (s, 3 H, OCH_3), 3.90 (s, 3 H, OCH_3), 4.82 (s, 2 H, CH_2), 6.92 (d, *J* = 8.5 Hz, 1 H_{arom}), 7.05 (d, *J* = 8.5 Hz, 1 H_{arom}), 7.91 (s, 1 H, CH).

^{13}C NMR ($CDCl_3$): δ = 20.9, 52.3, 56.0, 59.5, 60.3, 98.4, 112.0, 125.6, 126.4, 131.1, 148.4 (2 peaks), 152.8, 166.9, 170.6.

EIMS: *m*/*z* (%) = 420 (2) [M^+], 293 (92), 233 (10), 219 (80), 203 (22), 191 (62), 187 (15), 175 (18), 160 (10), 145 (13), 131 (21), 115 (14), 102 (11), 43 (100).

Anal. Calcd for $C_{15}H_{17}IO_6$: C, 42.88; H, 4.08. Found: C, 42.69; H, 3.87.

Morita–Baylis–Hillman Cinnamyl Alcohols 5; General Procedure

A mixture of the MBH cinnamyl acetate **4** (3 mmol) and K_2CO_3 (0.62 g, 4.5 mmol) in H_2O–MeOH (1:3, 12 mL) was stirred at r.t. for 20 min to 2 h. Then, the mixture was diluted with H_2O (20 mL) and extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were dried ($MgSO_4$) and the solvent was evaporated under reduced pressure. The resulting mixture was chromatographed on silica gel (hexane–EtOAc, 3:1) to yield **5**.

Methyl (*E*)-2-(Hydroxymethyl)-3-(2-iodophenyl)propenoate (5a)

Reaction time: 30 min; yield: 897 mg (94%); white solid; mp 90–91 °C (Et_2O–PE).

IR (KBr): 3494, 1704, 1627, 1580, 1557, 1463 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.64 (t, *J* = 6.7 Hz, 1 H, OH), 3.90 (s, 3 H, OCH_3), 4.34 (d, *J* = 6.7 Hz, 2 H, CH_2), 7.03–7.09 (m, 1 H_{arom}), 7.38–7.45 (m, 2 H_{arom}), 7.73 (s, 1 H, CH), 7.89–7.92 (m, 1 H_{arom}).

^{13}C NMR ($CDCl_3$): δ = 52.4, 58.1, 99.3, 128.2, 130.2, 130.3, 131.6, 138.5, 139.1, 145.2, 167.9.

EIMS: *m*/*z* (%) = 191 (100), 159 (9), 147 (7), 131 (30), 115 (12), 103 (24).

Anal. Calcd for $C_{11}H_{11}IO_3$: C, 41.53; H, 3.49. Found: C, 41.25; H, 3.21.

Methyl (*E*)-3-(2-Fluoro-6-iodophenyl)-2-(hydroxymethyl)propenoate (5b)

Reaction time: 30 min; yield: 766 mg (76%); white solid; mp 58–59 °C (Et_2O–PE).

IR (KBr): 3427, 1715, 1647, 1594, 1560, 1451, 1437 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.65 (t, *J* = 7.0 Hz, 1 H, OH), 3.91 (s, 3 H, OCH_3), 4.23 (dd, *J* = 7.0, 1.8 Hz, 2 H, CH_2), 7.04–7.17 (m, 2 H_{arom}), 7.34 (s, 1 H, CH), 7.69–7.72 (m, 1 H_{arom}).

^{13}C NMR ($CDCl_3$): δ = 52.4, 59.2, 99.3, 115.7 (d, *J* = 23.4 Hz), 126.9 (d, *J* = 17.4 Hz), 131.5 (d, *J* = 8.8 Hz), 134.5, 134.8 (d, *J* = 3.4 Hz), 136.8, 158.3 (d, *J* = 251.8 Hz), 167.1.

EIMS: *m*/*z* (%) = 209 (100), 177 (11), 165 (4), 149 (34), 133 (10), 120 (20), 101 (25).

Anal. Calcd for $C_{11}H_{10}FIO_3$: C, 39.31; H, 3.00. Found: C, 39.13; H, 2.79.

Methyl (*E*)-3-(5-Bromo-2-iodophenyl)-2-(hydroxymethyl)propenoate (5c)

Reaction time: 20 min; yield: 1.12 g (94%); white solid; mp 76–78 °C (Et_2O–PE).

IR (KBr): 3418, 1711, 1634, 1567, 1539, 1448 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.56 (t, *J* = 6.7 Hz, 1 H, OH), 3.90 (s, 3 H, OCH_3), 4.33 (d, *J* = 6.7 Hz, 2 H, CH_2), 7.20 (dd, *J* = 8.5, 2.4 Hz, 1 H_{arom}), 7.56 (d, *J* = 2.4 Hz, 1 H_{arom}), 7.62 (s, 1 H, CH), 7.74 (d, *J* = 8.5 Hz, 1 H_{arom}).

^{13}C NMR ($CDCl_3$): δ = 52.5, 57.9, 97.2, 122.5, 132.6, 132.7, 133.3, 140.4 (2 peaks), 143.6, 167.5.

EIMS: *m*/*z* (%) = 271 (95), 269 (100), 239 (9), 237 (10), 211 (16), 209 (18), 182 (11), 180 (10), 131 (45), 102 (62).

Anal. Calcd for $C_{11}H_{10}BrIO_3$: C, 33.28; H, 2.54. Found: C, 33.55; H, 2.71.

Methyl (*E*)-3-(4-Chloro-2-iodophenyl)-2-(hydroxymethyl)propenoate (5d)

Reaction time: 20 min; yield: 835 mg (79%); white solid; mp 119–120 °C (Et_2O–PE).

IR (KBr): 3476, 1707, 1631, 1573, 1464, 1434 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.56 (br s, 1 H, OH), 3.90 (s, 3 H, OCH_3), 4.31 (s, 2 H, CH_2), 7.38–7.39 (m, 2 H_{arom}), 7.67 (s, 1 H, CH), 7.90–7.91 (m, 1 H_{arom}).

^{13}C NMR ($CDCl_3$): δ = 52.5, 58.0, 99.4, 128.5, 130.8, 132.1, 135.3, 137.0, 138.6, 144.1, 167.7.

EIMS: *m*/*z* (%) = 227 (32), 225 (100), 195 (4), 193 (11), 167 (7), 165 (22), 138 (7), 136 (16), 131 (30), 101 (21).

Anal. Calcd for $C_{11}H_{10}ClIO_3$: C, 37.47; H, 2.86. Found: C, 37.22; H, 2.59.

Methyl (*E*)-2-(Hydroxymethyl)-3-(2-iodo-5-methylphenyl)propenoate (5e)

Reaction time: 1 h; yield: 717 mg (72%); white solid; mp 54–56 °C (Et_2O–PE).

IR (KBr): 3439, 1711, 1633, 1459, 1435 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.33 (s, 3 H, CH_3), 2.68 (t, *J* = 6.7 Hz, 1 H, OH), 3.89 (s, 3 H, OCH_3), 4.35 (d, *J* = 6.7 Hz, 2 H, CH_2), 6.88 (dd, *J* = 7.9, 1.8 Hz, 1 H_{arom}), 7.23 (d, *J* = 1.8 Hz, 1 H_{arom}), 7.72 (s, 1 H, CH), 7.75 (d, *J* = 7.9 Hz, 1 H_{arom}).

^{13}C NMR ($CDCl_3$): δ = 21.1, 52.4, 58.1, 95.2, 130.8, 131.4, 131.5, 138.2, 138.3, 138.8, 145.2, 168.0.

EIMS: *m*/*z* (%) = 332 (1) [M^+], 205 (100), 161 (17), 145 (26), 131 (13), 115 (41).

Anal. Calcd for $C_{12}H_{13}IO_3$: C, 43.39; H, 3.95. Found: C, 43.18; H, 4.07.

Methyl (*E*)-2-(Hydroxymethyl)-3-(2-iodo-5-methoxyphenyl)propenoate (5f)

Reaction time: 2 h; yield: 825 mg (79%); white solid; mp 123–125 °C (Et_2O–PE).

IR (KBr): 3499, 1691, 1629, 1584, 1564, 1463, 1433 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.55 (br s, 1 H, OH), 3.81 (s, 3 H, OCH_3), 3.90 (s, 3 H, OCH_3), 4.36 (s, 2 H, CH_2), 6.67 (dd, *J* = 8.8, 2.9 Hz, 1 H_{arom}), 7.05 (d, *J* = 2.9 Hz, 1 H_{arom}), 7.70 (s, 1 H, CH), 7.74 (d, *J* = 8.8 Hz, 1 H_{arom}).

^{13}C NMR ($CDCl_3$): δ = 52.4, 55.5, 58.1, 87.6, 115.8, 116.9, 131.8, 139.2, 139.6, 145.2, 159.7, 167.9.

EIMS: *m*/*z* (%) = 348 (5) [M^+], 221 (100), 206 (10), 189 (23), 177 (19), 161 (37), 133 (12), 118 (16), 102 (13).

Anal. Calcd for $C_{12}H_{13}IO_4$: C, 41.40; H, 3.76. Found: C, 41.23; H, 3.55.

Methyl (*E*)-2-(Hydroxymethyl)-3-(2-iodo-3,4-dimethoxyphenyl)propenoate (5g)

Reaction time: 30 min; yield: 930 mg (82%); white solid; mp 101–103 °C (Et_2O–PE).

IR (KBr): 3481, 1694, 1624, 1579, 1480 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.62 (t, *J* = 6.7 Hz, 1 H, OH), 3.85 (s, 3 H, OCH_3), 3.88 (s, 3 H, OCH_3), 3.90 (s, 3 H, OCH_3), 4.36 (d, *J* = 6.7 Hz, 2 H, CH_2), 6.93 (d, *J* = 8.5 Hz, 1 H_{arom}), 7.25 (d, *J* = 8.5 Hz, 1 H_{arom}), 7.75 (s, 1 H, CH).

^{13}C NMR ($CDCl_3$): δ = 52.2, 56.0, 58.2, 60.3, 98.4, 112.1, 126.3, 130.4, 131.4, 145.4, 149.0, 152.7, 168.2.

EIMS: *m*/*z* (%) = 378 (2) [M$^+$], 251 (100), 221 (12), 207 (12), 191 (17).

Anal. Calcd for $C_{13}H_{15}IO_5$: C, 41.29; H, 4.00. Found: C, 41.17; H, 3.94.

Methyl 2-Methoxy-1-(methoxycarbonylmethyl)-1,4-dihydro-2*H*-3-benzoxocine-5-carboxylates 10; General Procedure

A mixture of the MBH cinnamyl alcohol **5** (1 mmol), 2,5-dimethoxy-2,5-dihydrofuran (**6**; 0.24 mL, 2 mmol), DIPEA (0.53 mL, 3 mmol), BTEAC (0.23 g, 1 mmol), and $Pd(OAc)_2$ (7 mg, 3 mol%) in DMF (10 mL) was stirred at 80 °C for 1–24 h under nitrogen atmosphere. Then, the mixture was diluted with H_2O (20 mL) and extracted with Et_2O (3 × 30 mL). The combined organic layers were dried ($MgSO_4$) and the solvent was evaporated under reduced pressure. The resulting mixture was chromatographed on silica gel (hexane–EtOAc, 3:1) to provide **10**.

Methyl 2-Methoxy-1-(methoxycarbonylmethyl)-1,4-dihydro-2*H*-3-benzoxocine-5-carboxylate (10a)

Reaction time: 3 h; yield: 131 mg (41%); white solid; mp 94–95 °C (Et_2O–PE).

IR (KBr): 1738, 1706, 1644, 1436, 1251 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.75 (dd, *J* = 15.9, 7.6 Hz, 1 H, C_1CH_2), 2.92 (dd, *J* = 15.9, 7.6 Hz, 1 H, C_1CH_2), 3.35 (s, 3 H, OCH_3), 3.61 (s, 3 H, OCH_3), 3.71–3.76 (m, 1 H, C_1H), 3.82 (s, 3 H, OCH_3), 4.21 (d, *J* = 9.4 Hz, 1 H, C_2H), 4.41 (d, *J* = 19.0 Hz, 1 H, C_4H), 4.90 (dd, *J* = 19.0, 1.8 Hz, 1 H, C_4H), 7.18–7.32 (m, 4 H_{arom}), 7.76 (s, 1 H, C_6H).

^{13}C NMR ($CDCl_3$): δ = 34.6, 41.2, 51.7, 52.0, 55.5, 59.4, 104.6, 124.7, 126.8, 128.9, 130.6, 131.5, 135.5, 137.4, 138.0, 166.6, 172.4.

EIMS: *m*/*z* (%) = 320 (1) [M$^+$], 187 (100), 155 (80), 143 (38), 141 (64), 128 (58), 115 (42).

Anal. Calcd for $C_{17}H_{20}O_6$: C, 63.74; H, 6.29. Found: C, 63.45; H, 6.11.

Methyl 7-Fluoro-2-methoxy-1-(methoxycarbonylmethyl)-1,4-dihydro-2*H*-3-benzoxocine-5-carboxylate (10b)

Reaction time: 6 h; yield: 199 mg (59%); colorless oil.

IR (CH_2Cl_2): 1738, 1710, 1649, 1611, 1573, 1454, 1436, 1257 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.74 (dd, *J* = 15.8, 7.6 Hz, 1 H, C_1CH_2), 2.93 (dd, *J* = 15.8, 7.6 Hz, 1 H, C_1CH_2), 3.36 (s, 3 H, OCH_3), 3.61 (s, 3 H, OCH_3), 3.62–3.71 (m, 1 H, C_1H), 3.83 (s, 3 H, OCH_3), 4.18 (d, *J* = 9.7 Hz, 1 H, C_2H), 4.43 (d, *J* = 19.1 Hz, 1 H, C_4H), 4.91 (dd, *J* = 19.1, 2.3 Hz, 1 H, C_4H), 6.96–7.03 (m, 2 H_{arom}), 7.26–7.33 (m, 1 H_{arom}), 7.81 (d, *J* = 2.1 Hz, 1 H, C_6H).

^{13}C NMR ($CDCl_3$): δ = 34.6, 41.3, 51.8, 52.1, 55.5, 59.4, 104.2, 113.9 (d, *J* = 22.0 Hz), 120.1, 123.8, 129.5, 130.0 (d, *J* = 8.8 Hz), 133.3, 140.4, 160.6 (d, *J* = 249.3 Hz), 166.1, 172.2.

EIMS: *m*/*z* (%) = 338 (1) [M$^+$], 278 (10), 247 (10), 215 (10), 205 (100), 187 (15), 173 (80), 161 (41), 159 (64), 146 (64), 133 (39).

Anal. Calcd for $C_{17}H_{19}FO_6$: C, 60.35; H, 5.66. Found: C, 60.12; H, 5.38.

Methyl 8-Bromo-2-methoxy-1-(methoxycarbonylmethyl)-1,4-dihydro-2*H*-3-benzoxocine-5-carboxylate (10c)

Reaction time: 23 h; yield: 148 mg (37%); white solid; mp 124–125 °C (Et_2O–PE).

IR (KBr): 1737, 1707, 1646, 1488, 1435, 1251 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.71 (dd, *J* = 15.8, 8.4 Hz, 1 H, C_1CH_2), 2.92 (dd, *J* = 15.8, 6.7 Hz, 1 H, C_1CH_2), 3.56 (s, 3 H, OCH_3), 3.61 (s, 3 H, OCH_3), 3.63–3.70 (m, 1 H, C_1H), 3.82 (s, 3 H, OCH_3), 4.17 (d, *J* = 9.4 Hz, 1 H, C_2H), 4.40 (d, *J* = 19.1 Hz, 1 H, C_4H), 4.89 (dd, *J* = 19.1, 2.1 Hz, 1 H, C_4H), 7.04–7.07 (m, 1 H_{arom}), 7.41–7.46 (m, 2 H_{arom}), 7.66 (s, 1 H, C_6H).

^{13}C NMR ($CDCl_3$): δ = 34.3, 41.0, 51.8, 52.2, 55.6, 59.3, 104.2, 120.6, 126.3, 131.6, 133.0, 133.1, 135.7, 136.9, 137.7, 166.2, 172.1.

EIMS: *m*/*z* (%) = 336 (5), 334 (5), 308 (10), 306 (9), 267 (49), 265 (51), 235 (25), 233 (25), 221 (21), 219 (17), 207 (35), 155 (11), 142 (100), 115 (46).

Anal. Calcd for $C_{17}H_{19}BrO_6$: C, 51.14; H, 4.80. Found: C, 50.92; H, 4.64.

Methyl 9-Chloro-2-methoxy-1-(methoxycarbonylmethyl)-1,4-dihydro-2*H*-3-benzoxocine-5-carboxylate (10d)

Reaction time: 24 h; yield: 152 mg (43%); white solid; mp 101–102 °C (Et_2O–PE).

IR (KBr): 1738, 1710, 1645, 1590, 1436, 1251 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.70 (dd, *J* = 15.8, 7.6 Hz, 1 H, C_1CH_2), 2.91 (dd, *J* = 15.8, 7.0 Hz, 1 H, C_1CH_2), 3.36 (s, 3 H, OCH_3), 3.63 (s, 3 H, OCH_3), 3.66–3.75 (m, 1 H, C_1H), 3.82 (s, 3 H, OCH_3), 4.21 (d, *J* = 9.7 Hz, 1 H, C_2H), 4.40 (d, *J* = 19.4 Hz, 1 H, C_4H), 4.88 (dd, *J* = 19.1, 1.5 Hz, 1 H, C_4H), 7.15 (s, 1 H_{arom}), 7.25 (s, 2 H_{arom}), 7.69 (s, 1 H, C_6H).

^{13}C NMR ($CDCl_3$): δ = 34.3, 41.2, 51.8, 52.1, 55.5, 59.4, 104.2, 125.1, 127.0, 131.8, 132.1, 134.1, 134.7, 136.2, 140.0, 166.4, 172.0.

EIMS: *m*/*z* (%) = 354 (1) [M$^+$], 263 (10), 230 (11), 223 (32), 221 (100), 203 (14), 191 (25), 189 (74), 175 (47), 162 (23), 149 (16), 142 (60), 127 (25), 115 (33).

Anal. Calcd for $C_{17}H_{19}ClO_6$: C, 57.55; H, 5.40. Found: C, 57.69; H, 5.57.

Methyl 2-Methoxy-1-(methoxycarbonylmethyl)-8-methyl-1,4-dihydro-2*H*-3-benzoxocine-5-carboxylate (10e)

Reaction time: 2 h; yield: 144 mg (43%); white solid; mp 119–121 °C (Et_2O–PE).

IR (KBr): 1739, 1705, 1643, 1506, 1435, 1254 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.32 (s, 3 H, CH_3), 2.72 (dd, *J* = 15.8, 7.9 Hz, 1 H, C_1CH_2), 2.91 (dd, *J* = 15.8, 7.0 Hz, 1 H, C_1CH_2), 3.35 (s, 3 H, OCH_3), 3.60 (s, 3 H, OCH_3), 3.64–3.72 (m, 1 H, C_1H), 3.81 (s, 3 H, OCH_3), 4.18 (d, *J* = 9.4 Hz, 1 H, C_2H), 4.39 (d, *J* = 18.8 Hz, 1 H, C_4H), 4.88 (dd, *J* = 18.8, 1.6 Hz, 1 H, C_4H), 7.05–7.13 (m, 3 H_{arom}), 7.73 (s, 1 H, C_6H).

^{13}C NMR ($CDCl_3$): δ = 20.8, 34.6, 40.9, 51.7, 52.0, 55.4, 55.5, 59.4, 104.8, 124.6, 129.7, 131.3, 135.0, 135.3, 136.4, 137.6, 166.7, 172.5.

EIMS: *m*/*z* (%) = 334 (1) [M$^+$], 201 (100), 183 (10), 169 (96), 155 (41), 142 (54), 128 (21), 115 (23).

Anal. Calcd for $C_{18}H_{22}O_6$: C, 64.66; H, 6.63. Found: C, 64.47; H, 6.48.

Methyl 2,8-Dimethoxy-1-(methoxycarbonylmethyl)-1,4-dihydro-2*H*-3-benzoxocine-5-carboxylate (10f)

Reaction time: 1 h; yield: 147 mg (42%); white solid; mp 38–40 °C (Et_2O–PE).

IR (KBr): 1737, 1706, 1646, 1605, 1574, 1506, 1436, 1238 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.71 (dd, *J* = 15.8, 8.1 Hz, 1 H, C_1CH_2), 2.90 (dd, *J* = 15.8, 7.6 Hz, 1 H, C_1CH_2), 3.35 (s, 3 H, OCH_3), 3.60–3.69 (m, 1 H, C_1H), 3.61 (s, 3 H, OCH_3), 3.79 (s, 3 H, OCH_3), 3.82 (s, 3 H, OCH_3), 4.16 (d, *J* = 9.4 Hz, 1 H, C_2H), 4.39 (d, *J* = 19.0 Hz, 1 H, C_4H), 4.89 (d, *J* = 19.0 Hz, 1 H, C_4H), 6.84–6.86 (m, 2 H_{arom}), 7.08–7.11 (m, 1 H_{arom}), 7.71 (s, 1 H, C_6H).

^{13}C NMR ($CDCl_3$): δ = 34.7, 40.6, 51.7, 52.1, 55.3, 55.5, 59.3, 104.8, 114.8, 115.2, 125.8, 130.1, 131.8, 136.6, 137.2, 158.0, 166.6, 172.4.

EIMS: *m*/*z* (%) = 350 (1) [M$^+$], 259 (15), 227 (11), 216 (100), 199 (12), 185 (51), 171 (35), 158 (56), 141 (11), 128 (28), 115 (25).

Anal. Calcd for $C_{18}H_{22}O_7$: C, 61.71; H, 6.33. Found: C, 61.42; H, 6.21.

Methyl 2-Oxo-1,2,5,11b-tetrahydro-3a*H*-furo[3,2-*a*][3]benzoxocine-6-carboxylates 14; General Procedure

A mixture of the 3-benzoxocine **10** (1 mmol) and TFA (1.53 mL, 20 mmol) in CH_2Cl_2 was stirred at r.t. for 24–72 h. Then, the mixture was diluted with H_2O (20 mL) and extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were dried ($MgSO_4$) and the solvent was evaporated under reduced pressure. The resulting mixture was chromatographed on silica gel (hexane–EtOAc, 3:1) to provide **14**.

Methyl 2-Oxo-1,2,5,11b-tetrahydro-3a*H*-furo[3,2-*a*][3]benzoxocine-6-carboxylate (14a)

Reaction time: 24 h; yield: 189 mg (69%); white solid; mp 125–126 °C (Et_2O–PE).

IR (KBr): 1794, 1713, 1634, 1256 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 2.84 (dd, *J* = 17.3, 8.4 Hz, 1 H, C_1CH_2), 3.21 (dd, *J* = 17.3, 13.2 Hz, 1 H, C_1CH_2), 3.69–3.75 (m, 1 H, C_1H), 3.77–3.82 (m, 1 H, C_4H), 3.88 (s, 3 H, OCH_3), 4.90 (d, *J* = 14.4 Hz, 1 H, C_4H), 5.24 (d, *J* = 7.4 Hz, 1 H, C_2H), 7.38–7.50 (m, 4 H_{arom}), 8.00 (s, 1 H, C_6H).

^{13}C NMR ($CDCl_3$): δ = 33.2, 45.0, 52.6, 60.7, 106.0, 125.0, 127.7, 129.9, 130.3, 130.5, 133.1, 135.3, 141.3, 166.5, 171.6.

EIMS: *m*/*z* (%) = 274 (1) [M^+], 200 (33), 168 (30), 140 (100), 128 (46), 115 (49).

Anal. Calcd for $C_{15}H_{14}O_5$: C, 65.69; H, 5.15. Found: C, 65.58; H, 5.01.

Methyl 8-Fluoro-2-oxo-1,2,5,11b-tetrahydro-3a*H*-furo[3,2-*a*][3]benzoxocine-6-carboxylate (14b)

Reaction time: 72 h; yield: 199 mg (68%); white solid; mp 160–161 °C (Et_2O–PE).

IR (KBr): 1796, 1715, 1640, 1612, 1571, 1456, 1259 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 2.86 (dd, *J* = 17.3, 8.6 Hz, 1 H, C_1CH_2), 3.19 (dd, *J* = 17.3, 12.9 Hz, 1 H, C_1CH_2), 3.61–3.71 (m, 1 H, C_1H), 3.79–3.86 (m, 1 H, C_4H), 3.89 (s, 3 H, OCH_3), 4.94 (d, *J* = 14.7 Hz, 1 H, C_4H), 5.21 (d, *J* = 7.3 Hz, 1 H, C_2H), 7.10–7.23 (m, 2 H_{arom}), 7.45–7.53 (m, 1 H_{arom}), 8.00 (s, 1 H, C_6H).

^{13}C NMR ($CDCl_3$): δ = 33.3, 44.9, 52.7, 60.9, 105.8, 115.0 (d, *J* = 21.7 Hz), 120.6, 123.4, 123.6, 131.5 (d, *J* = 10.0 Hz), 132.0, 135.6, 160.9 (d, *J* = 252.1 Hz), 166.0, 171.3.

EIMS: *m*/*z* (%) = 292 (1) [M^+], 218 (19), 186 (35), 173 (8), 158 (100), 146 (38), 133 (39).

Anal. Calcd for $C_{15}H_{13}FO_5$: C, 61.64; H, 4.48. Found: C, 61.37; H, 4.28.

Methyl 9-Bromo-2-oxo-1,2,5,11b-tetrahydro-3a*H*-furo[3,2-*a*][3]benzoxocine-6-carboxylate (14c)

Reaction time: 24 h; yield: 247 mg (70%); white solid; mp 171–172 °C (Et_2O–PE).

IR (KBr): 1795, 1713, 1635, 1435, 1256 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 2.85 (dd, *J* = 17.3, 8.5 Hz, 1 H, C_1CH_2), 3.15 (dd, *J* = 17.3, 13.0 Hz, 1 H, C_1CH_2), 3.62–3.72 (m, 1 H, C_1H), 3.78–3.83 (m, 1 H, C_4H), 3.88 (s, 3 H, OCH_3), 4.90 (d, *J* = 14.7 Hz, 1 H, C_4H), 5.19 (d, *J* = 7.3 Hz, 1 H, C_2H), 7.30 (s, 1 H_{arom}), 7.54–7.62 (m, 2 H_{arom}), 7.89 (s, 1 H, C_6H).

^{13}C NMR ($CDCl_3$): δ = 33.2, 44.6, 52.7, 60.7, 105.8, 121.6, 126.6, 131.7, 132.1, 132.8, 133.0, 137.2, 139.4, 166.1, 171.2.

EIMS: *m*/*z* (%) = 354 (1), 352 (1) [M^+], 294 (9), 292 (10), 280 (29), 278 (30), 250 (10), 248 (28), 220 (66), 218 (56), 208 (11), 206 (10), 199 (21), 195 (10), 168 (10), 155 (11), 145 (14), 141 (95), 139 (58), 128 (57), 115 (100).

Anal. Calcd for $C_{15}H_{13}BrO_5$: C, 51.01; H, 3.71. Found: C, 49.76; H, 3.61.

Methyl 10-Chloro-2-oxo-1,2,5,11b-tetrahydro-3a*H*-furo[3,2-*a*][3]benzoxocine-6-carboxylate (14d)

Reaction time: 48 h; yield: 234 mg (76%); white solid; mp 151–153 °C (Et_2O–PE).

IR (KBr): 1797, 1713, 1636, 1592, 1488, 1435, 1256 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 2.86 (dd, *J* = 17.3, 8.5 Hz, 1 H, C_1CH_2), 3.14 (dd, *J* = 17.3, 12.9 Hz, 1 H, C_1CH_2), 3.66–3.75 (m, 1 H, C_1H), 3.78–3.83 (m, 1 H, C_4H), 3.88 (s, 3 H, OCH_3), 4.90 (d, *J* = 14.7 Hz, 1 H, C_4H), 5.23 (d, *J* = 7.3 Hz, 1 H, C_2H), 7.32–7.39 (m, 3 H_{arom}), 7.92 (s, 1 H, C_6H).

^{13}C NMR ($CDCl_3$): δ = 33.2, 44.8, 52.7, 60.8, 105.6, 125.5, 128.1, 131.0, 131.8, 133.7, 135.0, 136.1, 139.9, 166.3, 171.0.

EIMS: *m*/*z* (%) = 308 (1) [M^+], 278 (5), 276 (16), 248 (12), 234 (29), 230 (16), 207 (10), 202 (38), 189 (16), 176 (47), 174 (100), 162 (22), 149 (24), 141 (64), 127 (35), 115 (62).

Anal. Calcd for $C_{15}H_{13}ClO_5$: C, 58.36; H, 4.24. Found: C, 58.59; H, 4.55.

Methyl 9-Methyl-2-oxo-1,2,5,11b-tetrahydro-3a*H*-furo[3,2-*a*][3]benzoxocine-6-carboxylate (14e)

Reaction time: 24 h; yield: 181 mg (63%); white solid; mp 134–135 °C (Et_2O–PE).

IR (KBr): 1796, 1714, 1633, 1435, 1251 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 2.39 (s, 3 H, CH_3), 2.81 (dd, *J* = 17.3, 8.6 Hz, 1 H, C_1CH_2), 3.17 (dd, *J* = 17.3, 13.0 Hz, 1 H, C_1CH_2), 3.61–3.71 (m, 1 H, C_1H), 3.73–3.82 (m, 1 H, C_4H), 3.88 (s, 3 H, OCH_3), 4.89 (d, *J* = 14.4 Hz, 1 H, C_4H), 5.20 (d, *J* = 7.3 Hz, 1 H, C_2H), 7.19–7.29 (m, 3 H_{arom}), 7.96 (s, 1 H, C_6H).

^{13}C NMR ($CDCl_3$): δ = 20.9, 33.3, 44.8, 52.6, 60.8, 106.1, 124.9, 130.1, 130.4, 130.7 (2), 135.1, 137.6, 141.6, 166.6, 171.7.

EIMS: *m*/*z* (%) = 288 (1) [M^+], 228 (10), 214 (48), 182 (18), 169 (18), 154 (100), 142 (50), 128 (40), 115 (43).

Anal. Calcd for $C_{16}H_{16}O_5$: C, 66.66; H, 5.59. Found: C, 66.43; H, 5.31.

Methyl 9-Methoxy-2-oxo-1,2,5,11b-tetrahydro-3a*H*-furo[3,2-*a*][3]benzoxocine-6-carboxylate (14f)

Reaction time: 24 h; yield: 185 mg (61%); white solid; mp 193–194 °C (Et_2O–PE).

IR (KBr): 1795, 1713, 1636, 1605, 1502, 1254 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 2.81 (dd, *J* = 17.3, 8.5 Hz, 1 H, C_1CH_2), 3.15 (dd, *J* = 17.3, 13.2 Hz, 1 H, C_1CH_2), 3.59–3.68 (m, 1 H, C_1H), 3.74–3.81 (m, 1 H, C_4H), 3.84 (s, 3 H, OCH_3), 3.88 (s, 3 H, OCH_3), 4.89 (d, *J* = 14.4 Hz, 1 H, C_4H), 5.25 (d, *J* = 7.3 Hz, 1 H, C_2H), 6.88 (d, *J* = 2.6 Hz, 1 H_{arom}), 7.01 (dd, *J* = 8.8, 2.6 Hz, 1 H_{arom}), 7.31 (d, *J* = 8.5 Hz, 1 H_{arom}), 7.94 (s, 1 H, C_6H).

^{13}C NMR ($CDCl_3$): δ = 33.4, 44.5, 52.6, 55.4, 60.7, 106.2, 114.8, 115.8, 125.1, 126.3, 130.7, 136.4, 141.2, 158.6, 166.5, 171.7.

EIMS: *m*/*z* (%) = 304 (3) [M^+], 230 (53), 204 (13), 199 (26), 185 (17), 171 (100), 158 (45), 145 (22), 141 (15), 128 (46), 115 (44).

Anal. Calcd for $C_{16}H_{16}O_6$: C, 63.15; H, 5.30. Found: C, 63.27; H, 5.53.

Acknowledgment

This work was supported in part by the Brain Korea 21 program, Republic of Korea.

References

(1) For reviews of medium-ring cyclic ethers, see: (a) Elliott, M. C. *Contemp. Org. Synth.* **1994**, *1*, 457. (b) Moody, C. J.;

Davies, M. J. In *Studies in Natural Products Chemistry*; Vol. 10; Atta-Ur-Rahman, Ed.; Elsevier: New York, **1992**, 201.
(2) (a) Ohno, H.; Hamaguchi, H.; Ohata, M.; Kosaka, S.; Tanaka, T. *Heterocycles* **2003**, *61*, 65. (b) Ohno, H.; Hamaguchi, H.; Ohata, M.; Kosaka, S.; Tanaka, T. *J. Am. Chem. Soc.* **2004**, *126*, 8744.
(3) Kurita, J.; Aruga, T.; Tsuchiya, T. *Heterocycles* **1990**, *31*, 1769.
(4) Chaudhuri, R.; Das, A.; Liao, H.-Y.; Liu, R.-S. *Chem. Commun.* **2010**, *46*, 4601.
(5) Samizu, K.; Ogasawara, K. *Heterocycles* **1994**, *38*, 1745.
(6) (a) Samizu, K.; Ogasawara, K. *Synlett* **1994**, 499. (b) Sakagami, H.; Ogasawara, K. *Heterocycles* **1999**, *51*, 1131.
(7) For reviews of the Morita–Baylis–Hillman reaction, see: (a) Drewes, S. E.; Roos, G. H. P. *Tetrahedron* **1988**, *44*, 4653. (b) Basavaiah, D.; Rao, P. D.; Hyma, R. S. *Tetrahedron* **1996**, *52*, 8001. (c) Ciganek, E. *Org. React.* **1997**, *51*, 201. (d) Langer, P. *Angew. Chem. Int. Ed.* **2000**, *39*, 3049. (e) Basavaiah, D.; Rao, A. J.; Satyanarayana, T. *Chem. Rev.* **2003**, *103*, 811. (f) Kataoka, T.; Kinoshita, H. *Eur. J. Org. Chem.* **2005**, 45. (g) Basavaiah, D.; Rao, K. V.; Reddy, R. J. *Chem. Soc. Rev.* **2007**, *36*, 1581. (h) Singh, V.; Batra, S. *Tetrahedron* **2008**, *64*, 4511. (i) Declerck, V.; Martinez, J.; Lamaty, F. *Chem. Rev.* **2009**, *109*, 1. (j) Gowrisankar, S.; Lee, H. S.; Kim, S. H.; Lee, K. Y.; Kim, J. N. *Tetrahedron* **2009**, *65*, 8769. (k) Ma, G.-N.; Jiang, J.-J.; Shi, M.; Wei, Y. *Chem. Commun.* **2009**, 5496. (l) Basavaiah, D.; Reddy, B. S.; Badsara, S. S. *Chem. Rev.* **2010**, *110*, 5447. (m) Zhong, W.; Liu, Y.; Wang, G.; Hong, L.; Chen, Y.; Chen, X.; Zheng, Y.; Zhang, W.; Ma, Y.; Shen, Y.; Yao, Y. *Org. Prep. Proced. Int.* **2011**, *43*, 1.
(8) For our recent examples, see: (a) Hong, W. P.; Lim, H. N.; Park, H. W.; Lee, K.-J. *Bull. Korean Chem. Soc.* **2005**, *26*, 655. (b) Hong, W. P.; Lee, K.-J. *Synthesis* **2005**, 33. (c) Hong, W. P.; Lee, K.-J. *Synthesis* **2006**, 963. (d) Song, Y. S.; Lee, K.-J. *J. Heterocycl. Chem.* **2006**, *43*, 1721. (e) Ji, S.-H.; Hong, W. P.; Ko, S. H.; Lee, K.-J. *J. Heterocycl. Chem.* **2006**, *43*, 799. (f) Lim, H. N.; Ji, S.-H.; Lee, K.-J. *Synthesis* **2007**, 2454. (g) Song, Y. S.; Lee, K.-J. *Synthesis* **2007**, 3037. (h) Lim, H. N.; Song, Y. S.; Lee, K.-J. *Synthesis* **2007**, 3376. (i) Jeon, K. J.; Lee, K.-J. *J. Heterocycl. Chem.* **2008**, *45*, 615. (j) Park, S. P.; Song, Y. S.; Lee, K.-J. *Tetrahedron* **2009**, *65*, 4703. (k) Han, E.-G.; Kim, H. J.; Lee, K.-J. *Tetrahedron* **2009**, *65*, 9616. (l) Park, S. P.; Ahn, S.-H.; Lee, K.-J. *Tetrahedron* **2010**, *66*, 3490. (m) Ahn, S.-H.; Jang, S. S.; Han, E.-G.; Lee, K.-J. *Synthesis* **2011**, 377.
(9) (a) Park, J. B.; Ko, S. H.; Hong, W. P.; Lee, K.-J. *Bull. Korean Chem. Soc.* **2004**, *25*, 927. (b) Park, J. B.; Ko, S. H.; Kim, B. G.; Hong, W. P.; Lee, K.-J. *Bull. Korean Chem. Soc.* **2004**, *25*, 27.
(10) Mason, P. H.; Emslie, N. D. *Tetrahedron* **1994**, *50*, 12001.
(11) Lee, K. Y.; Gowrisankar, S.; Kim, J. N. *Bull. Korean Chem. Soc.* **2004**, *25*, 413.
(12) Palladium is very sensitive to steric effects and generally forms less hindered complexes where possible. Thus, coordination of the palladium(II) intermediate occurs at the face of the dimethoxydihydrofuran *anti* to the methoxy group.
(13) The NMR numbering systems used for compounds **10** and **14** are shown in Schemes 2 and 3.
(14) Hartree–Fock 3-21G calculation data using Spartan are as follows: (a) *cis*-**10a**: dihedral angle = 76.80°, $J_{1,2}$ = 2.34 Hz; *trans*-**10a**: dihedral angle = 50.21°, $J_{1,2}$ = 6.84 Hz; *cis*-**14a**: dihedral angle = 38.19°, $J_{1,2}$ = 8.70 Hz; *trans*-**14a**: dihedral angle = 154.14°, $J_{1,2}$ = 7.26 Hz. (b) Observed *J* values: **10a**: $J_{1,2}$ = 9.4 Hz; **14a**: $J_{1,2}$ = 7.4 Hz.
(15) (a) Zhou, N.; Wang, L.; Thompson, D. W.; Zhao, Y. *Org. Lett.* **2008**, *10*, 3001. (b) Akgün, E.; Glinski, M. B.; Dhawan, K. L.; Durst, T. *J. Org. Chem.* **1981**, *46*, 2730. (c) Dong, L.-C.; Crowe, M.; West, J.; Ammann, J. R. *Tetrahedron Lett.* **2004**, *45*, 2731.

