

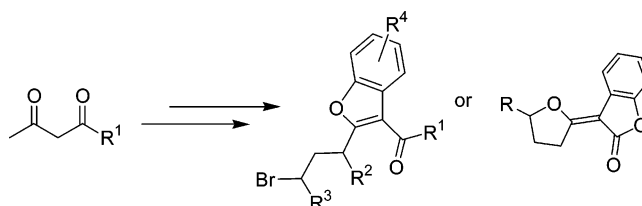
# Synthesis of Benzofurans with Remote Bromide Functionality by Domino “Ring-Cleavage-Deprotection-Cyclization” Reactions of 2-Alkylidenetetrahydrofurans with Boron Tribromide

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Bromination and subsequent Suzuki reactions of 2-alkylidenetetrahydrofurans, readily available by [3+2] cyclizations, afforded 1'-(2''-methoxyphenyl)-2-alkylidenetetrahydrofurans. Treatment of the latter with boron tribromide and subsequent addition of water resulted in the chemoselective formation of functionalized benzofurans containing a remote bromide functionality. The products are formed by a new domino “ring-cleavage-deprotection-cyclization” reaction. The addition of an aqueous solution of potassium *tert*-butoxide, rather than water, afforded saturated analogues of calycine by a “ring-cleavage-deprotection-ring-closure-lactonization” reaction.

## Introduction

Functionalized benzofurans<sup>1,2</sup> represent important synthetic building blocks and occur in a variety of pharmacologically relevant natural products, such as diazonamide A, anigopreissin A (Figure 1), euparin (Figure 2), coumestrol (Figure 3), dehydrotremetone, or cicerfuran (Figure 4).<sup>1</sup> Synthetic amiodarone represents a potent antiarrhythmic and antianginal drug that is used in the clinic.<sup>3</sup>

2-Alkylidenetetrahydrofurans represent useful synthetic building blocks.<sup>4–6</sup> We and others have reported a

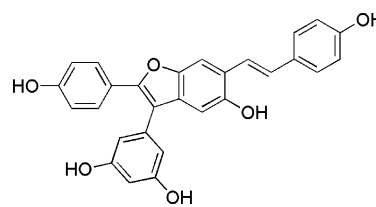


FIGURE 1. Anigopreissin A.

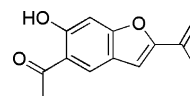


FIGURE 2. Euparin.

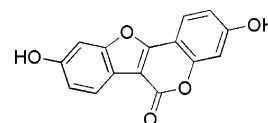


FIGURE 3. Coumestrol.

number of one-pot syntheses of 2-alkylidenetetrahydrofurans by [3+2] cyclizations of 1,3-dicarbonyl dianions and 1,3-bis-silyl enol ethers with 1,2-dielectrophiles,<sup>7</sup> and

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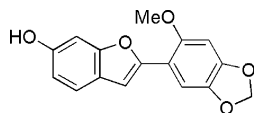
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(1) For benzofuran natural products: (a) Fuerst, D. E.; Stoltz, B. M.; Wood, J. L. *Org. Lett.* **2000**, *22*, 3521. (b) Schneider, B. *Phytochemistry* **2003**, *64*, 459. (c) Katritzky, A. R.; Kirichenko, K.; Ji, Y.; Steel, P. J.; Karelson, M. *ARKIVOC* **2003**, *vi*, 49. (d) Czekei, M.; Novák, Z.; Timári, G.; Kotschy, A. *ARKIVOC* **2004**, *vii*, 285 and references therein.

(2) For benzofuran syntheses: (a) Miyata, O.; Takeda, N.; Morikami, Y.; Naito, T. *Org. Biomol. Chem.* **2003**, *1*, 254. (b) Xie, X.; Chen, B.; Lu, J.; Han, J.; She, X.; Pan, X. *Tetrahedron Lett.* **2004**, *45*, 6235. (c) Zhang, H.; Ferreira, E. M.; Stoltz, B. M. *Angew. Chem., Int. Ed.* **2004**, *43*, 6144. (d) Kurfurst, P.; Marek, J.; Vanco, J.; Csöllei, J. *Acta Crystallogr.* **2004**, *E60*, 1989. For a review, see: (e) Butin, A. V.; Gutnow, A. V.; Abaev, V. T.; Krapivin, G. D. *Molecules* **1999**, *4*, 52.

**FIGURE 4.** Cicerfuran.

also by other methods.<sup>8c-e</sup> 2-Alkylidenetetrahydrofurans have been functionalized by lithiation and subsequent alkylations,<sup>8a,b</sup> in addition, the bromination of the exocyclic double bond and subsequent cross-coupling reactions have been reported.<sup>8f</sup> Recently, we have reported the synthesis of 6-bromo-3-oxoalkanoates by reaction of 2-alkylidenetetrahydrofurans with boron tribromide ( $\text{BBr}_3$ ).<sup>9</sup> Herein, we wish to report the synthesis of benzofurans by  $\text{BBr}_3$ -mediated domino “ring-cleavage-deprotection-cyclization” reactions of 2-alkylidenetetrahydrofurans. In addition, the synthesis of calyxine analogues,<sup>10</sup> based on Suzuki-cross-coupling and  $\text{BBr}_3$  reactions, is reported. From a preparative viewpoint, our methodology allows a convenient access to functionalized benzofurans, containing a remote bromide functionality, which are not readily available by other methods. The chemistry reported herein complements our recently reported synthetic approach to benzofurans based on a “[3+2] cyclization/oxidation”<sup>11</sup> strategy. The reactions

(3) (a) Wendt, B.; Ha, H. R.; Hesse, M. *Helv. Chim. Acta* **2002**, *85*, 2990. (b) Carlsson, B.; Singh, B. N.; Temciuc, M.; Nilsson, S.; Li, Y. L.; Mellin, C.; Malm, J. *J. Med. Chem.* **2002**, *45*, 623 and references therein. (c) Kwiecien, H.; Baumann, E. *J. Heterocycl. Chem.* **1997**, *34*, 1587. (d) Larock, R. C.; Harrison, L. W. *J. Am. Chem. Soc.* **1984**, *106*, 4218. (e) Mátyus, P.; Varga, I.; Reteggi, T.; Simay, A.; Kallay, N.; Károlyházy, L.; Kocsis, A.; Varro, A.; Penzes, I.; Papp, J. *G. Curr. Med. Chem.* **2004**, *1*, 61.

(4) For cycloadditions, see: (a) Weichert, A.; Hoffmann, H. M. R. *J. Org. Chem.* **1991**, *56*, 4098. (b) Tchelitcheff, P. *Bull. Soc. Chim. Fr.* **1954**, 672. (c) Ireland, R. E.; Haebich, D. *Chem. Ber.* **1981**, *114*, 1418. (d) Audrain, H.; Thorhauge, J.; Hazell, R. G.; Jørgensen, K. A. *J. Org. Chem.* **2000**, *65*, 4487. For reactions with amines, see: (e) Detty, M. R. *J. Org. Chem.* **1979**, *44*, 2073. (f) Batra, S.; Srivastava, S.; Singh, K.; Chander, R.; Khanna, A. K.; Bhaduri, A. P. *Bioorg. Med. Chem.* **2000**, *8*, 2195. For cyclopropanations: (g) Kirmse, W.; Rode, K. *Chem. Ber.* **1987**, *120*, 847. For hydrogenations: (h) Ohta, T.; Miyake, T.; Seido, N.; Kumobayashi, H.; Takaya, H. *J. Org. Chem.* **1995**, *60*, 357. See also ref 2.

(5) Reviews: (a) Oivin, T. L. B. *Tetrahedron* **1987**, *43*, 3309. (b) Barrett, A. G. M.; Sheth, H. G. *J. Org. Chem.* **1983**, *48*, 5017. (c) Rao, Y. S. *Chem. Rev.* **1976**, *76*, 625. (d) Pattenden, G. *Prog. Chem. Nat. Prod.* **1978**, *35*, 133. (e) Knight, D. W. *Contemp. Org. Synth.* **1994**, *1*, 287. (f) Gerlach, H.; Wetter, H. *Helv. Chim. Acta* **1974**, *57*, 2306. (g) Schmidt, U.; Gombos, J.; Haslinger, E.; Zak, H. *Chem. Ber.* **1976**, *109*, 2628. (h) Bartlett, P. A.; Meadows, J. D.; Ottow, E. *J. Am. Chem. Soc.* **1984**, *106*, 5304. (i) Lygo, B. *Tetrahedron* **1988**, *44*, 6889.

(6) (a) Ley, S. V.; Lygo, B.; Organ, H. M.; Wonnacott, A. *Tetrahedron* **1985**, *41*, 3825. (b) Booth, P. M.; Fox, C. M. J.; Ley, S. V. *J. Chem. Soc., Perkin Trans. 1* **1987**, 121. (c) Mori, K.; Sasaki, M.; Tamada, S.; Suguro, T.; Masuda, S. *Tetrahedron* **1979**, *35*, 1601.

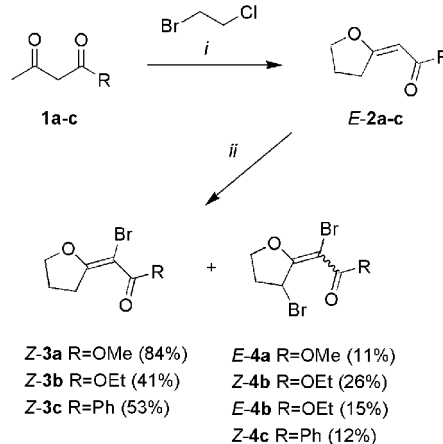
(7) For reviews of cyclization reactions of free and masked dianions, see: (a) Langer, P. *Chem.-Eur. J.* **2001**, *7*, 3858. (b) Langer, P. *Synthesis* **2002**, 441. (c) Langer, P.; Freiberg, W. *Chem. Rev.* **2004**, *104*, 4125.

(8) (a) Langer, P.; Bellur, E. *J. Org. Chem.* **2003**, *68*, 9742. See also: (b) Edwards, G. L.; Sinclair, D. *J. Tetrahedron Lett.* **1999**, *40*, 3933. (c) Krueger, S. A.; Bryson, T. A. *J. Org. Chem.* **1974**, *39*, 3167. (d) Gabriele, B.; Salerno, G.; Pascali, F. D.; Costa, M.; Chiusoli, G. P. *J. Organomet. Chem.* **2000**, *593*, 1, 409. (e) Pflieger, D.; Muckensturn, B. *Tetrahedron* **1989**, *45*, 7, 2031. (f) Bellur, E.; Langer, P. *Synlett* **2004**, 2169.

(9) For an isolated example of the domino “ring-cleavage-deprotection-cyclization” reaction, see: (a) Bellur, E.; Langer, P. *Synlett* **2004**, 2172. For open-chained products: (b) Bellur, E.; Langer, P. *J. Org. Chem.* **2005**, *70*, 3819.

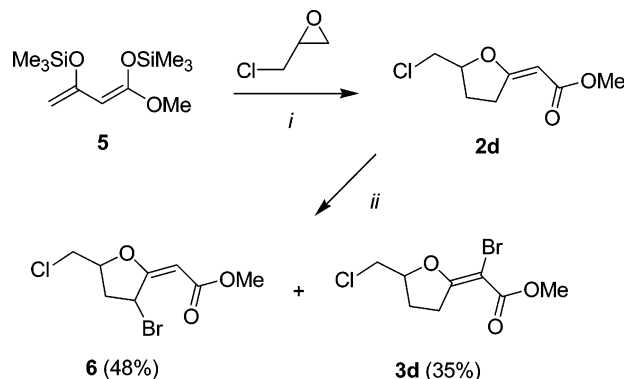
(10) (a) Akermarck, B. *Acta Chem. Scand.* **1961**, *15*, 1695. (b) The 2,3'-bifuranylidene subunit is present in the natural products charlic acid, charolic acid, and terrestric acid: Arai, H.; Miyajima, H.; Mushiroda, T.; Yamamoto, Y. *Chem. Pharm. Bull.* **1989**, *12*, 3229.

## SCHEME 1. Bromination of 2-Alkylidenetetrahydrofurans **2a–c**<sup>a</sup>



<sup>a</sup> (i) (1) 2.3 equiv of LDA, THF, 0 °C, 1 h, (2)  $\text{Br}(\text{CH}_2)_2\text{Cl}$ ,  $-78 \rightarrow 20$  °C, 14 h, then reflux, 12 h; (ii) NBS (1.1–1.3 equiv),  $\text{CCl}_4$ , reflux, 3 h.

## SCHEME 2. Bromination of 2-Alkylidenetetrahydrofuran **2d**<sup>a</sup>



<sup>a</sup> (i) 2 equiv of  $\text{TiCl}_4$ ,  $\text{CH}_2\text{Cl}_2$ ,  $-78 \rightarrow 20$  °C; (ii) NBS (1.1 equiv),  $\text{CCl}_4$ , reflux, 3 h.

reported herein are of interest also from a methodology viewpoint: whereas the  $\text{BBr}_3$ -mediated cleavage of methylaryl ethers is well known and broadly used,<sup>12</sup> reactions of other ethers are more rare. Known examples include the formation of  $\omega$ -bromoalkanol by ring-opening of cyclic ethers with  $\text{BBr}_3/\text{MeOH}$ ,<sup>13a</sup> or the transformation of lactones into  $\omega$ -halocarboxylic acids.<sup>13b</sup>

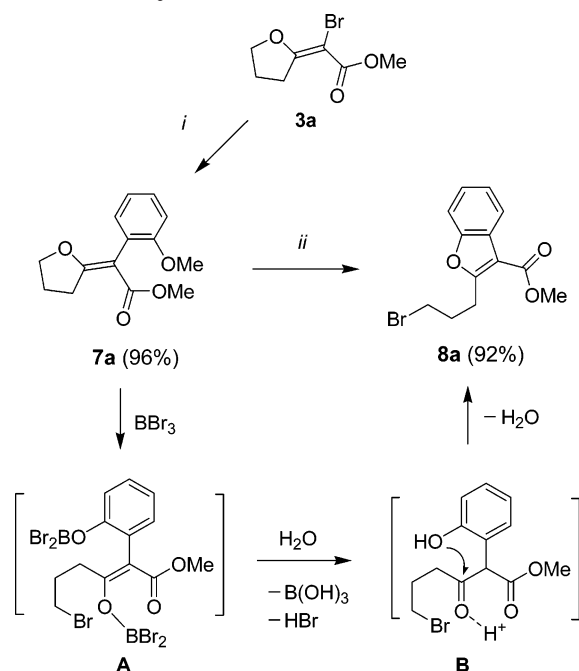
## Results and Discussion

Our first aim was the synthesis of the required starting materials (Schemes 1 and 2). The reaction of 2-alkylidenetetrahydrofurans **2a–c**, prepared by cyclization of 1-bromo-2-chloroethane with the dianions of 1,3-dicarbonyl compounds **1a–c**,<sup>8a,14</sup> with NBS (1.1–1.3 equiv)

(11) (a) Bellur, E.; Freifeld, I.; Langer, P. *Tetrahedron Lett.* **2005**, *46*, 2185. (b) Bellur, E.; Görls, H.; Langer, P. *Eur. J. Org. Chem.* **2005**, 2074.

(12) Review: (a) Bhatt, M. V.; Kulkarni, S. U. *Synthesis* **1983**, 249. See also: (b) McOmie, J. F. W.; Watts, M. L.; West, D. E. *Tetrahedron* **1968**, *24*, 2289.

(13) For the cleavage of cyclic ethers, see: (a) Kulkarni, S. U.; Patil, V. D. *Heterocycles* **1982**, *18*, 163. For the cleavage of lactones, see: (b) Olah, G. A.; Karpeles, R.; Narang, S. C. *Synthesis* **1982**, 963.

SCHEME 3. Synthesis of Benzofuran 8a<sup>a</sup>

<sup>a</sup> (i) [2-(MeO)C<sub>6</sub>H<sub>4</sub>]B(OH)<sub>2</sub> (3.0 equiv), Pd(PPh<sub>3</sub>)<sub>4</sub> (3 mol-%), K<sub>3</sub>PO<sub>4</sub> (6.0 equiv), 1,4-dioxane, reflux, 6 h; (ii) (1) 4 equiv of BBr<sub>3</sub>, CH<sub>2</sub>Cl<sub>2</sub>, 0 → 20 °C, 12 h, 20 °C, 6 h; (2) H<sub>2</sub>O.

afforded the 1'-bromo-2-alkylidenetetrahydrofurans **3a–c** and the 1',3-dibromo-2-alkylidenetetrahydrofurans **4a–c** (Scheme 1).

The NBS-mediated (1.1 equiv) bromination of 5-chloromethyl-2-alkylidenetetrahydrofuran **2d**, prepared by TiCl<sub>4</sub>-mediated cyclization of 1,3-bis-silyl enol ether **5** with epichlorohydrin,<sup>15</sup> afforded the 1'-bromo-2-alkylidenetetrahydrofuran **3d** and the 1',3-dibromo-2-alkylidenetetrahydrofuran **6** (Scheme 2). The desired product **3d** could be isolated in pure form when 1.1 equiv of NBS was employed; however, the formation of **6** could not be entirely avoided. The use of 1.3 equiv of NBS resulted in a decrease of the yield of **3d** and gave an inseparable mixture of **3d** and **6**.

The synthesis of functionalized benzofurans by sequential Suzuki and BBr<sub>3</sub> reactions was studied next (Scheme 3, Table 1). The Pd(PPh<sub>3</sub>)<sub>4</sub> (3 mol-%) catalyzed Suzuki reaction of **3a** with (2-methoxyphenyl)boronic acid gave the desired 2-alkylidenetetrahydrofuran **7a** with excellent *E*-diastereoselectivity. Treatment of **7a** with BBr<sub>3</sub> afforded the benzofuran **8a**.<sup>9a</sup> We propose a mechanism that involves the formation of **8a** (Scheme 3). The latter is formed by BBr<sub>3</sub>-mediated ring-opening of **7a** and cleavage of the arylmethyl ether to give intermediate **A**. Addition of water results in hydrolysis of the boronic ester moieties, to give boronic and hydrobromic acid (intermediate **B**), and subsequent acid-mediated cyclization and aromatization by extrusion of water. During the optimization, the use of an excess of BBr<sub>3</sub> (4 equiv) proved to be important.

(14) Langer, P.; Holtz, E.; Karimé, I.; Saleh, N. N. *R. J. Org. Chem.* **2001**, *66*, 6057.

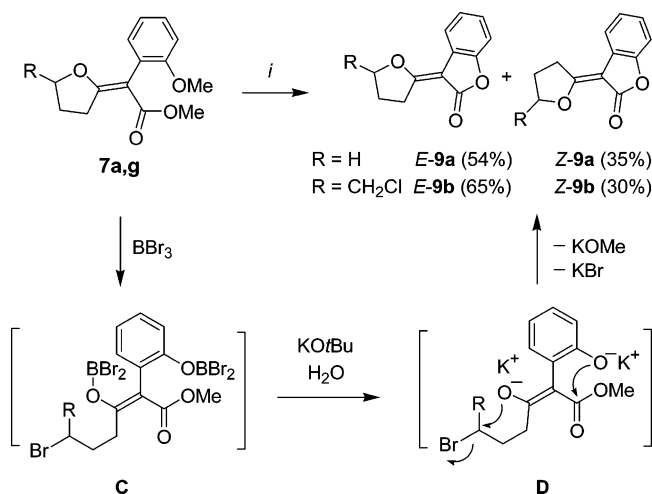
(15) (a) Langer, P.; Armbrust, H.; Eckardt, T.; Magull, J. *Chem.-Eur. J.* **2002**, *8*, 1443. (b) For an alternative synthesis of **2d**, see: Pound, M. K.; Davies, D. L.; Pilkington, M.; de Pina Vaz Sousa, M. M.; Wallis, J. D. *Tetrahedron Lett.* **2002**, *43*, 1915.

TABLE 1. Synthesis of Benzofuran Derivatives

entry	substrate	% ( <b>7</b> ) <sup>a, b</sup>	% ( <b>8</b> ) <sup>a</sup>
1	<b>3a</b>	 <b>7b</b> (87%)	 <b>8b</b> (97%)
2	<b>3b</b>	 <b>7c</b> (93%)	 <b>8c</b> (84%)
3	<b>3b</b>	 <b>7d</b> (96%)	 <b>8d</b> (97%)
4	<b>3b</b>	 <b>7e</b> (87%)	 <b>8e</b> (92%)
5	<b>3c</b>	 <b>7f</b> (77%)	 <b>8f</b> (71%)
6	<b>3d</b>	 <b>7g</b> (96%)	 <b>8g</b> (80%)
7	<b>4a</b>	 <b>7h</b> (92%)	 <b>8h</b> (58%)

<sup>a</sup> Yields of isolated products. <sup>b</sup> *E/Z* > 98:2.

The preparative scope of our methodology was studied (Table 1). The Suzuki reaction of **3a** with 2,5-dimethoxyphenylboronic acid gave 2-alkylidenetetrahydrofuran **7b**.

SCHEME 4. Lactonization of **7a,g**<sup>a</sup>

<sup>a</sup> (i) (1) 4 equiv of  $\text{BBr}_3$ ,  $\text{CH}_2\text{Cl}_2$ ,  $0 \rightarrow 20^\circ\text{C}$ , 12 h,  $20^\circ\text{C}$ , 6 h; (2)  $\text{KOtBu}$ ,  $\text{H}_2\text{O}$  (1 M), 1 h,  $20^\circ\text{C}$ .

Treatment of the latter with  $\text{BBr}_3$  afforded the benzofuran **8b**. The reaction of **3b** with 2-methoxyphenyl-, 2,4-dimethoxyphenyl-, and 2,6-dimethoxyphenylboronic acid afforded the functionalized 2-alkylenetetrahydrofurans **7c–e**, which were transformed into **8c–e**. Likewise, the reaction of **3c** with 2-methoxyphenylboronic acid afforded **7f**, which was transformed into the 3-benzoylbenzofuran **8f** by treatment with  $\text{BBr}_3$ . 2-Alkylenetetrahydrofuran **7g** was prepared by reaction of **3d** with 2-methoxyphenylboronic acid; treatment of **7g** with  $\text{BBr}_3$  gave the benzofuran **8g**. The Suzuki reaction of dibromide **4a** with 2-methoxyphenylboronic acid afforded 2-alkylen-1',3-diaryltetrahydrofuran **7h**, which was formed by a double-Suzuki reaction of the 1,3-dibromoprop-1-ene moiety; the reaction of **7h** with  $\text{BBr}_3$  afforded the benzofuran **8h**. All reactions proceeded in good to very good yields and with very good chemoselectivity. In addition, all Suzuki reactions proceeded with excellent *E*-diastereoselectivity.

The application of our methodology to the synthesis of 3-(dihydrofuran-2(3*H*)-ylidene)-3*H*-benzofuran-2-one **9a** and of 3-[(5-chloromethyl)dihydrofuran-2(3*H*)-ylidene]-3*H*-benzofuran-2-one **9b**, saturated analogues of calycine,<sup>10</sup> was studied next (Scheme 4).<sup>8c</sup> Treatment of **7a** and **7g** with  $\text{BBr}_3$  ( $\text{CH}_2\text{Cl}_2$ ) and subsequent addition of an aqueous solution of  $\text{KOtBu}$  (1 M) afforded **9a** and **9b** as separable mixtures of *E/Z*-isomers, respectively. We propose a mechanism that involves the formation of **9a** and **9b** by  $\text{BBr}_3$ -mediated ring-cleavage of **7a,g** and cleavage of the arylmethyl ether (intermediate **C**). Addition of the aqueous solution of  $\text{KOtBu}$  ( $\text{KOtBu} + \text{H}_2\text{O} \rightarrow \text{KOH} + t\text{BuOH}$ ) results in hydrolysis of the boronic ester moieties (intermediate **D**) and subsequent base-mediated recyclization of the tetrahydrofuran moiety and lactonization. The formation of **9a,b** as a mixture of *E/Z*-isomers can be explained by keto–enol tautomerism of intermediate **C**.

In summary, we have reported a convenient and chemoselective formation of functionalized benzofurans containing a remote bromide functionality. The products are formed by a new  $\text{BBr}_3$ -mediated domino “ring-cleavage-deprotection-cyclization” reaction. The starting materials, 1'-(2'-methoxyphenyl)-2-alkylenetetrahydro-

furans, were prepared by bromination and subsequent Suzuki reactions of 2-alkylenetetrahydrofurans available by [3+2] cyclizations. In addition, we have reported the synthesis of saturated analogues of calycine, prepared by reaction of 1'-(2'-methoxyphenyl)-2-alkylenetetrahydrofurans with  $\text{BBr}_3$  and subsequent addition of an aqueous solution of  $\text{KOtBu}$ .

## Experimental Section

**General Procedure for the Reaction of 2-Alkylenetetrahydrofurans with *N*-Bromosuccinimide (NBS).** To a  $\text{CCl}_4$ -solution (5 mL/mmol) of the 2-alkylenetetrahydrofuran **2** (1 equiv) was added *N*-bromosuccinimide (1.1 equiv) at  $20^\circ\text{C}$ . The reaction mixture was heated and stirred at reflux for 3 h. The reaction mixture was then allowed to cool to ambient temperature, and the solvent was removed in vacuo. The residue was purified by chromatography (silica gel, *n*-hexane/ $\text{EtOAc}$ ) to give the bromo-2-alkylenetetrahydrofurans **3,4,6**.

**Synthesis of **3,4a**.** Starting with **2a** (4.000 g, 28.0 mmol) and NBS (6.511 g, 36.6 mmol) in  $\text{CCl}_4$  (40 mL), **3-3a** (5.212 g, 84%) and **4-4a** (0.937 g, 11%) were isolated after chromatography (silica gel, *n*-hexane/ $\text{EtOAc}$  = 100:1  $\rightarrow$  1:1) as yellowish and colorless solids, respectively.

**Methyl Bromo(dihydrofuran-2(3*H*)-ylidene)acetate (**Z-3a**).**  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  2.23 (quint,  $J$  = 7.2 Hz, 2H,  $\text{CH}_2$ ), 3.19 (t,  $J$  = 7.8 Hz, 2H,  $\text{CH}_2$ ), 3.78 (s, 3H,  $\text{OCH}_3$ ), 4.41 (t,  $J$  = 7.2 Hz, 2H,  $\text{OCH}_2$ ).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz):  $\delta$  24.8, 32.3, 52.2, 73.0, 82.7, 164.7, 172.2. IR (KBr,  $\text{cm}^{-1}$ ):  $\nu$  = 2951 (w), 1699 (s), 1609 (s), 1435 (m), 1281 (s), 1213 (s), 1188 (m), 1073 (s), 973 (w), 925 (w), 879 (w), 770 (w), 759 (w). MS (EI, 70 eV):  $m/z$  (%) = 221 ( $\text{M}^+$  [ $^{81}\text{Br}$ ], 72), 219 ( $\text{M}^+$  [ $^{79}\text{Br}$ ], 71), 190 (87), 162 (3). Anal. Calcd for  $\text{C}_7\text{H}_9\text{O}_3\text{Br}$  (221.050): C, 38.04; H, 4.10. Found: C, 38.19; H, 3.64.

**Methyl Bromo(3-bromodihydrofuran-2(3*H*)-ylidene)-acetate (**E-4a**).**  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  2.43–2.49 (m, 1H,  $\text{CH}_2$ ), 2.53–2.61 (m, 1H,  $\text{CH}_2$ ), 3.80 (s, 3H,  $\text{OCH}_3$ ), 4.74–4.76 (m, 1H,  $\text{OCH}_2$ ), 4.78–4.79 (m, 1H,  $\text{OCH}_2$ ), 5.20 (d,  $J$  = 5.4 Hz, 1H,  $\text{CH}-\text{Br}$ ).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz):  $\delta$  34.7, 48.4, 52.1, 73.8, 87.1, 162.0, 167.0. IR (KBr,  $\text{cm}^{-1}$ ):  $\nu$  = 2950 (w), 1706 (s), 1605 (s), 1433 (m), 1271 (s), 1204 (s), 1174 (s), 1057 (w), 1039 (s), 1027 (s), 1004 (w), 765 (w). MS (EI, 70 eV):  $m/z$  (%) = 302 ( $\text{M}^+$  [ $2 \times ^{81}\text{Br}$ ], 17), 300 ( $\text{M}^+$  [ $^{81}\text{Br}^{79}\text{Br}$ ], 34), 298 ( $\text{M}^+$  [ $2 \times ^{79}\text{Br}$ ], 17), 269 (19), 241 (2), 221 (100), 189 (22), 161 (18). Anal. Calcd for  $\text{C}_7\text{H}_8\text{O}_3\text{Br}_2$  (299.946): C, 28.03; H, 2.69. Found: C, 28.88; H, 2.85.

**Synthesis of **3,4b**.** Starting with **2b** (1.432 g, 9.2 mmol) and NBS (2.122 g, 11.92 mmol) in  $\text{CCl}_4$  (25 mL), **Z-4b** (0.740 g, 26%), **Z-3b** (0.886 g, 41%), and **E-4b** (0.430 g, 15%) were isolated after chromatography (silica gel, *n*-hexane/ $\text{EtOAc}$  = 100:1  $\rightarrow$  1:1) as slightly yellowish solid, yellowish solid, and yellowish oil, respectively.

**Ethyl Bromo(3-bromodihydrofuran-2(3*H*)-ylidene)acetate (**Z-4b**).**  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  1.36 (t,  $J$  = 7.2 Hz, 3H,  $\text{CH}_3$ ), 2.55–2.63 (m, 2H,  $\text{CH}_2$ ), 4.29 (dq,  $J$  = 2.1, 7.2 Hz, 2H,  $\text{OCH}_2\text{CH}_3$ ), 4.56–4.66 (m, 2H,  $\text{OCH}_2$ ), 5.81 (dd,  $J$  = 4.5, 1.5 Hz, 1H,  $\text{CH}-\text{Br}$ ).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz):  $\delta$  13.9, 36.8, 44.1, 61.7, 70.6, 87.1, 162.5, 168.5. IR (KBr,  $\text{cm}^{-1}$ ):  $\nu$  = 2933 (w), 1701 (s), 1616 (s), 1371 (w), 1274 (s), 1216 (s), 1189 (m), 1160 (w), 1069 (s), 1026 (w), 953 (w), 928 (w), 872 (w), 757 (w). MS (EI, 70 eV):  $m/z$  (%) = 315 ( $\text{M}^+$  [ $2 \times ^{81}\text{Br}$ ], 11), 313 ( $\text{M}^+$  [ $^{81}\text{Br}^{79}\text{Br}$ ], 33), 311 ( $\text{M}^+$  [ $2 \times ^{79}\text{Br}$ ], 12), 269 (11), 235 (65), 305 (100), 189 (29), 161 (23). Anal. Calcd for  $\text{C}_8\text{H}_{10}\text{O}_3\text{Br}_2$  (313.973): C, 30.60; H, 3.21. Found: C, 30.32; H, 3.51.

**Ethyl Bromo(dihydrofuran-2(3*H*)-ylidene)acetate (**Z-3b**).**  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  1.32 (t,  $J$  = 7.2 Hz, 3H,  $\text{CH}_3$ ), 2.23 (quint,  $J$  = 7.5 Hz,  $\text{CH}_2$ ), 3.18 (t,  $J$  = 7.8 Hz, 2H,  $\text{CH}_2$ ), 4.23 (q,  $J$  = 7.2 Hz, 2H,  $\text{OCH}_2\text{CH}_3$ ), 4.40 (t,  $J$  = 7.2 Hz, 2H,  $\text{OCH}_2$ ).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 150 MHz):  $\delta$  14.0, 24.6, 32.2, 60.8, 72.7, 83.0, 163.7, 171.7. IR (KBr,  $\text{cm}^{-1}$ ):  $\nu$  = 2995 (w),



2975 (w), 2907 (w), 1691 (s), 1608 (s), 1395 (w), 1374 (m), 1294 (s), 1276 (s), 1240 (w), 1194 (s), 1065 (s), 1038 (m), 953 (w), 931 (m), 874 (w), 762 (m). MS (EI, 70 eV):  $m/z$  (%) = 236 ( $M^+$  [ $^{81}\text{Br}$ ], 75), 234 ( $M^+$  [ $^{79}\text{Br}$ ], 76), 206 (44), 189 (100), 161 (5), 110 (40), 81 (12). Anal. Calcd for  $\text{C}_8\text{H}_{11}\text{O}_3\text{Br}$  (235.077): C, 40.88; H, 4.72. Found: C, 41.04; H, 4.61.

**E-4b.**  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  1.32 (t,  $J$  = 7.2 Hz, 3H,  $\text{CH}_3$ ), 2.43–2.48 (m, 1H,  $\text{CH}_2$ ), 2.52–2.61 (m, 1H,  $\text{CH}_2$ ), 4.27 (q,  $J$  = 7.2 Hz, 2H,  $\text{OCH}_2\text{CH}_3$ ), 4.76 (dt,  $J$  = 8.7, 0.9 Hz, 2H,  $\text{OCH}_2$ ), 5.20 (d,  $J$  = 5.4 Hz, 1H,  $\text{CH}-\text{Br}$ ).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 150 MHz):  $\delta$  14.1, 35.2, 48.7, 61.5, 74.0, 87.9, 162.0, 176.1. IR (neat,  $\text{cm}^{-1}$ ):  $\nu$  = 2983 (m), 2938 (w), 2905 (m), 1737 (s), 1703 (s), 1660 (m), 1616 (s), 1471 (m), 1440 (m), 1371 (s), 1316 (m), 1283 (s), 1272 (s), 1206 (s), 1184 (s), 1157 (s), 1117 (m), 1094 (m), 1088 (s), 935 (m), 925 (m), 865 (w), 847 (w), 763 (m), 700 (w). MS (EI, 70 eV):  $m/z$  (%) = 316 ( $M^+$  [ $2 \times ^{81}\text{Br}$ ], 17), 314 ( $M^+$  [ $^{81}\text{Br}^{79}\text{Br}$ ], 37), 312 ( $M^+$  [ $2 \times ^{79}\text{Br}$ ], 18), 269 (29), 241 (3), 233 (6), 205 (100), 189 (35), 161 (23). The exact molecular mass  $m/z$  = 311.8997  $\pm$  2 ppm [ $M^+$ ] for  $\text{C}_8\text{H}_{10}\text{O}_3\text{Br}_2$  was confirmed by HRMS (EI, 70 eV).

**Synthesis of 3,4c.** Starting with **2c** (0.400 g, 2.13 mmol) and NBS (0.416 g, 2.34 mmol) in  $\text{CCl}_4$  (30 mL), **Z-4c** (0.087 g, 12%) and **Z-3c** (0.302 g, 53%) were isolated after chromatography (silica gel,  $n$ -hexane/EtOAc = 100:1  $\rightarrow$  1:1) as yellowish oils.

**2-Bromo-2-(3-bromodihydrofuran-2(3H)-ylidene)-1-phenylethanone (Z-4c).**  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  2.51–2.72 (m, 2H,  $\text{CH}_2$ ), 4.60–4.71 (m, 2H,  $\text{OCH}_2$ ), 5.60 (d,  $J$  = 5.4 Hz, 1H,  $\text{CH}-\text{Br}$ ), 7.41–7.55 (m, 3H,  $3 \times \text{CH of Ph}$ ), 7.75 (d,  $J$  = 3.9 Hz, 2H,  $2 \times \text{CH of Ph}$ ).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz):  $\delta$  36.8, 43.6, 70.5, 92.8, 127.7, 128.7, 132.0, 137.7, 166.9, 191.0. IR (neat,  $\text{cm}^{-1}$ ):  $\nu$  = 3059 (w), 2998 (w), 2962 (w), 2906 (m), 1659 (s), 1653 (s), 1598 (s), 1584 (s), 1581 (s), 1570 (s), 1473 (w), 1444 (m), 1370 (m), 1311 (s), 1276 (s), 1220 (s), 1174 (s), 1161 (s), 1115 (w), 1076 (w), 1055 (m), 1017 (s), 964 (s), 931 (s), 909 (m), 882 (m), 836 (m), 815 (w), 794 (m), 741 (m), 687 (s), 654 (s), 522 (m). MS (EI, 70 eV):  $m/z$  (%) = 348 ( $M^+$  [ $2 \times ^{81}\text{Br}$ ], 7), 346 ( $M^+$  [ $^{81}\text{Br}^{79}\text{Br}$ ], 15), 344 ( $M^+$  [ $2 \times ^{79}\text{Br}$ ], 7), 267 (36), 186 (100). Anal. Calcd for  $\text{C}_{12}\text{H}_{10}\text{O}_2\text{Br}_2$  (346.018): C, 41.65; H, 2.91. Found: C, 41.35; H, 3.60.

**2-Bromo-2-(dihydrofuran-2(3H)-ylidene)-1-phenylethanone (Z-3c).**  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  2.21 (quint,  $J$  = 7.5 Hz, 2H,  $\text{CH}_2$ ), 2.94 (t,  $J$  = 7.8 Hz, 2H,  $\text{CH}_2$ ), 4.45 (t,  $J$  = 7.2 Hz, 2H,  $\text{OCH}_2$ ), 7.38–7.53 (m, 3H,  $3 \times \text{CH of Ph}$ ), 7.61–7.71 (m, 2H,  $2 \times \text{CH of Ph}$ ).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz):  $\delta$  25.2, 32.7, 72.9, 91.3, 127.9 (2C), 128.5 (2C), 131.4, 139.2, 171.5, 191.8. IR (neat,  $\text{cm}^{-1}$ ):  $\nu$  = 2959 (w), 2927 (w), 1684 (s), 1646 (s), 1596 (s), 1448 (m), 1420 (w), 1312 (m), 1285 (m), 1253 (w), 1210 (s), 1183 (m), 1118 (w), 1075 (w), 1033 (m), 995 (w), 965 (w), 930 (w), 693 (w), 649 (w). MS (EI, 70 eV):  $m/z$  (%) = 267 ( $M^+$  [ $^{81}\text{Br}$ ], 22), 265 ( $M^+$  [ $^{79}\text{Br}$ ], 21), 186 (35), 162 (3), 146 (11), 129 (2), 105 (100), 77 (64), 70 (18).

**Synthesis of 3d,6.** Starting with **2d** (1.000 g, 5.25 mmol) and NBS (1.027 g, 5.77 mmol) in  $\text{CCl}_4$  (50 mL), **6** (0.680 g, 48%) and **3d** (0.492 g, 35%) were isolated after chromatography (silica gel,  $n$ -hexane/EtOAc = 100:1  $\rightarrow$  2:1) as a yellowish oil and a white solid, respectively.

**Methyl (3-Bromo-5-chloromethyldihydrofuran-2(3H)-ylidene)acetate (6).**  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  2.38–2.71 (m, 2H,  $\text{CH}_2$ ), 3.73 (s, 3H,  $\text{OCH}_3$ ), 3.79 (dd,  $J$  = 9.4, 4.9 Hz, 2H,  $\text{CH}_2-\text{Cl}$ ), 5.03 (sext,  $J$  = 4.9 Hz, 1H,  $\text{OCH}$ ), 5.33 (s, 1H,  $\text{CH}=\text{C}$ ), 5.81 (d,  $J$  = 5.6 Hz, 1H,  $\text{CH}-\text{Br}$ ).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz):  $\delta$  38.3, 43.8, 50.5, 52.2, 79.9, 90.7, 166.0, 171.8. IR (neat,  $\text{cm}^{-1}$ ):  $\nu$  = 2953 (w), 1708 (s), 1653 (s), 1625 (m), 1436 (m), 1407 (w), 1358 (m), 1335 (w), 1284 (m), 1243 (w), 1215 (m), 1194 (m), 1164 (w), 1125 (s), 1071 (m), 1048 (m), 999 (w), 944 (w), 889 (w), 837 (w), 757 (w), 716 (w). MS (EI, 70 eV):  $m/z$  (%) = 272 ( $M^+$  [ $^{81}\text{Br}^{37}\text{Cl}$ ], 21), 270 ( $M^+$  [ $^{81}\text{Br}^{35}\text{Cl}$ ], 99), 268 ( $M^+$  [ $^{79}\text{Br}^{35}\text{Cl}$ ], 72), 239 (99), 189 (100), 157 (56), 139 (27), 125 (11), 110 (20), 101 (35), 81 (25).

**Methyl Bromo(5-chloromethyldihydrofuran-2(3H)-ylidene)acetate (3d).** mp = 40  $^\circ\text{C}$ .  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300

MHz):  $\delta$  2.11–2.22 (m, 1H,  $\text{CH}_2$ ), 2.35–2.46 (m, 1H,  $\text{CH}_2$ ), 3.09–3.21 (m, 1H,  $\text{CH}_2$ ), 3.30–3.41 (m, 1H,  $\text{CH}_2$ ), 3.63–3.73 (m, 2H,  $\text{CH}_2-\text{Cl}$ ), 3.78 (s, 3H,  $\text{OCH}_3$ ), 4.80–4.87 (m, 1H,  $\text{OCH}$ ).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz):  $\delta$  27.3, 31.9, 45.1, 52.1, 82.8, 82.9, 164.2, 171.1. IR (KBr,  $\text{cm}^{-1}$ ):  $\nu$  = 2953 (w), 1701 (s), 1614 (s), 1434 (m), 1346 (w), 1280 (s), 1221 (m), 1192 (m), 1122 (w), 1075 (s), 1037 (m), 883 (w), 760 (w), 748 (w), 738 (w). MS (EI, 70 eV):  $m/z$  (%) = 272 ( $M^+$  [ $^{81}\text{Br}^{37}\text{Cl}$ ], 8), 270 ( $M^+$  [ $^{81}\text{Br}^{35}\text{Cl}$ ], 48), 268 ( $M^+$  [ $^{79}\text{Br}^{35}\text{Cl}$ ], 39), 238 (100), 235 (72), 219 (5), 201 (14), 191 (5), 159 (23), 117 (11), 69 (36). Anal. Calcd for  $\text{C}_8\text{H}_{10}\text{BrClO}_3$  (269.522): C, 35.65; H, 3.74. Found: C, 35.38; H, 4.00.

**General Procedure for the Suzuki Reaction of 2-Alkylidenetetrahydrofurans with Arylboronic Acids.** To a 1,4-dioxane solution (3 mL/mmol) of the bromo-2-alkylidenetetrahydrofuran (**3,4**) (1 equiv) were added potassium phosphate ( $\text{K}_3\text{PO}_4$ , 6 equiv), the boronic acid ( $\text{ArB}(\text{OH})_2$ , 3 equiv), and  $\text{Pd}(\text{PPh}_3)_4$  (0.03 equiv) at 20  $^\circ\text{C}$ . The reaction mixture was heated and stirred at reflux for 6 h. The reaction mixture was then allowed to cool to ambient temperature, and diethyl ether (10 mL/mmol) was added. The precipitate was filtered off, washed with diethyl ether, and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel,  $n$ -hexane/EtOAc) to give the aryl-substituted 2-alkylidenetetrahydrofurans **7**.

**Methyl (Dihydrofuran-2(3H)-ylidene)-(2-methoxyphenyl)acetate (7a).** Starting with **3a** (0.100 g, 0.45 mmol), 2-methoxyphenylboronic acid (0.213 g, 1.36 mmol),  $\text{K}_3\text{PO}_4$  (0.575 g, 2.71 mmol), and  $\text{Pd}(\text{PPh}_3)_4$  (0.016 g, 0.014 mmol) in 1,4-dioxane (5 mL), **7a** was isolated after chromatography (silica gel,  $n$ -hexane/EtOAc = 100:1  $\rightarrow$  1:1) as a slightly yellowish solid (0.107 g, 96%).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  2.12 (quint,  $J$  = 7.2 Hz, 2H,  $\text{CH}_2$ ), 3.28 (t,  $J$  = 7.8 Hz, 2H,  $\text{CH}_2$ ), 3.63 (s, 3H,  $\text{OCH}_3$ ), 3.77 (s, 3H,  $\text{OCH}_3$ ), 4.19 (t,  $J$  = 7.2 Hz, 2H,  $\text{OCH}_2$ ), 6.90–6.98 (m, 2H,  $2 \times \text{CH}$ ), 7.19 (d,  $J$  = 9.3 Hz, 1H,  $\text{CH}$ ), 7.24–7.30 (m, 1H,  $\text{CH}$ ).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz):  $\delta$  24.0, 31.1, 51.0, 55.5, 71.9, 100.4, 110.9, 120.1, 124.6, 128.3, 131.8, 157.1, 168.9, 171.5. IR (KBr,  $\text{cm}^{-1}$ ):  $\nu$  = 2943 (w), 1704 (s), 1623 (s), 1599 (w), 1492 (m), 1464 (w), 1435 (m), 1376 (w), 1315 (m), 1271 (m), 1244 (m), 1184 (s), 1114 (w), 1075 (s), 1068 (s), 1024 (m), 979 (m). MS (EI, 70 eV):  $m/z$  (%) = 248 ( $M^+$ , 100), 216 (25), 189 (57), 174 (7), 158 (3). Anal. Calcd for  $\text{C}_{14}\text{H}_{16}\text{O}_4$  (248.278): C, 67.73; H, 6.50. Found: C, 67.51; H, 6.83.

**Methyl (Dihydrofuran-2(3H)-ylidene)-(2,5-dimethoxyphenyl)acetate (7b).** Starting with **3a** (0.100 g, 0.45 mmol), 2,5-dimethoxybenzeneboronic acid (0.253 g, 1.36 mmol),  $\text{K}_3\text{PO}_4$  (0.576 g, 2.71 mmol), and  $\text{Pd}(\text{PPh}_3)_4$  (0.016 g, 0.014 mmol) in 1,4-dioxane (5 mL), **7b** was isolated after chromatography (silica gel,  $n$ -hexane/EtOAc = 50:1  $\rightarrow$  1:1) as a yellowish solid (0.109 g, 87%).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  2.13 (quint,  $J$  = 7.5 Hz, 2H,  $\text{CH}_2$ ), 3.27 (t,  $J$  = 7.8 Hz, 2H,  $\text{CH}_2$ ), 3.64 (s, 3H,  $\text{OCH}_3$ ), 3.73 (s, 3H,  $\text{OCH}_3$ ), 3.77 (s, 3H,  $\text{OCH}_3$ ), 4.20 (t,  $J$  = 7.2 Hz, 2H,  $\text{OCH}_2$ ), 6.77–6.86 (m, 3H,  $3 \times \text{CH}$ ).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 150 MHz):  $\delta$  24.2, 31.4, 51.3, 55.7, 56.5, 72.3, 100.5, 112.2, 112.8, 118.1, 125.9, 151.8, 153.3, 169.0, 171.9. IR (KBr,  $\text{cm}^{-1}$ ):  $\nu$  = 3009 (w), 2986 (w), 2953 (m), 2900 (w), 2837 (w), 1700 (s), 1621 (s), 1609 (s), 1497 (s), 1464 (m), 1428 (m), 1377 (w), 1306 (s), 1279 (s), 1236 (s), 1217 (s), 1185 (s), 1160 (m), 1137 (s), 1072 (s), 1053 (s), 1026 (m), 983 (w), 983 (w), 964 (m), 936 (w), 899 (w), 805 (m), 779 (w), 724 (w). MS (EI, 70 eV):  $m/z$  (%) = 278 ( $M^+$ , 100), 247 (8), 231 (3), 219 (15), 217 (1), 204 (1), 155 (28), 91 (7), 77 (5), 70 (13). Anal. Calcd for  $\text{C}_{15}\text{H}_{18}\text{O}_5$  (278.304): C, 64.74; H, 6.52. Found: C, 64.75; H, 6.75.

**Ethyl (Dihydrofuran-2(3H)-ylidene)-(2-methoxyphenyl)acetate (7c).** Starting with **3b** (0.200 g, 0.85 mmol), 2-methoxybenzeneboronic acid (0.400 g, 2.55 mmol),  $\text{K}_3\text{PO}_4$  (1.085 g, 5.11 mmol), and  $\text{Pd}(\text{PPh}_3)_4$  (0.030 g, 0.026 mmol) in 1,4-dioxane (8 mL), **7c** was isolated after chromatography (silica gel,  $n$ -hexane/EtOAc = 50:1  $\rightarrow$  1:1) as a slightly yellowish solid (0.207 g, 93%), mp = 59  $^\circ\text{C}$ .  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  1.17 (t,  $J$  = 7.2 Hz, 3H,  $\text{CH}_3$ ), 2.12 (quint,  $J$  =

7.5 Hz, 2H, CH<sub>2</sub>), 3.27 (t,  $J$  = 7.8 Hz, 2H, CH<sub>2</sub>), 3.77 (s, 3H, OCH<sub>3</sub>), 4.13 (q,  $J$  = 7.2 Hz, 2H, OCH<sub>2</sub>CH<sub>3</sub>), 4.18 (t,  $J$  = 7.2 Hz, 2H, OCH<sub>2</sub>), 6.88–6.97 (m, 2H, 2 × CH), 7.18–7.29 (m, 2H, 2 × CH). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 150 MHz):  $\delta$  14.6, 24.3, 31.4, 55.6, 59.6, 72.1, 101.1, 110.9, 120.3, 125.0, 128.4, 132.1, 157.4, 168.7, 171.4. IR (KBr, cm<sup>-1</sup>):  $\nu$  = 29.82 (m), 2958 (m), 2940 (m), 2900 (m), 2836 (w), 1697 (s), 1627 (s), 1603 (m), 1492 (s), 1462 (m), 1437 (m), 1371 (m), 1304 (s), 1267 (s), 1241 (s), 1185 (s), 1115 (m), 1069 (s), 1028 (m), 1008 (m), 955 (w), 933 (m), 876 (w), 849 (w), 782 (w), 755 (m), 647 (w). MS (EI, 70 eV):  $m/z$  (%) = 262 (M<sup>+</sup>, 100), 217 (13), 216 (15), 189 (53), 91 (31). Anal. Calcd for C<sub>15</sub>H<sub>18</sub>O<sub>4</sub> (262.305): C, 68.69; H, 6.92. Found: C, 68.78; H, 6.81.

**Ethyl (Dihydrofuran-2(3H)-ylidene)-(2,4-dimethoxyphenyl)acetate (7d).** Starting with **3b** (0.150 g, 0.64 mmol), 2,4-dimethoxybenzeneboronic acid (0.355 g, 1.91 mmol), K<sub>3</sub>PO<sub>4</sub> (0.813 g, 3.83 mmol), and Pd(PPh<sub>3</sub>)<sub>4</sub> (0.022 g, 0.019 mmol) in 1,4-dioxane (10 mL), **7d** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 50:1 → 1:1) as a white solid (0.180 g, 96%), mp = 91 °C. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz):  $\delta$  1.17 (t,  $J$  = 7.2 Hz, 3H, CH<sub>3</sub>), 2.11 (quint,  $J$  = 7.5 Hz, 2H, CH<sub>2</sub>), 3.25 (t,  $J$  = 7.8 Hz, 2H, CH<sub>2</sub>), 3.75 (s, 3H, OCH<sub>3</sub>), 3.81 (s, 3H, OCH<sub>3</sub>), 4.12 (q,  $J$  = 7.2 Hz, 2H, OCH<sub>2</sub>CH<sub>3</sub>), 4.18 (t,  $J$  = 7.2 Hz, 2H, OCH<sub>2</sub>), 6.48–6.51 (m, 2H, 2 × CH), 7.08–7.11 (m, 1H, CH). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 150 MHz):  $\delta$  14.4, 24.1, 31.1, 55.1, 55.3, 59.4, 71.8, 98.5, 100.5, 103.9, 117.4, 132.1, 158.1, 159.9, 168.6, 171.09. IR (KBr, cm<sup>-1</sup>):  $\nu$  = 3000 (w), 2977 (w), 1690 (s), 1616 (s), 1584 (w), 1511 (m), 1464 (w), 1309 (m), 1289 (m), 1265 (m), 1209 (m), 1187 (m), 1167 (m), 1108 (w), 1069 (s), 1032 (m), 1008 (w), 947 (w), 819 (w). MS (EI, 70 eV):  $m/z$  (%) = 292 (M<sup>+</sup>, 100), 246 (20), 231 (1), 219 (16), 190 (8). Anal. Calcd for C<sub>16</sub>H<sub>20</sub>O<sub>5</sub> (292.331): C, 65.74; H, 6.90. Found: C, 65.91; H, 6.87.

**Ethyl (Dihydrofuran-2(3H)-ylidene)-(2,6-dimethoxyphenyl)acetate (7e).** Starting with **3b** (0.170 g, 0.72 mmol), 2,6-dimethoxybenzeneboronic acid (0.403 g, 2.17 mmol), K<sub>3</sub>PO<sub>4</sub> (0.921 g, 4.34 mmol), and Pd(PPh<sub>3</sub>)<sub>4</sub> (0.025 g, 0.022 mmol) in 1,4-dioxane (10 mL), **7e** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 100:1 → 1:1) as a yellowish solid (0.182 g, 87%), mp = 82 °C. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz):  $\delta$  1.15 (t,  $J$  = 7.2 Hz, 3H, CH<sub>3</sub>), 2.11 (quint,  $J$  = 7.2 Hz, 2H, CH<sub>2</sub>), 3.29 (t,  $J$  = 7.5 Hz, 2H, CH<sub>2</sub>), 3.76 (s, 6H, 2 × OCH<sub>3</sub>), 4.11 (q,  $J$  = 7.2 Hz, 2H, OCH<sub>2</sub>CH<sub>3</sub>), 4.16 (t,  $J$  = 7.2 Hz, 2H, OCH<sub>2</sub>), 6.59 (d,  $J$  = 8.4 Hz, 2H, 2 × CH), 7.22 (t,  $J$  = 8.4 Hz, 1H, CH). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 150 MHz):  $\delta$  14.7, 24.3, 31.3, 56.2, 59.5, 72.0, 96.3, 104.4, 113.8, 128.7, 158.4, 168.8, 171.8. IR (KBr, cm<sup>-1</sup>):  $\nu$  = 2976 (m), 2926 (m), 2855 (w), 1696 (s), 1630 (s), 1589 (m), 1468 (s), 1436 (m), 1378 (w), 1286 (m), 1248 (s), 1182 (s), 1112 (s), 1067 (s), 1030 (m), 931 (w), 746 (w). MS (EI, 70 eV):  $m/z$  (%) = 292 (M<sup>+</sup>, 95), 263 (6), 219 (100), 204 (4), 190 (15), 188 (4), 173 (8), 157 (3), 137 (5). Anal. Calcd for C<sub>16</sub>H<sub>20</sub>O<sub>5</sub> (292.331): C, 65.74; H, 6.90. Found: C, 65.61; H, 6.24.

**2-(Dihydrofuran-2(3H)-ylidene)-2-(2-methoxyphenyl)-1-phenyl-ethanone (7f).** Starting with **3c** (0.100 g, 0.374 mmol), 2-methoxyphenylboronic acid (0.176 g, 1.12 mmol), K<sub>3</sub>PO<sub>4</sub> (0.478 g, 2.25 mmol), and Pd(PPh<sub>3</sub>)<sub>4</sub> (0.013 g, 0.011 mmol) in 1,4-dioxane (10 mL), **7f** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 100:1 → 2:1) as a yellowish solid (0.085 g, 77%), mp = 123 °C. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz):  $\delta$  2.16 (quint,  $J$  = 7.5 Hz, 2H, CH<sub>2</sub>), 3.22 (t,  $J$  = 7.8 Hz, 2H, CH<sub>2</sub>), 3.44 (s, 3H, OCH<sub>3</sub>), 4.27 (t,  $J$  = 7.2 Hz, 2H, OCH<sub>2</sub>), 6.63 (dd,  $J$  = 5.1, 1.2 Hz, 1H, CH), 6.94 (dt,  $J$  = 7.5, 1.2 Hz, 1H, CH), 7.11–7.18 (m, 3H, 3 × CH of Ar), 7.22–7.28 (m, 1H, CH), 7.45 (dt,  $J$  = 7.5, 1.5 Hz, 3H, 3 × CH of Ar). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 50 MHz):  $\delta$  24.2, 31.4, 54.8, 71.8, 108.5, 110.7, 120.2, 126.3, 127.0 (2C), 128.1 (2C), 128.2, 130.1, 131.8, 140.6, 156.3, 171.3, 196.1. IR (KBr, cm<sup>-1</sup>):  $\nu$  = 2992 (w), 2987 (w), 2936 (w), 1654 (s), 1595 (s), 1581 (s), 1487 (m), 1458 (m), 1443 (w), 1322 (m), 1300 (w), 1260 (s), 1249 (s), 1186 (s), 1114 (m), 1051 (w), 1022 (m), 967 (s), 932 (m), 889 (m), 760 (m), 712 (w), 712 (w), 663

(w). MS (EI, 70 eV):  $m/z$  (%) = 294 (M<sup>+</sup>, 88), 263 (29), 217 (39), 189 (28), 171 (4), 157 (1), 105 (100), 91 (17), 77 (62).

**Methyl (5-Chloromethyl-dihydrofuran-2(3H)-ylidene)-(2-methoxyphenyl)acetate (7g).** Starting with **3d** (0.150 g, 0.56 mmol), 2-methoxyphenylboronic acid (0.262 g, 1.67 mmol), K<sub>3</sub>PO<sub>4</sub> (0.709 g, 3.34 mmol), and [Pd(PPh<sub>3</sub>)<sub>4</sub>] (0.019 g, 0.017 mmol) in 1,4-dioxane (5 mL), **7g** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 100:1 → 1:1) as a slightly yellowish oil (0.159 g, 96%). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz):  $\delta$  2.02–2.14 (m, 1H, CH<sub>2</sub>), 2.19–2.31 (m, 1H, CH<sub>2</sub>), 3.26–3.36 (m, 2H, CH<sub>2</sub>), 3.54 (d,  $J$  = 5.1 Hz, 2H, CH<sub>2</sub>–Cl), 3.60 (s, 3H, OCH<sub>3</sub>), 3.75 (s, 3H, OCH<sub>3</sub>), 4.58 (quint,  $J$  = 7.2 Hz, 1H, OCH), 6.87–6.96 (m, 2H, 2 × CH of Ar), 7.18–7.27 (m, 2H, 2 × CH of Ar). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz):  $\delta$  26.6, 30.7, 45.4, 51.0, 53.3, 81.6, 100.9, 110.6, 120.0, 124.2, 128.3, 131.8, 157.0, 168.7, 170.3. IR (neat, cm<sup>-1</sup>):  $\nu$  = 2950 (w), 1704 (s), 1632 (s), 1492 (m), 1460 (m), 1435 (s), 1346 (w), 1308 (m), 1265 (m), 1244 (s), 1185 (s), 1116 (m), 1072 (s), 1026 (m), 926 (w), 755 (m). MS (EI, 70 eV):  $m/z$  (%) = 298 (M<sup>+</sup> [<sup>37</sup>Cl], 33), 296 (M<sup>+</sup> [<sup>35</sup>Cl], 100), 264 (50), 237 (58), 200 (7).

**Methyl (2-Methoxyphenyl)-[3-(2-methoxyphenyl)-dihydrofuran-2(3H)-ylidene]acetate (7h).** Starting with **Z-4a** (0.300 g, 1.0 mmol), 2-methoxybenzeneboronic acid (0.940 g, 6.0 mmol), K<sub>3</sub>PO<sub>4</sub> (1.274 g, 6.0 mmol), and [Pd(PPh<sub>3</sub>)<sub>4</sub>] (0.058 g, 0.05 mmol) in 1,4-dioxane (5 mL), **7h** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 100:1 → 2:1) as a white solid (0.325 g, 92%), mp = 112 °C. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz):  $\delta$  1.58–2.05 (m, 1H, CH<sub>2</sub>), 2.41–2.56 (m, 1H, CH), 3.43 (s, 3H, OCH<sub>3</sub>), 3.82 (s, 3H, OCH<sub>3</sub>), 3.91 (s, 3H, OCH<sub>3</sub>), 4.04–4.18 (m, 1H, OCH<sub>2</sub>), 4.24 (dt,  $J$  = 8.4, 1.8 Hz, 1H, OCH<sub>2</sub>), 5.34 (dd,  $J$  = 8.7, 1.5 Hz, 1H, CH), 6.86–7.05 (m, 4H, 4 × CH), 7.19–7.32 (m, 2H, 2 × CH), 7.37–7.45 (m, 1H, CH), 7.81–7.85 (m, 1H, CH). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz):  $\delta$  32.7, 42.7, 50.9, 55.4, 55.6, 70.0, 101.9, 110.4, 111.0, 120.1, 120.2, 125.0, 127.0, 127.6, 128.4, 130.0, 131.8, 156.5, 157.3, 167.7, 172.7. IR (KBr, cm<sup>-1</sup>):  $\nu$  = 2946 (w), 1705 (m), 1631 (m), 1600 (s), 1577 (m), 1489 (s), 1461 (s), 1436 (s), 1402 (m), 1368 (s), 1344 (s), 1296 (m), 1270 (m), 1234 (s), 1197 (w), 1166 (m), 1109 (m), 1076 (s), 1054 (s), 1024 (s), 982 (w), 779 (m), 758 (s), 704 (w), 656 (m), 528 (w). MS (EI, 70 eV):  $m/z$  (%) = 354 (M<sup>+</sup>, 100), 322 (39), 295 (25), 247 (32). The exact molecular mass  $m/z$  = 354.1467 ± 2 ppm [M<sup>+</sup>] for C<sub>21</sub>H<sub>22</sub>O<sub>5</sub> was confirmed by HRMS (EI, 70 eV).

**General Procedure for the Synthesis of Benzofurans by Reaction of 2-Alkylidenetetrahydrofurans with Borontribromide.** To a CH<sub>2</sub>Cl<sub>2</sub>-solution (10 mL/mmol) of the 2-alkylidenetetrahydrofuran **7** (1 equiv) was added BBr<sub>3</sub> (4 equiv) at 0 °C. The reaction mixture was allowed to warm to 20 °C over 12 h and was stirred for 6 h at 20 °C. Water (15 mL/mmol substrate) was slowly added to the reaction mixture, and the organic layer was separated. The aqueous layer was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 × 30 mL/mmol substrate). The combined organic extracts were dried (Na<sub>2</sub>SO<sub>4</sub>), filtered, and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, *n*-hexane/EtOAc) to give **8**.

**Methyl 2-(3'-Bromopropyl)benzofuran-3-carboxylate (8a).** Starting with **7a** (0.150 g, 0.60 mmol) and BBr<sub>3</sub> (0.605 g, 2.42 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (6 mL), **8a** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 100:1 → 1:1) as a yellowish oil (0.163 g, 92%). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz):  $\delta$  2.34 (quint,  $J$  = 7.2 Hz, 2H, CH<sub>2</sub>), 3.35 (t,  $J$  = 7.5 Hz, 2H, CH<sub>2</sub>), 3.47 (t,  $J$  = 6.9 Hz, 2H, CH<sub>2</sub>–Br), 3.95 (s, 3H, OCH<sub>3</sub>), 7.28–7.33 (m, 2H, 2 × CH), 7.42–7.45 (m, 1H, CH), 7.95–7.98 (m, 1H, CH). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz):  $\delta$  26.8, 30.8, 32.4, 51.4, 109.2, 110.9, 121.9, 123.9, 124.6, 125.8, 153.6, 164.5, 165.2. IR (neat, cm<sup>-1</sup>):  $\nu$  = 2952 (m), 1714 (s), 1593 (s), 1478 (m), 1451 (s), 1437 (s), 1386 (m), 1342 (w), 1284 (m), 1235 (s), 1174 (s), 1127 (w), 1106 (m), 1073 (s), 1010 (w), 959 (w), 935 (w), 861 (w), 790 (m), 752 (s). MS (EI, 70 eV):  $m/z$  (%) = 298 (M<sup>+</sup> [<sup>81</sup>Br], 38), 296 (M<sup>+</sup> [<sup>79</sup>Br], 39), 266 (7), 217 (16), 203 (10),



188 (100), 174 (5), 170 (29), 158 (47), 144 (4). Anal. Calcd for  $C_{13}H_{13}BrO_3$  (297.148): C, 52.55; H, 4.41. Found: C, 52.84; H, 4.74.

**Methyl 2-(3'-Bromopropyl)-5-hydroxybenzofuran-3-carboxylate (8b).** Starting with **7b** (0.070 g, 0.25 mmol) and  $BBr_3$  (0.504 g, 2.0 mmol) in  $CH_2Cl_2$  (5 mL), **8b** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 100:1 → 5:1) as a white solid (0.076 g, 97%), mp = 154 °C.  $^1H$  NMR ( $CDCl_3$ , 300 MHz):  $\delta$  2.34 (quint,  $J$  = 7.05 Hz, 2H,  $CH_2$ ), 3.33 (t,  $J$  = 7.5 Hz, 2H,  $CH_2$ ), 3.47 (t,  $J$  = 6.6 Hz, 2H,  $CH_2$ -Br), 3.95 (s, 3H,  $OCH_3$ ), 5.31 (broad s, 1H, OH), 6.83 (dd,  $J$  = 8.7, 2.4 Hz, 1H, CH), 7.30 (d,  $J$  = 8.7 Hz, 1H, CH), 7.46 (d,  $J$  = 2.4 Hz, 1H, CH).  $^{13}C$  NMR ( $CDCl_3$ /DMSO- $d_6$ , 150 MHz):  $\delta$  26.4, 30.2, 32.2, 50.8, 106.3, 108.4, 110.6, 112.9, 126.1, 147.4, 153.7, 163.9, 165.0. IR (KBr,  $cm^{-1}$ ):  $\nu$  = 3326 (s), 2962 (w), 2947 (w), 1687 (s), 1624 (w), 1605 (w), 1578 (m), 1488 (m), 1468 (s), 1441 (s), 1408 (m), 1382 (m), 1306 (m), 1267 (s), 1239 (m), 1224 (m), 1197 (m), 1169 (s), 1133 (w), 1111 (w), 1077 (m), 1048 (m), 955 (w), 867 (m), 816 (m), 789 (m), 731 (w), 664 (m), 623 (w). MS (EI, 70 eV):  $m/z$  (%) = 314 ( $M^+$  [ $^{81}Br$ ], 89), 312 ( $M^+$  [ $^{79}Br$ ], 92), 281 (7), 233 (6), 219 (6), 205 (100), 175 (18), 147 (8). The exact molecular mass  $m/z$  = 311.9997  $\pm$  2 ppm [ $M^+$ ] for  $C_{13}H_{13}O_4Br$  was confirmed by HRMS (EI, 70 eV). Anal. Calcd for  $C_{13}H_{13}BrO_4$  (313.147): C, 49.86; H, 4.18. Found: C, 50.14; H, 4.88.

**Ethyl 2-(3'-Bromopropyl)benzofuran-3-carboxylate (8c).** Starting with **7c** (0.080 g, 0.30 mmol) and  $BBr_3$  (0.306 g, 1.2 mmol) in  $CH_2Cl_2$  (3 mL), **8c** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 100:1 → 50:1) as a slightly yellowish oil (0.078 g, 84%).  $^1H$  NMR ( $CDCl_3$ , 300 MHz):  $\delta$  1.46 (t,  $J$  = 7.2 Hz, 3H,  $CH_3$ ), 2.36 (quint,  $J$  = 6.6 Hz, 2H,  $CH_2$ ), 3.36 (t,  $J$  = 7.2 Hz, 2H,  $CH_2$ ), 3.48 (t,  $J$  = 6.6 Hz, 2H,  $CH_2$ -Br), 4.42 (q,  $J$  = 7.2 Hz, 2H,  $OCH_2$ ), 7.29–7.32 (m, 2H, 2  $\times$  CH), 7.44–7.47 (m, 1H, CH), 7.97–8.00 (m, 1H, CH).  $^{13}C$  NMR ( $CDCl_3$ , 150 MHz):  $\delta$  14.7, 27.2, 31.1, 32.7, 60.7, 109.6, 111.2, 122.2, 124.1, 124.8, 126.3, 153.9, 164.4, 165.3. IR (neat,  $cm^{-1}$ ):  $\nu$  = 2979 (w), 2931 (w), 1711 (s), 1593 (m), 1479 (w), 1451 (m), 1404 (w), 1380 (m), 1347 (w), 1283 (w), 1234 (s), 1176 (m), 1128 (w), 1104 (w), 1070 (s), 1012 (w), 789 (w), 751 (m). MS (EI, 70 eV):  $m/z$  (%) = 312 ( $M^+$  [ $^{81}Br$ ], 88) 310 ( $M^+$  [ $^{79}Br$ ], 95), 281 (17), 265 (14), 231 (7), 217 (3), 203 (27), 189 (4), 175 (100), 157 (36), 128 (15). HRMS (FT-ICR): calcd for  $C_{14}H_{15}BrO_3$  [ $M^+$ ]: 313.02623 ( $^{81}Br$ ); 311.02828 ( $^{79}Br$ ); found: 313.02576 ( $^{81}Br$ ), 311.02779 ( $^{79}Br$ ).

**Methyl 2-(3'-Bromopropyl)-6-hydroxybenzofuran-3-carboxylate (8d).** Starting with **7d** (0.080 g, 0.27 mmol) and  $BBr_3$  (0.549 g, 2.2 mmol) in  $CH_2Cl_2$  (3 mL), **8d** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 100:1 → 5:1) as a white solid (0.085 g, 97%), mp = 132 °C.  $^1H$  NMR ( $CDCl_3$ , 300 MHz):  $\delta$  1.44 (t,  $J$  = 7.2 Hz, 3H,  $CH_3$ ), 2.33 (quint,  $J$  = 7.05 Hz, 2H,  $CH_2$ ), 3.31 (t,  $J$  = 7.5 Hz, 2H,  $CH_2$ ), 3.47 (t,  $J$  = 6.6 Hz, 2H,  $CH_2$ -Br), 4.41 (q,  $J$  = 7.2 Hz, 2H,  $OCH_2$ ), 4.97 (broad s, 1H, OH), 6.84 (dd,  $J$  = 8.7, 2.1 Hz, 1H, CH), 6.94 (d,  $J$  = 2.1 Hz, 1H, CH), 7.80 (d,  $J$  = 8.7 Hz, 1H, CH).  $^{13}C$  NMR ( $CDCl_3$ + $d_6$ -DMSO, 150 MHz):  $\delta$  14.3, 26.7, 30.8, 32.6, 60.1, 97.8, 109.1, 113.1, 118.0, 121.7, 154.6, 155.5, 163.3, 164.2. IR (KBr,  $cm^{-1}$ ):  $\nu$  = 3304 (s), 2987 (w), 1676 (s), 1628 (m), 1594 (m), 1510 (w), 1495 (w), 1443 (s), 1406 (w), 1367 (m), 1301 (m), 1284 (m), 1262 (m), 1247 (m), 1196 (m), 1140 (m), 1113 (s), 1076 (s), 950 (w), 838 (w), 817 (w). MS (EI, 70 eV):  $m/z$  (%) = 328 ( $M^+$  [ $^{81}Br$ ], 97), 326 ( $M^+$  [ $^{79}Br$ ], 100), 297 (2%), 281 (9), 219 (75), 191 (88), 173 (19). The exact molecular mass  $m/z$  = 326.0154  $\pm$  2 ppm [ $M^+$ ] for  $C_{14}H_{15}O_4Br$  was confirmed by HRMS (EI, 70 eV). Anal. Calcd for  $C_{14}H_{15}BrO_4$  (327.174): C, 51.40; H, 4.62. Found: C, 51.30; H, 4.97.

**Ethyl 2-(3'-Bromopropyl)-4-hydroxybenzofuran-3-carboxylate (8e).** Starting with **7e** (0.070 g, 0.24 mmol) and  $BBr_3$  (0.480 g, 1.92 mmol) in  $CH_2Cl_2$  (3 mL), **8e** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 100:1 → 50:1) as a white solid (0.073 g, 92%); mp = 86 °C.  $^1H$  NMR ( $CDCl_3$ , 300 MHz):  $\delta$  1.40 (t,  $J$  = 7.2 Hz, 3H,  $CH_3$ ), 2.27 (quint,  $J$  = 7.05 Hz, 2H,  $CH_2$ ), 3.23 (t,  $J$  = 7.5 Hz, 2H,  $CH_2$ ), 3.41 (t,  $J$  =

6.6 Hz, 2H,  $CH_2$ -Br), 4.41 (q,  $J$  = 7.2 Hz, 2H,  $OCH_2$ ), 6.70 (dd,  $J$  = 8.1, 0.9 Hz, 1H, CH), 6.88 (dd,  $J$  = 8.1 Hz, 0.9 Hz, 1H, CH), 7.12 (t,  $J$  = 8.1 Hz, 1H, CH), 10.40 (s, 1H, OH).  $^{13}C$  NMR ( $CDCl_3$ , 150 MHz):  $\delta$  14.5, 27.6, 31.0, 32.7, 62.5, 102.4, 109.5, 110.3, 113.7, 126.9, 151.5, 155.3, 163.8, 167.4. IR (KBr,  $cm^{-1}$ ):  $\nu$  = 3417 (w), 3146 (w), 3126 (w), 3068 (w), 3043 (w), 2974 (w), 2933 (w), 1667 (s), 1630 (m), 1595 (m), 1481 (m), 1420 (m), 1384 (m), 1353 (w), 1328 (w), 1284 (m), 1240 (m), 1201 (m), 1155 (w), 1084 (m), 1045 (m), 1022 (w), 769 (m), 750 (m), 728 (w). MS (EI, 70 eV):  $m/z$  (%) = 328 ( $M^+$  [ $^{81}Br$ ], 61), 326 ( $M^+$  [ $^{79}Br$ ], 62), 282 (100), 219 (14), 200 (7), 186 (4), 173 (38). The exact molecular mass  $m/z$  = 326.0154  $\pm$  2 ppm [ $M^+$ ] for  $C_{14}H_{15}O_4Br$  was confirmed by HRMS (EI, 70 eV). Anal. Calcd for  $C_{14}H_{15}BrO_4$  (327.174): C, 51.40; H, 4.62. Found: C, 52.15; H, 4.73.

**3-Benzoyl-2-(3'-bromopropyl)benzofuran (8f).** Starting with **7f** (0.050 g, 0.17 mmol) and  $BBr_3$  (0.171 g, 0.68 mmol) in  $CH_2Cl_2$  (3 mL), **8f** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 100:1 → 1:1) as a slightly yellowish oil (0.036 g, 71%).  $^1H$  NMR ( $CDCl_3$ , 300 MHz):  $\delta$  2.35 (quint,  $J$  = 7.1 Hz, 2H,  $CH_2$ ), 3.10 (t,  $J$  = 7.4 Hz, 2H,  $CH_2$ ), 3.44 (t,  $J$  = 6.8 Hz, 2H,  $CH_2$ -Br), 7.16–7.40 (m, 3H, 3  $\times$  CH), 7.47–7.64 (m, 4H, 4  $\times$  CH), 7.81–7.84 (m, 2H, 2  $\times$  CH).  $^{13}C$  NMR ( $CDCl_3$ , 75 MHz):  $\delta$  27.0, 31.0, 32.4, 111.1, 117.4, 121.5, 123.7, 124.6, 126.6, 128.6 (2C), 129.2 (2C), 132.9, 139.1, 153.7, 163.5, 191.9. IR (neat,  $cm^{-1}$ ):  $\nu$  = 2968 (m), 2925 (s), 2857 (m), 1730 (m), 1652 (s), 1573 (m), 1451 (s), 1377 (m), 1281 (m), 1242 (m), 1178 (m), 1117 (s), 1075 (w), 1017 (w), 937 (w), 899 (w), 753 (m), 700 (w). MS (EI, 70 eV):  $m/z$  (%) = 344 ( $M^+$  [ $^{81}Br$ ], 29), 342 ( $M^+$  [ $^{79}Br$ ], 30), 263 (17), 249 (40), 135 (90), 221 (159), 205 (10), 178 (13), 160 (10), 148 (100), 131 (12), 105 (44), 77 (32). HRMS (ESI): calcd for  $C_{18}H_{15}BrO_2$  [ $M^+$ ]: 344.02349 ( $^{81}Br$ ), 342.02554 ( $^{79}Br$ ); found: 344.02303 ( $^{81}Br$ ), 342.02576 ( $^{79}Br$ ).

**Methyl 2-(3'-Bromo-4'-chlorobutyl)benzofuran-3-carboxylate (8g).** Starting with **7g** (0.050 g, 0.17 mmol) and  $BBr_3$  (0.171 g, 0.67 mmol) in  $CH_2Cl_2$  (3 mL), **8g** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 100:1 → 10:1) as a slightly yellowish oil (0.047 g, 80%).  $^1H$  NMR ( $CDCl_3$ , 300 MHz):  $\delta$  2.21–2.34 (m, 1H,  $CH_2$ ), 2.57–2.69 (m, 1H,  $CH_2$ ), 3.31–3.42 (m, 1H,  $CH_2$ ), 3.44–3.54 (m, 1H,  $CH_2$ ), 3.80 (dd,  $J$  = 11.4, 8.4 Hz, 1H,  $CH_2$ -Cl), 3.97 (dd,  $J$  = 11.4, 4.8 Hz, 1H,  $CH_2$ -Cl), 3.97 (s, 3H,  $OCH_3$ ), 4.14–4.22 (m, 1H, CH-Br), 7.30–7.33 (m, 2H, 2  $\times$  CH of Ar), 7.44–7.48 (m, 1H, CH of Ar), 7.96–7.99 (m, 1H, CH of Ar).  $^{13}C$  NMR ( $CDCl_3$ , 75 MHz):  $\delta$  26.0, 33.5, 48.0, 51.6, 51.9, 109.4, 111.0, 122.0, 124.0, 124.7, 125.9, 153.9, 164.6, 164.8. IR (neat,  $cm^{-1}$ ):  $\nu$  = 2952 (w), 2926 (w), 1714 (s), 1594 (m), 1446 (m), 1383 (w), 1285 (w), 1237 (s), 1176 (m), 1106 (w), 1070 (s), 794 (w), 751 (m). MS (EI, 70 eV):  $m/z$  (%) = 348 ( $M^+$  [ $^{81}Br^{37}Cl$ ], 6), 346 ( $M^+$  [ $^{81}Br^{35}Cl$ ], 34), 344 ( $M^+$  [ $^{79}Br^{35}Cl$ ], 24), 314 (2), 229 (18), 203 (24), 189 (100), 169 (13), 159 (22), 131 (12), 114 (8). HRMS (ESI): calcd for  $C_{14}H_{14}BrClO_3$  [ $M^+$ ]: 345.97944 ( $^{81}Br$ ), 343.98148 ( $^{79}Br$ ); found: 345.96002 ( $^{81}Br$ ), 343.98353 ( $^{79}Br$ ).

**Methyl 2-[3'-Bromo-1'-(2''-hydroxyphenyl)propyl]benzofuran-3-carboxylate (8h).** Starting with **7h** (0.030 g, 0.085 mmol) and  $BBr_3$  (0.129 g, 0.51 mmol) in  $CH_2Cl_2$  (9 mL), **8h** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 100:1 → 4:1) as a colorless oil (0.019 g, 58%).  $^1H$  NMR ( $CDCl_3$ , 300 MHz):  $\delta$  2.68–2.81 (m, 1H,  $CH_2$ ), 2.84–2.95 (m, 1H,  $CH_2$ ), 3.25–3.41 (m, 2H,  $CH_2$ -Br), 4.06 (s, 3H,  $OCH_3$ ), 5.53 (t,  $J$  = 7.6 Hz, 1H, CH), 6.91–6.97 (m, 2H, 2  $\times$  CH), 7.13–7.19 (m, 1H, CH), 7.29–7.35 (m, 2H, 2  $\times$  CH), 7.45–7.50 (m, 2H, 2  $\times$  CH), 7.86–7.89 (m, 1H, CH), 7.91 (s, 1H, OH).  $^{13}C$  NMR ( $CDCl_3$ , 75 MHz):  $\delta$  30.6, 35.0, 35.3, 52.5, 111.3, 117.9, 120.9, 121.1, 122.1, 124.3, 124.5, 124.8, 125.2, 127.7, 128.8, 153.9, 154.5, 165.5, 167.1. IR (neat,  $cm^{-1}$ ):  $\nu$  = 3354 (br), 2974 (m), 2956 (m), 2928 (m), 2858 (w), 1738 (w), 1712 (s), 1688 (s), 1588 (m), 1482 (m), 1454 (s), 1368 (m), 1288 (m), 1239 (s), 1174 (s), 1154 (m), 1108 (s), 1069 (s), 1020 (m), 984 (w), 793 (w), 754 (s). MS (EI, 70 eV):  $m/z$  (%) = 390 ( $M^+$  [ $^{81}Br$ ], 18), 388 ( $M^+$  [ $^{79}Br$ ], 19), 356 (17), 329 (5), 281 (44), 263 (11), 249 (100), 221 (65), 205 (5), 134 (25), 107 (13). The exact molecular mass

$m/z = 388.0310 \pm 2$  ppm [ $M^+$ ] for  $C_{19}H_{17}BrO_4$  was confirmed by HRMS (EI, 70 eV).

**General Procedure for the Synthesis of 9 by Reaction of 2-Alkylidenetetrahydrofurans with Borontribromide.** To a  $CH_2Cl_2$ -solution (10 mL/mmol) of the 2-alkylidenetetrahydrofuran (**7**) (1 equiv) was added  $BBr_3$  (4 equiv) at 0 °C. The reaction mixture was allowed to warm to 20 °C over 12 h and was stirred for 12 h at 20 °C. The reaction mixture was then poured into an aqueous solution of  $KOtBu$  (1 M, 10 mL/mmol). The mixture was stirred for 1 h and later extracted with  $CH_2Cl_2$  ( $3 \times 30$  mL/mmol). The combined organic extracts were dried ( $Na_2SO_4$ ), filtered, and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel,  $n$ -hexane/EtOAc) to give **9**.

**3-(Dihydro-furan-2(3H)-ylidene)-3H-benzofuran-2-one (9a).** Starting with **7a** (0.070 g, 0.282 mmol) and  $BBr_3$  (0.283 g, 1.13 mmol) in  $CH_2Cl_2$  (3 mL), **E-9a** and **Z-9a** were isolated after chromatography (silica gel,  $n$ -hexane/EtOAc = 50:1  $\rightarrow$  1:1) as yellowish solids (0.031 g, 54%; 0.020 g, 35%).

**E-9a.** mp = 170 °C.  $^1H$  NMR ( $CDCl_3$ , 300 MHz):  $\delta$  2.28 (quint,  $J = 7.5$  Hz, 2H,  $CH_2$ ), 3.37 (t,  $J = 7.8$  Hz, 2H,  $CH_2$ ), 4.62 (t,  $J = 7.2$  Hz, 2H,  $OCH_2$ ), 7.06–7.21 (m, 3H,  $3 \times CH$  of Ar), 7.60 (dd,  $J = 7.2$ , 1.2 Hz, 1H, CH of Ar).  $^{13}C$  NMR ( $CDCl_3$ , 75 MHz):  $\delta$  23.5, 31.4, 75.0, 95.9, 110.0, 122.0, 123.5, 124.1, 126.7, 151.0, 169.8, 175.2. IR (KBr,  $cm^{-1}$ ):  $\nu = 2911$  (w), 1750 (s), 1652 (s), 1611 (w), 1589 (w), 1479 (w), 1459 (m), 1420 (w), 1392 (m), 1247 (s), 1220 (m), 1166 (m), 1032 (m), 977 (s), 939 (m), 866 (m), 780 (m), 751 (m). MS (EI, 70 eV):  $m/z$  (%) = 202 ( $M^+$ , 100), 159 (10). The exact molecular mass  $m/z = 202.0630 \pm 2$  ppm [ $M^+$ ] for  $C_{12}H_{10}O_3$  was confirmed by HRMS (EI, 70 eV).

**Z-9a.** mp = 106 °C.  $^1H$  NMR ( $CDCl_3$ , 300 MHz):  $\delta$  2.34 (quint,  $J = 7.5$  Hz, 2H,  $CH_2$ ), 3.19 (t,  $J = 7.8$  Hz, 2H,  $CH_2$ ), 4.68 (t,  $J = 7.2$  Hz, 2H,  $OCH_2$ ), 7.06–7.25 (m, 4H,  $4 \times CH$  of Ar).  $^{13}C$  NMR ( $CDCl_3$ , 75 MHz):  $\delta$  23.1, 32.4, 75.3, 95.9, 110.6, 119.6, 123.4, 124.7, 126.5, 151.3, 165.9, 172.9. IR (KBr,  $cm^{-1}$ ):  $\nu = 2958$  (w), 2928 (w), 2855 (w), 1814 (w), 1760 (s), 1638 (s), 1457 (s), 1422 (w), 1392 (w), 1349 (w), 1308 (w), 1288 (w), 1245 (s), 1221 (m), 1192 (m), 1158 (w), 1133 (s), 1084 (s), 1028 (s), 997 (m), 976 (w), 924 (s), 868 (w), 776 (m), 750 (s). MS (EI, 70 eV):  $m/z$  (%) = 202 ( $M^+$ , 87), 159 (100). The exact molecular mass  $m/z = 202.0630 \pm 2$  ppm [ $M^+$ ] for  $C_{12}H_{10}O_3$  was confirmed by HRMS (EI, 70 eV).

**3-(5-Chloromethyl-dihydro-furan-2(3H)-ylidene)-3H-benzofuran-2-one (9b).** Starting with **7g** (0.050 g, 0.17 mmol)

and  $BBr_3$  (0.171 g, 0.67 mmol) in  $CH_2Cl_2$  (3 mL), **E-9b** and **Z-9b** were isolated after chromatography (silica gel,  $n$ -hexane/EtOAc = 100:1  $\rightarrow$  1:1) as yellowish solids (0.028 g, 65%; 0.013 g, 30%).

**E-9b.** mp = 61 °C.  $^1H$  NMR ( $CDCl_3$ , 300 MHz):  $\delta$  2.12–2.23 (m, 1H,  $CH_2$ ), 2.39–2.52 (m, 1H,  $CH_2$ ), 3.25–3.38 (m, 1H,  $CH_2$ ), 3.52–3.60 (m, 1H,  $CH_2$ ), 3.80 (d,  $J = 5.1$  Hz, 1H,  $CH_2-Cl$ ), 3.84 (d,  $J = 5.1$  Hz, 1H,  $CH_2-Cl$ ), 5.02–5.08 (m, 1H,  $OCH$ ), 7.07–7.21 (m, 3H,  $3 \times CH$  of Ar), 7.61 (dd,  $J = 7.5$ , 1.2 Hz, 1H, CH of Ar).  $^{13}C$  NMR ( $CDCl_3$ , 75 MHz):  $\delta$  26.1, 31.0, 45.3, 85.2, 96.3, 109.8, 122.0, 123.4, 126.8, 126.8, 150.8, 169.4, 173.3. IR (KBr,  $cm^{-1}$ ):  $\nu = 2976$  (s), 2932 (w), 2866 (m), 1758 (s), 1746 (s), 1655 (s), 1612 (w), 1455 (s), 1378 (m), 1360 (m), 1296 (w), 1242 (s), 1206 (s), 1151 (s), 1118 (s), 1076 (m), 1015 (s), 964 (s), 933 (w), 874 (w), 832 (w), 752 (s). MS (EI, 70 eV):  $m/z$  (%) = 252 ( $M^+$  [ $^{37}Cl$ ], 20), 250 ( $M^+$  [ $^{35}Cl$ ], 73), 215 (20), 187 (8), 160 (100), 104 (25), 85 (76), 76 (26). HRMS (ESI): calcd for  $C_{13}H_{11}ClO_3$  [ $M^+$ ]: 252.03672 ( $^{37}Cl$ ), 250.03967 ( $^{35}Cl$ ); found: 252.03800 ( $^{37}Cl$ ), 250.03903 ( $^{35}Cl$ ).

**Z-9b.**  $^1H$  NMR ( $CDCl_3$ , 300 MHz):  $\delta$  2.34–2.39 (m, 1H,  $CH_2$ ), 2.45–2.58 (m, 1H,  $CH_2$ ), 3.14–3.39 (m, 2H,  $CH_2$ ), 3.86 (d,  $J = 0.9$  Hz, 1H,  $CH_2-Cl$ ), 3.87 (d,  $J = 1.8$  Hz, 1H,  $CH_2-Cl$ ), 5.13–5.19 (m, 1H,  $OCH$ ), 7.08–7.23 (m, 4H,  $4 \times CH$  of Ar).  $^{13}C$  NMR ( $CDCl_3$ , 75 MHz):  $\delta$  25.5, 31.0, 45.6, 85.1, 95.9, 110.5, 119.6, 123.3, 124.2, 126.6, 151.2, 167.3, 171.6. IR (KBr,  $cm^{-1}$ ):  $\nu = 2927$  (w), 1756 (s), 1644 (s), 1459 (w), 1243 (m), 1140 (m), 1086 (m), 1014 (m), 938 (w), 777 (w), 747 (m). MS (EI, 70 eV):  $m/z$  (%) = 252 ( $M^+$  [ $^{37}Cl$ ], 2), 250 ( $M^+$  [ $^{35}Cl$ ], 12), 215 (12), 187 (7), 160 (100), 104 (35), 85 (86), 76 (24). HRMS (ESI): calcd for  $C_{13}H_{11}ClO_3$  [ $M^+$ ]: 252.03672 ( $^{37}Cl$ ), 250.03967 ( $^{35}Cl$ ); found: 252.03800 ( $^{37}Cl$ ), 250.03903 ( $^{35}Cl$ ).

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**Supporting Information Available:** Experimental procedures, spectroscopic data, and copies of NMR spectra. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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