Synthesis of Functionalized Furans Based on a '[3+2] Cyclization/ Bromination/Elimination' Strategy

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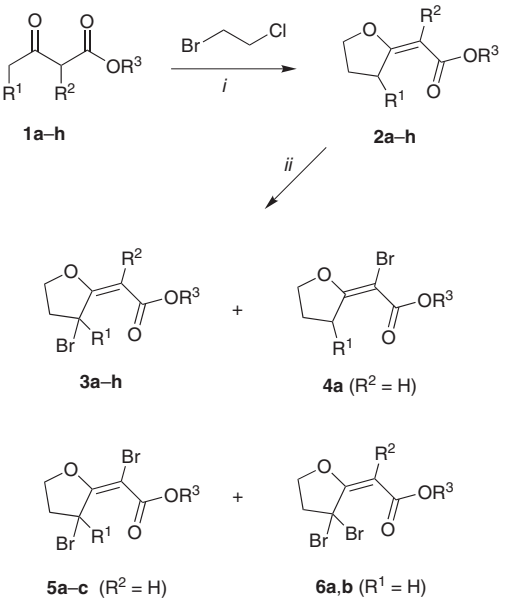
Abstract: The bromination of 2-alkylidenetetrahydrofurans – readily available via one-pot [3+2] cyclizations – afforded 2-alkylidene-3-bromotetrahydrofurans. Elimination of hydrogen bromide and subsequent aromatization of these compounds provided a convenient approach to functionalized furans.

Keywords: bromination, elimination, furans, *O*-heterocycles, tetrahydrofurans

2-Alkylidenetetrahydrofurans represent important synthetic building blocks,[1,2] which have been used for cycloadditions,[1a–d] nucleophilic additions,[1e,f] cyclopropanations,[1g] hydrogenations,[1h,2h–i] and spiroketal formation.[3] In recent years, we have reported a number of one-pot syntheses of 2-alkylidenetetrahydrofurans by [3+2] cyclizations of 1,3-dicarbonyl dianions and 1,3-bissilyl enol ethers.[4] In this context, we have also reported the functionalization of 2-alkylidenetetrahydrofurans by lithiation/alkylation,[5a,b] by BBr_3-mediated ring-openings,[5c,d] and by bromination of the exocyclic double bond and subsequent Suzuki cross-coupling reactions.[6] Herein, we wish to report a new approach to functionalized furans based on elimination reactions of 2-alkylidene-3-bromotetrahydrofurans. The synthesis and reactivity of 2-alkylidene-3-bromotetrahydrofurans has, to the best of our knowledge, not yet been studied.[7,8] Functionalized furans are of considerable pharmacological relevance and occur in a variety of natural products, such as terpenes. This includes, for instance, the calicogorgins, furan fatty acids, cyctotoxic furanocembranes, gersolanes, pseudopteranes, rosefuran, agassizin, furodysin, mikanifuran, or α-clausenan.[9] Although numerous synthetic approaches to furans have been reported,[10] the development of new and convenient strategies is of considerable interest.

The required starting materials, 2-alkylidenetetrahydrofurans **2a**–**h**, were prepared by our recently reported cyclization of 1-bromo-2-chloroethane with the dianions of 1,3-dicarbonyl compounds **1a**–**h** (Scheme 1, Table 1).[5a,11] These cyclizations proceed by attack of C-4 of the dianion onto the bromide group at low temperature and, upon heating, regioselective attack of the oxygen atom onto the chloride group.



Scheme 1 Preparation and bromination of 2-alkylidenetetrahydrofurans **2a**–**h**: *i*: 1) LDA (2.3 equiv), THF, 0 °C, 1 h, 2) $Br(CH_2)_2Cl$, –78→20 °C, 14 h, then reflux, 12 h; *ii*: NBS (see Table 1), CCl_4, reflux, 3 h

The reaction of **2a** with NBS (1.1 equivalents) resulted in the formation of a separable mixture of bromination products **3a**, **4a**, and (*E*)-**5a** (Scheme 1).[6] The use of an excess of NBS (3.0 equivalents) resulted in selective formation of the dibrominated product **5a**; the latter was isolated in high yield as a separable mixture of *E*/*Z* isomers. The employment of other bromination agents (e.g. Br_2) was unsuccessful. Besides the stoichiometry, the reaction time (three hours), temperature (reflux), and solvent (CCl_4) proved to be important parameters in the optimization of the bromination reactions. No conversion was observed when the reaction was carried out at 20 °C. Shorter reaction times resulted in incomplete conversion; in contrast, decomposition was observed with extended reaction times. The bromination of **2b**–**e**, containing an alkyl substituent at C-3, resulted in bromination of C-3 and formation of the monobromides **3b**–**e**. The best yields of **3b** and **3c** were obtained when 1.5 and 1.8 equivalents of NBS was employed. In contrast, employment of only 1.1 equiv-

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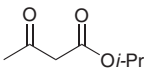
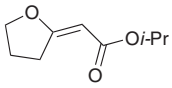
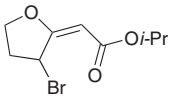
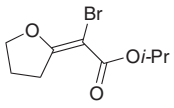
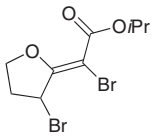
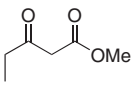
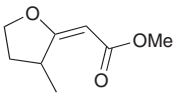
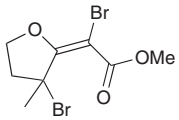
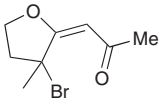
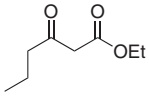
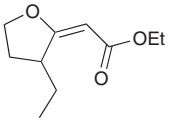
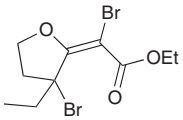
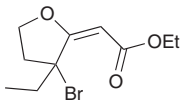
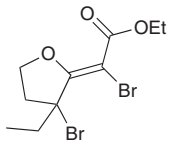
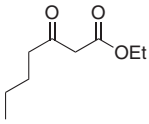
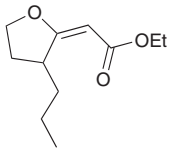
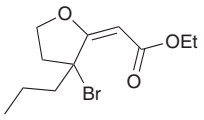
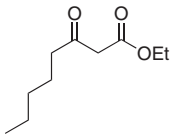
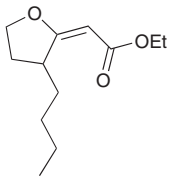
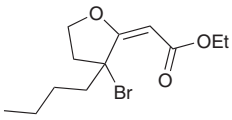
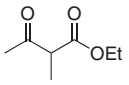
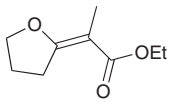
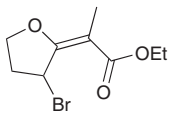
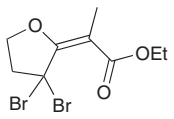
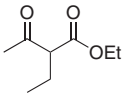
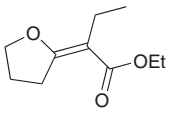
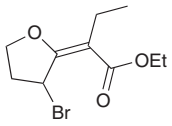
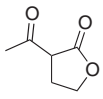
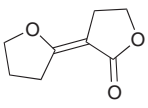
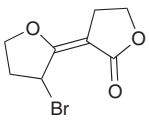
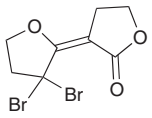
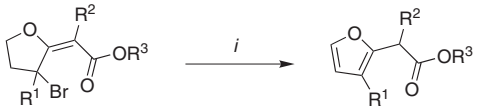
Table 1 Bromination of 2-Alkylidenetetrahydrofurans

Entry	Substrate **1**	Substrate **2**	Products **3**, **4**, **5**, and **6** (%)[a]			NBS (equiv)
1	 **1a**	 **2a**	 (*E*)-**3a** (21%)	 (*Z*)-**4a** (65%)	 (*E*)-**5a** (6%)	1.1
2	 **1b**	 **2b**	 (*Z*)-**5b** (44%)	 (*E*)-**3b** (47%)		1.5
3	 **1c**	 **2c**	 (*Z*)-**5c** (60%)	 (*E*)-**3c** (31%)	 (*E*)-**5c** (6%)	1.8
4	 **1d**	 **2d**		 **3d** (87%)		1.3
5	 **1e**	 **2e**		 **3e** (91%)		1.3
6	 **1f**	 **2f**	 **3f** (56%)	 **6a** (12%)		1.1
7	 **1g**	 **2g**		 **3g** (80%)		1.1
8	 **1h**	 **2h**	 **3h** (76%)	 **6b** (22%)		1.2

[a] Yields of isolated products.

alents of NBS again resulted in the formation of a mixture of products and, thus, a decreased yield. The yields of dibrominated products **5b** and **5c** were significantly improved by employing an excess of NBS. The bromination of 2-alkylidenetetrahydrofurans **2f** and **2g**, containing methyl and ethyl groups located on the exocyclic double bond, resulted in monobromination of C-3 (**3f** and **3g**) and in double bromination (**6a**). Bromination (NBS, 1.2 equivalents) of tetrahydro-2,3′-bifuranyliden-2′-one (**2h**)[5a,11] afforded the monobromide **3h** (76%) and the dibromide **6b** (22%).

2-Alkylidene-3-bromotetrahydrofurans proved to be excellent starting materials for the synthesis of functionalized furans (Scheme 2, Table 2). Treatment of **3a–h** with DBU (two equivalents) resulted in the elimination of hydrogen bromide and subsequent aromatization gave the known[10] furans **7a–h**. Likewise, the functionalized furans **7i–k** were prepared. Notably, the dehydrobromination of **5c** proceeded with very good regioselectivity to give the bromofuran **7i**. The reaction of DBU with 2-alkylidene-3,3-dibromotetrahydrofurans **6a** and **6b** afforded the 3-bromofurans **7j** and **7k** which represent useful synthetic building blocks for functionalization by a cross-coupling reaction. In fact, 3-bromofurans are more difficult to prepare than 2-bromofurans (vide supra).[12] All furans **7a–k** were isolated in good yields.



3a–h, **5c**, **6a**,**b** **7a–k**

Scheme 2 Synthesis of furans **7a–k**: *i*: DBU (2 equiv), THF, 20 °C, 12 h

Table 2 Synthesis of Furans from 2-Alkylidene-3-bromotetrahydrofurans

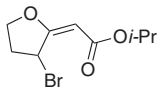
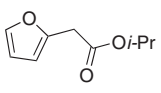
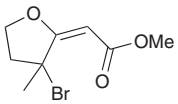
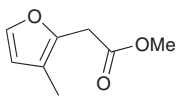
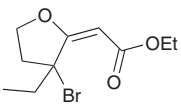
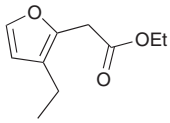
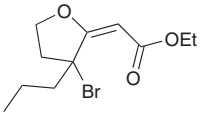
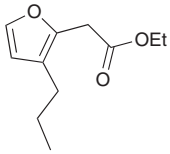
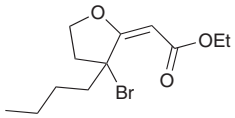
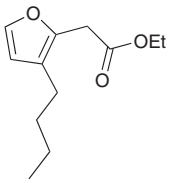
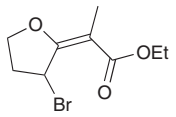
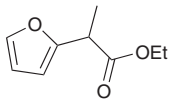
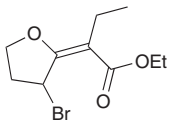
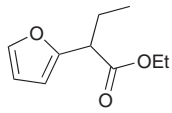
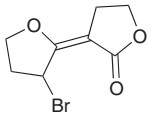
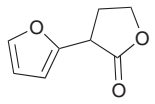
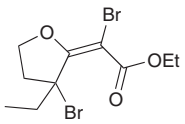
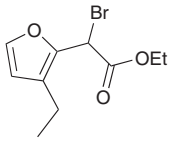
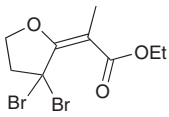
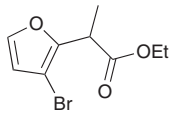
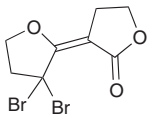
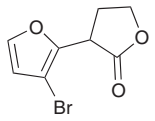
Entry	Substrate	Product **7** (%) [a]
1	 **3a**	 **7a** (72%)
2	 **3b**	 **7b** (75%)
3	 **3c**	 **7c** (64%)
4	 **3d**	 **7d** (55%)
5	 **3e**	 **7e** (53%)

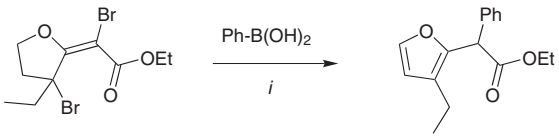
Table 2 Synthesis of Furans from 2-Alkylidene-3-bromotetrahydrofurans (continued)

Entry	Substrate	Product **7** (%) [a]
6	 **3f**	 **7f** (52%)
7	 **3g**	 **7g** (66%)
8	 **3h**	 **7h** (63%)
9	 **5c**	 **7i** (61%)
10	 **6a**	 **7j** (76%)
11	 **6b**	 **7k** (83%)

[a] Yields of isolated products.

The Suzuki reaction of dibromide (*Z*)-**5c** was next studied (Scheme 3). The reaction of phenylboronic acid (3 equivalents) with (*Z*)-**5c**, containing an ethyl group located at C-3, exclusively afforded furan **8** (60%). The formation of **8** occurs through a Suzuki reaction of the alkenyl bromide, thermal elimination of hydrogen bromide, and subsequent aromatization. Due to steric reasons, elimination is favored over a double Suzuki reaction.[6b]

In summary, we have reported the synthesis of 2-alkylidene-3-bromotetrahydrofurans by NBS bromination of



(*Z*)-**5c** **8** (60%)

Scheme 3 Elimination and Suzuki reaction of 2-alkylidene-1′,3-dibromotetrahydrofuran (*Z*)-**5c**: *i*: $PhB(OH)_2$ (3 equiv), $Pd(PPh_3)_4$ (3 mol%), K_3PO_4 (6 equiv), 1,4-dioxane, reflux, 6 h

2-alkylidenetetrahydrofurans, which are readily available by one-pot [3+2] cyclizations. Elimination reactions of 2-alkylidene-3-bromotetrahydrofurans and 2-alkylidene-1′,3-dibromotetrahydrofurans provided a convenient approach to functionalized furans.

All solvents were dried by standard methods and all reactions were carried out under an inert atmosphere. MS were obtained by EI (70 eV), CI (H_2O), or ESI. For preparative scale chromatography silica gel (60–200 mesh) was used. Mps are uncorrected.

Isopropyl (Dihydrofuran-2-ylidene)acetate (2a)[5a]
Isopropyl acetoacetate (**1a**; 7.28 mL, 50 mmol), *i*-Pr_2NH (17.5 mL, 125 mmol), *n*-BuLi (15% in *n*-hexane; 78.5 mL, 125 mmol), and 1-bromo-2-chloroethane (4.97 mL, 60 mmol) in THF (300 mL) gave (*E*)-**2a** and (*Z*)-**2a** after chromatography (*n*-hexane–EtOAc, 100:1→1:1).

(*E*)-2a
Yield: 5.42 g (64%); slightly yellowish oil.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.26 (d, *J* = 6.3 Hz, 6 H, 2 × CH_3), 2.09 (quint, *J* = 7.5 Hz, 2 H, CH_2), 3.10 (dt, *J* = 7.8 Hz, 1.9, 2 H, CH_2), 4.21 (t, *J* = 6.9 Hz, 2 H, OCH_2), 5.02 (sept, *J* = 6.3 Hz, 1 H, OCH), 5.27 (t, *J* = 1.8 Hz, 1 H, CH=C).

(*Z*)-2a
Yield: 1.09 g (13%); slightly yellowish oil.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.26 (d, *J* = 6.3 Hz, 6 H, 2 × CH_3), 2.04 (quint, *J* = 7.5 Hz, 2 H, CH_2), 2.69 (dt, *J* = 7.8 Hz, 1.2, 2 H, CH_2), 4.44 (t, *J* = 6.9 Hz, 2 H, OCH_2), 4.89 (t, *J* = 1.1 Hz, 1 H, CH=C), 5.03 (sept, *J* = 6.3 Hz, 1 H, OCH).

Ethyl [3-Propyldihydrofuran-2(3*H*)-ylidene]acetate (2d)[5a]
Substrate **1d** (3.200 g, 18.6 mmol), *i*-Pr_2NH (6.53 mL, 46.5 mmol), *n*-BuLi (15% in *n*-hexane; 29.2 mL, 46.5 mmol), and 1-bromo-2-chloroethane (1.85 mL, 22.3 mmol) in THF (100 mL), gave (*E*)-**2d** and (*Z*)-**2d** after chromatography (*n*-hexane–EtOAc, 100:1→1:1).

(*E*)-2d
Yield: 1.554 g (42%); yellowish oil.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.96 (t, *J* = 7.2 Hz, 3 H, CH_3), 1.25 (t, *J* = 7.2 Hz, 3 H, CH_3), 1.31–1.49 (m, 3 H, 2 × CH_2), 1.62–1.71 (m, 1 H, CH_2), 1.97 (dd, *J* = 12.6, 6.3 Hz, 1 H, CH_2), 2.04–2.15 (m, 1 H, CH_2), 3.60–3.65 (m, 1 H, CH), 4.09–4.20 (m, 3 H, OCH_2CH_3, OCH_2), 4.26–4.32 (m, 1 H, OCH_2), 5.23 (s, 1 H, CH=C).

(*Z*)-2d
Yield: 0.64 g (17%); yellowish oil.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.95 (t, *J* = 7.2 Hz, 3 H, CH_3), 1.26 (t, *J* = 7.2 Hz, 3 H, CH_3), 1.31–1.49 (m, 4 H, 2 × CH_2), 1.60–1.77 (m, 1 H, CH_2), 2.14–2.25 (m, 1 H, CH_2), 2.75–2.85 (m, 1 H, CH), 4.15 (q, *J* = 7.2 Hz, 2 H, OCH_2CH_3), 4.26–4.34 (m, 1 H, OCH_2), 4.45–4.52 (m, 1 H, OCH_2), 4.85 (d, *J* = 1.5 Hz, 1 H, CH=C).

MS (EI, 70 eV): *m*/*z* (%) = 198 (M^+, 5), 183 (1), 169 (20), 156 (100), 153 (61), 141 (10), 128 (6), 114 (17), 109 (14), 97 (8), 84 (35).

Ethyl (3-Butyldihydrofuran-2-ylidene)acetate (2e)[5a]
Substrate **1e** (2.200 g, 11.8 mmol), *i*-Pr_2NH (4.2 mL, 29.5 mmol), *n*-BuLi (15% in *n*-hexane; 18.5 mL, 29.5 mmol), and 1-bromo-2-chloroethane (1.2 mL, 14.2 mmol) in THF (50 mL), gave **2e** after chromatography (*n*-hexane–EtOAc, 100:1→1:1).

Yield: 1.723 (69%); yellowish oil.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.91 (t, *J* = 7.2 Hz, 3 H, CH_3), 1.26 (t, *J* = 7.2 Hz, 3 H, CH_3), 1.30–1.43 (m, 5 H, 3 × CH_2), 1.62–1.72 (m, 1 H, CH_2), 1.97 (dd, *J* = 12.6, 6.0 Hz, 1 H, CH_2), 2.04–2.14 (m, 1 H, CH_2), 3.58–3.63 (m, 1 H, CH), 4.05–4.21 (m, 3 H, OCH_2CH_3, OCH_2), 4.26–4.33 (m, 1 H, OCH_2), 5.23 (s, 1 H, CH=C).

MS (EI, 70 eV): *m*/*z* (%) = 212 (M^+, 6), 197 (9), 184 (7), 169 (32), 167 (42), 156 (37), 141 (100), 128 (15), 114 (25), 97 (42), 84 (24).

Reaction of 2-Alkylidenetetrahydrofurans or Furans with NBS; General Procedure
To a CCl_4 solution (5 mL/mmol) of 2-alkylidenetetrahydrofuran (**2** or **9**) or furan (**10**) (1 equiv) was added NBS (1.1–1.8 equiv, see Table 1) at 20 °C. The reaction mixture was heated and stirred under reflux for 3 h, allowed to cool to ambient temperature, and the solvent was removed in vacuo. The residue was purified by chromatography (*n*-hexane–EtOAc) to give the brominated 2-alkylidenetetrahydrofuran (**3**, **4**, **5**, or **6**) or furan (**11**).

2-Alkylidenetetrahydrofurans 3a, 4a, and 5a
Isopropyl [dihydrofuran-2(3*H*)-ylidene]acetic acid isopropyl ester (**2a**; 0.936 g, 5.5 mmol) and NBS (1.077 g, 6.05 mmol) in CCl_4 (20 mL) at 20 °C gave (*E*)-**3a**, (*Z*)-**4a**, and (*E*)-**5a** after chromatography (*n*-hexane–EtOAc, 100:1→1:1).

Isopropyl [3-Bromodihydrofuran-2(3*H*)-ylidene]acetate [(*E*)-3a]
Yield: 0.281 g (21%); yellowish oil.

IR (neat): 2981 (m), 2935 (w), 2912 (w), 1701 (s), 1650 (s), 1464 (w), 1438 (w), 1375 (s), 1333 (w), 1302 (m), 1276 (m), 1246 (m), 1217 (w), 1179 (m), 1153 (m), 1127 (s), 1103 (s), 1060 (m), 1036 (s), 1008 (w), 958 (w), 888 (w), 834 (w), 705 (w) cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.27 (d, *J* = 6.3 Hz, 6 H, 2 × CH_3), 2.43–2.50 (m, 2 H, CH_2), 4.38–4.50 (m, 2 H, OCH_2), 5.08 (quint, *J* = 6.3 Hz, 1 H, CH), 5.25 (s, 1 H, CH=C), 5.76–5.78 (m, CHBr).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 21.9, 22.0 (CH_3), 36.0 (CH_2), 43.0 (CHBr), 67.1 (CH), 69.6 (C-5), 91.9 (*C*H=C), 166.3 (O=CO), 172.8 (O*C*CH=).

MS (EI, 70 eV): *m*/*z* (%) = 250 (M^+ [^{81}Br], 6), 248 (M^+ [^{79}Br], 6), 208 (20), 207 (29), 206 (21), 205 (26), 191 (54), 190 (15), 189 (64), 188 (11), 187 (4), 164 (32), 162 (32), 161 (5), 159 (2), 148 (2), 146 (1), 133 (3), 131 (2), 127 (46), 110 (15), 109 (75), 108 (46), 97 (4), 83 (28), 81 (24), 70 (100).

Anal. calcd for $C_9H_{13}BrO_3$ (249.104): C, 43.40; H, 5.26. Found: C, 43.28; H, 5.48.

Isopropyl Bromo[dihydrofuran-2(3*H*)-ylidene]acetate [(*Z*)-4a]
Yield: 0.888 g (65%); yellowish oil.

IR (neat): 2982 (s), 2938 (m), 2905 (m), 1732 (m), 1699 (s), 1690 (s), 1658 (m), 1612 (s), 1525 (w), 1462 (m), 1455 (m), 1427 (m), 1374 (m), 1355 (m), 1335 (m), 1276 (s), 1232 (s), 1211 (s), 1182 (s), 1147 (m), 1109 (m), 1067 (s), 1022 (m), 990 (w), 960 (m), 924 (m), 896 (w), 875 (w), 856 (w), 824 (w), 805 (w), 781 (m), 760 (m), 719 (w) cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.30 (d, *J* = 6.3 Hz, 6 H, 2 × CH_3), 2.22 (quint, *J* = 7.5 Hz, 2 H, CH_2), 3.17 (t, *J* = 7.8 Hz, 2 H, CH_2), 4.39 (t, *J* = 7.2 Hz, 2 H, OCH_2), 5.06 (quint, *J* = 6.3 Hz, 1 H, CH).

^{13}C NMR ($CDCl_3$, 150 MHz): δ = 22.0 (CH_3), 25.0, 32.5 (CH_2), 68.9 (CH), 72.9 (C-5), 84.2 (Br*C*=C), 163.8 (O=CO), 171.6 (O*C*=C).

MS (EI, 70 eV): *m*/*z* (%) = 249 (M^+ [^{81}Br], 26), 247 (M^+ [^{79}Br], 26), 207 (84), 205 (88), 189 (90), 187 (88), 171 (7), 165 (12), 163 (14), 148 (29), 146 (29), 122 (8), 120 (8), 110 (17), 87 (18), 70 (33), 43 (100).

HRMS (EI, 70 eV): *m*/*z* calcd for $C_9H_{13}BrO_3$ [M^+]: 248.0048; found: 248.0048 ± 2 ppm.

Anal. calcd for $C_9H_{13}BrO_3$ (249.104): C, 43.40; H, 5.26. Found: C, 43.28; H, 5.48.

Isopropyl Bromo[3-bromodihydrofuran-2(3*H*)-ylidene]acetate [(*E*)-5a]

Yield: 0.219 g (12%); yellowish oil.

IR (neat): 2982 (s), 2937 (m), 2906 (m), 2883 (w), 1733 (s), 1702 (s), 1663 (m), 1615 (s), 1464 (m), 1440 (m), 1375 (s), 1315 (m), 1279 (s), 1208 (s), 1184 (s), 1159 (s), 1105 (s), 1061 (s), 1034 (s), 986 (m), 962 (w), 936 (m), 904 (m), 854 (w), 831 (w), 809 (w), 764 (w), 699 (w) cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz): δ = 1.30 (d, *J* = 6.3 Hz, 6 H, 2 × CH_3), 2.11–2.48 (m, 1 H, CH_2), 2.52–2.60 (m, 1 H, CH_2), 4.73–4.78 (m, 2 H, OCH_2), 5.07 (quint, *J* = 6.3 Hz, 1 H, CH), 5.20 (d, *J* = 5.7 Hz, 1 H, CHBr).

^{13}C NMR ($CDCl_3$, 150 MHz): δ = 21.8 (CH_3), 35.3 (CH_2), 48.8 (CHBr), 69.2 (CH), 74.0 (C-5), 88.3 (Br*C*=C), 161.7 (O=CO), 166.9 (O*C*=C).

MS (EI, 70 eV): *m*/*z* (%) = 330 (M^+ [2 × ^{81}Br], 12), 328 (M^+ [^{81}Br, ^{79}Br], 26), 326 (M^+ [2 × ^{79}Br], 13), 288 (31), 286 (62), 284 (32), 271 (16), 269 (33), 267 (17), 249 (10), 247 (9), 241 (3), 207 (100), 205 (98), 191 (17), 189 (40), 187 (23), 163 (13), 161 (28), 159 (15), 148 (12), 146 (11), 133 (13), 131 (12), 108 (4), 106 (3), 87 (17), 70 (16), 43 (70).

HRMS (EI, 70 eV): *m*/*z* calcd for $C_9H_{12}Br_2O_3$ [M^+]: 325.9153; found: 325.9153

2-Alkylidenetetrahydrofurans 3b and 5b

Methyl [3-methyldihydrofuran-2(3*H*)-ylidene]acetate (**2b**; 1.650 g, 10.6 mmol) and NBS (2.830 g, 15.9 mmol) in CCl_4 (50 mL) gave (*Z*)-**5b** and (*E*)-**3b** after chromatography (*n*-hexane–EtOAc, 100:1→1:1).

Methyl Bromo[3-bromo-3-methyldihydrofuran-2(3*H*)-ylidene]acetate [(*Z*)-5b]

Yield: 1.462 g (44%); yellowish oil.

IR (neat): 2996 (w), 2953 (m), 2907 (w), 1709 (s), 1656 (w), 1600 (s), 1437 (s), 1377 (m), 1330 (w), 1277 (s), 1214 (s), 1186 (s), 1109 (s), 1068 (s), 1010 (s), 974 (w), 920 (m), 838 (m), 768 (m), 755 (m), 710 (w), 495 (w), 405 (w) cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz): δ = 2.16 (s, 3 H, CH_3), 2.45–2.56 (m, 1 H, CH_2), 2.76–2.82 (m, 1 H, CH_2), 3.83 (s, 3 H, OCH_3), 4.45–4.50 (m, 2 H, OCH_2).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 27.6 (CH_3), 47.8 (CH_2), 52.5 (OCH_3), 58.7 (CBr), 69.0 (C-5), 86.7 (Br*C*=C), 163.2 (O=CO) 168.8 (O*C*=C).

MS (EI, 70 eV): *m*/*z* (%) = 316 (M^+ [2 × ^{81}Br], 9), 314 (M^+ [^{81}Br, ^{79}Br], 19), 312 (M^+ [2 × ^{79}Br], 10), 283 (9), 236 (15), 235 (86), 234 (17), 233 (90), 204 (26), 203 (100), 202 (27), 201 (92), 176 (3), 175 (8), 174 (3), 148 (15), 146 (16), 70 (13).

HRMS (EI, 70 eV): *m*/*z* calcd for $C_8H_{10}Br_2O_3$: 311.8997; found: 311.8997.

Methyl [3-Bromo-3-methyldihydrofuran-2(3*H*)-ylidene]acetate [(*E*)-3b]

Yield: 1.180 g (47%); brownish oil.

IR (neat): 2989 (w), 2951 (m), 2925 (w), 2907 (w), 1719 (s), 1655 (s), 1476 (w), 1437 (s), 1387 (m), 1333 (m), 1302 (s), 1278 (s), 1246 (s), 1211 (s), 1186 (s), 1161 (s), 1101 (s), 1088 (s), 1035 (s), 1014 (s), 973 (w), 930 (w), 903 (w), 808 (s), 698 (w), 495 (w) cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz): δ = 2.02 (s, 3 H, CH_3), 2.11–2.22 (m, 1 H, CH_2), 2.53–2.59 (m, 1 H, CH_2), 3.71 (s, 3 H, OCH_3), 4.55–4.60 (m, 2 H, OCH_2), 5.14 (s, 1 H, CH=C).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 28.2 (CH_3), 42.2 (CH_2), 50.4 (OCH_3), 61.6 (CBr), 70.5 (C-5), 87.2 (*C*H=CO), 165.4 (O=CO), 172.6 (O*C*=CH).

MS (EI, 70 eV): *m*/*z* (%) = 236 (M^+ [^{81}Br], 12), 234 (M^+ [^{79}Br], 12), 205 (11), 203 (14), 155 (100), 139 (1), 123 (83), 95 (12), 81 (4), 70 (43).

Anal. calcd for $C_8H_{11}BrO_3$ (235.077): C, 40.88; H, 4.72. Found: C, 41.47; H, 5.18.

2-Alkylidenetetrahydrofurans 3c and 5c

Ethyl [3-ethyldihydrofuran-2(3*H*)-ylidene]acetate (**2c**; 2.400 g, 13 mmol) and NBS (4.165 g, 23.4 mmol) in CCl_4 (60 mL) gave (*Z*)-**5c**, (*E*)-**3c**, and (*E*)-**5c** after chromatography (*n*-hexane–EtOAc, 100:1→1:1).

Ethyl Bromo[3-bromo-3-ethyldihydrofuran-2(3*H*)-ylidene]acetate [(*Z*)-5c]

Yield: 2.681 g (60%); yellowish oil.

IR (neat): 2977 (m), 2938 (w), 2905 (w), 1706 (s), 1603 (s), 1460 (m), 1385 (w), 1367 (m), 1262 (s), 1209 (s), 1182 (s), 1114 (s), 1089 (s), 1066 (s), 1025 (m), 938 (m), 862 (w), 789 (w), 754 (w) cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz): δ = 1.03 (t, *J* = 7.2 Hz, 3 H, CH_3), 1.34 (t, *J* = 7.2 Hz, 3 H, OCH_2CH_3), 2.14 (sext, *J* = 7.2 Hz, 1 H, CH_2), 2.42–2.53 (m, 1 H, CH_2), 2.62–2.69 (m, 1 H, CH_2), 2.71 (sext, *J* = 7.2 Hz, 1 H, CH_2), 4.27 (dq, *J* = 7.2, 1.5 Hz, 2 H, OCH_2CH_3), 4.43–4.48 (m, 2 H, OCH_2).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 10.0, 13.7 (CH_3), 31.5, 43.8 (CH_2), 61.4 (C-5), 65.4 (CBr), 68.8 (OCH_2), 87.1 (Br*C*=C), 162.7 (O=CO), 166.8 (O*C*=C).

MS (EI, 70 eV): *m*/*z* (%) = 344 (M^+ [2 × ^{81}Br], 7), 342 (M^+ [^{81}Br, ^{79}Br], 17), 340 (M^+ [2 × ^{79}Br], 8), 299 (4), 297 (10), 295 (4), 263 (87), 261 (86), 235 (22), 233 (23), 217 (100), 215 (97), 203 (8), 201 (8), 189 (6), 187 (4), 153 (7), 148 (12), 146 (13), 137 (5), 107 (12), 70 (20).

Anal. calcd for $C_{10}H_{14}Br_2O_3$ (342.027): C, 35.12; H, 4.13. Found: C, 35.89; H, 4.11.

Ethyl [3-Bromo-3-ethyldihydrofuran-2(3*H*)-ylidene]acetate [(*E*)-3c]

Yield: 1.072 g (31%; brownish oil.

IR (neat): 2978 (s), 2940 (m), 2907 (m), 1715 (s), 1652 (s), 1461 (m), 1444 (m), 1400 (m), 1386 (m), 1369 (m), 1326 (m), 1300 (m), 1271 (m), 1209 (s), 1181 (s), 1155 (s), 1108 (m), 1096 (m), 1079 (m), 1046 (s), 976 (w), 955 (w), 860 (w), 807 (m) cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz): δ = 1.16 (t, *J* = 7.2 Hz, 3 H, CH_3), 1.28 (t, *J* = 7.2 Hz, 3 H, OCH_2CH_3), 1.88 (sext, *J* = 7.2 Hz, 1 H, CH_2), 2.04–2.15 (m, 1 H, CH_2), 2.30 (sext, *J* = 7.2 Hz, 1 H, CH_2), 2.43 (ddd, *J* = 13.8, 4.8, 1.2 Hz, 1 H, CH_2), 4.17 (q, *J* = 7.2 Hz, 2 H, OCH_2CH_3), 4.49–4.62 (m, 2 H, OCH_2), 5.09 (s, 1 H, CH=C).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 10.4, 14.2 (CH_3), 33.7, 39.3 (CH_2), 59.5 (C-5), 68.7 (CBr), 71.0 (OCH_2), 88.3 (*C*H=CO), 165.65 (O=CO), 172.23 (O*C*=CH).

MS (EI, 70 eV): *m*/*z* (%) = 264 (M^+ [^{81}Br], 2), 262 (M^+ [^{79}Br], 2), 236 (1), 234 (1), 219 (6), 217 (7), 203 (1), 183 (100), 155 (10), 137 (20), 123 (11), 110 (5), 108 (5), 70 (24).

Anal. calcd for $C_{10}H_{15}BrO_3$ (263.131): C, 45.65; H, 5.75. Found: C, 45.97; H, 5.81.

Ethyl Bromo[3-bromo-3-ethyldihydrofuran-2(3*H*)-ylidene]acetate [(*E*)-5c]
Yield: 0.265 g (6%); brownish oil.

IR (neat): 2977 (m), 2938 (w), 2904 (w), 1707 (s), 1594 (s), 1461 (m), 1370 (m), 1321 (w), 1275 (s), 1255 (s), 1233 (m), 1201 (s), 1176 (s), 1112 (s), 1089 (m), 1047 (s), 1006 (m), 972 (w), 946 (w), 846 (w), 761 (w), 710 (w) cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz): δ = 1.05 (t, *J* = 7.2 Hz, 3 H, CH_3), 1.33 (t, *J* = 7.2 Hz, 3 H, OCH_2CH_3), 2.44–2.54 (m, 3 H, 2 × CH_2), 2.74 (sext, *J* = 7.2 Hz, 1 H, CH_2), 4.25 (q, *J* = 7.2 Hz, 2 H, OCH_2CH_3), 4.37–4.45 (m, 1 H, OCH_2), 4.53 (dt, *J* = 9.0, 1.5 Hz, 1 H, OCH_2).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 10.1, 14.0 (CH_3), 34.1, 41.7 (CH_2), 61.7 (C-5), 69.1 (CBr), 70.2 (OCH_2), 88.0 (BrC=C), 163.0 (O=CO), 166.3 (OC=C).

MS (EI, 70 eV): *m*/*z* (%) = 344 (M^+ [2 × ^{81}Br], 7), 342 (M^+ [^{81}Br, ^{79}Br], 17), 340 (M^+ [2 × ^{79}Br], 8), 299 (9), 297 (19), 295 (9), 263 (85), 261 (87), 235 (25), 233 (26), 217 (100), 215 (99), 203 (9), 201 (9), 189 (7), 187 (5), 153 (17), 148 (14), 146 (14), 137 (5), 108 (12), 70 (18).

Anal. calcd for $C_{10}H_{14}Br_2O_3$ (342.027): C, 35.12; H, 4.13. Found: C, 35.22; H, 4.33.

Ethyl [3-Bromo-3-propyldihydrofuran-2(3*H*)-ylidene]acetate (3d)
Ethyl [3-propyldihydrofuran-2(3*H*)-ylidene]acetate (**2d**; 0.099 g, 0.50 mmol) and NBS (0.116 g, 0.65 mmol) in CCl_4 (10 mL) gave **3d** after chromatography (*n*-hexane–EtOAc, 50:1→1:1).

Yield: 0.121 g (87%); yellowish oil.

IR (neat): 2964 (m), 2935 (w), 2875 (w), 1715 (s), 1652 (s), 1463 (w), 1442 (w), 1401 (w), 1374 (w), 1332 (w), 1301 (w), 1272 (w), 1246 (w), 1208 (s), 1182 (s), 1157 (m), 1115 (m), 1100 (w), 1077 (w), 1050 (s), 1029 (m) cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz): δ = 1.03 (t, *J* = 7.2 Hz, 3 H, CH_3),1.28 (t, *J* = 6.9 Hz, 3 H, OCH_2CH_3), 1.35–1.50 (m, 1 H, CH_2), 1.71–1.85 (m, 2 H, CH_2), 2.05–2.23 (m, 2 H, CH_2), 2.43 (dd, *J* = 13.8, 4.5 Hz, 1 H, CH_2), 4.17 (q, *J* = 7.2 Hz, 2 H, OCH_2CH_3), 4.51–4.59 (m, 2 H, OCH_2), 5.10 (s, 1 H, CH=C).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.9, 14.3 (CH_3), 19.5, 39.9, 42.8 (CH_2), 59.7 (CBr), 71.1 (OCH_2), 88.4 (CH=CO), 165.8 (O=CO), 172.4 (OC=CH).

MS (EI, 70 eV): *m*/*z* (%) = 278 (M^+ [^{81}Br], 4), 276 (M^+ [^{79}Br], 3), 236 (40), 234 (42), 233 (24), 231 (24), 197 (92), 183 (5), 169 (34), 150 (78), 123 (100), 114 (18), 108 (14), 95 (26), 70 (74).

HRMS (EI, 70 eV): *m*/*z* calcd for $C_{11}H_{17}BrO_3$ [M^+]: 276.0361; found: 276.0361 ± 2 ppm.

Ethyl [3-Bromo-3-butyldihydrofuran-2(3*H*)-ylidene]acetate (3e)
Ethyl [3-butyldihydrofuran-2(3*H*)-ylidene]acetate (**2e**; 0.127 g, 0.6 mmol) and NBS (0.139 g, 0.78 mmol) in CCl_4 (15 mL) gave **3e** after chromatography (*n*-hexane–EtOAc, 50:1→1:1).

Yield: 0.160 g (91%); yellowish oil.

IR (neat): 2958 (s), 2932 (s), 2869 (m), 1717 (s), 1652 (s), 1463 (m), 1437 (m), 1388 (m), 1329 (m), 1298 (m), 1272 (m), 1206 (s), 1181 (s), 1156 (s), 1116 (m), 1102 (m), 1951 (s), 1021 (m), 964 (w), 807 (m) cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz): δ = 0.96 (t, *J* = 6.9 Hz, 3 H, CH_3), 1.28 (t, *J* = 7.2 Hz, 3 H, OCH_2CH_3), 1.32–1.46 (m, 3 H, 2 × CH_2), 1.60–1.74 (m, 1 H, CH_2), 1.77–1.87 (m, 1 H, CH_2), 2.05–2.16 (m, 1 H, CH_2), 2.20–2.30 (m, 1 H, CH_2), 2.44 (dd, *J* = 14.1, 4.8 Hz, 1 H, CH_2), 4.17 (q, *J* = 7.2 Hz, 2 H, OCH_2CH_3), 4.49–4.61 (m, 2 H, OCH_2), 5.10 (s, 1 H, CH=C).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.8 (CH_3), 22.5, 28.2, 39.9, 40.4 (CH_2), 59.7 (C-5), 67.9 (CBr), 71.2 (OCH_2), 88.1 (CH=CO), 16.2 (O=CO), 172.5 (OC=CH).

MS (EI, 70 eV): *m*/*z* (%) = 292 (M^+ [^{81}Br], 4), 290 (M^+ [^{79}Br], 4), 278 (5), 276 (5), 247 (24), 245 (23), 236 (12), 234 (12), 222 (15), 220 (16), 211 (22), 197 (35), 183 (10), 181 (9), 179 (9), 169 (83), 167 (17), 165 (47), 155 (100), 137 (31), 127 (11), 123 (71), 121 (6), 119 (11), 112 (28), 110 (12), 108 (17), 98 (24), 81 (22), 70 (64).

2-Alkylidenetetrahydrofurans 3f and 6a
Ethyl 2-[dihydrofuran-2(3*H*)-ylidene]propionate (**2f**; 0.100 g, 0.59 mmol) and NBS (0.115 g, 0.65 mmol) in CCl_4 (5 mL) gave **3f** and **6a** after chromatography (*n*-hexane–EtOAc, 100:1→5:1).

Ethyl 2-[3-Bromodihydrofuran-2(3*H*)-ylidene]propionate (3f)
Yield: 0.082 g (56%); slightly yellowish oil.

IR (neat): 2984 (m), 2930 (w), 2904 (w), 1699 (s), 1644 (s), 1469 (w), 1441 (m), 1390 (w), 1369 (m), 1288 (s), 1212 (m), 1185 (m), 1170 (m), 1107 (s), 1082 (s), 1024 (m), 972 (w), 933 (w), 880 (w), 767 (w), 704 (w) cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz): δ = 1.30 (t, *J* = 7.2 Hz, 3 H, CH_3), 1.85 (s, 3 H, CH_3), 2.43–2.49 (m, 2 H, CH_2), 4.22 (dq, *J* = 7.2, 2.7 Hz, 2 H, OCH_2CH_3), 4.39–4.54 (m, 2 H, OCH_2), 5.81 (m, 1 H, CHBr).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 11.6, 14.3 (CH_3), 36.7 (CH_2), 45.1 (CHBr), 60.1 (OCH_2), 69.1 (C-5), 100.4 (C=CO), 167.1 (O=CO), 167.6 (OC=C).

MS (EI, 70 eV): *m*/*z* (%) = 250 (M^+ [^{81}Br], 29), 248 (M^+ [^{79}Br], 34), 205 (14), 203 (16), 169 (83), 141 (100), 123 (54), 99 (3), 97 (3), 95 (32), 83 (49), 68 (33).

HRMS (ESI): *m*/*z* calcd for $C_9H_{13}BrO_3$ [M^+]: 250.00276 (^{81}Br), 248.00481 (^{79}Br); found: 250.00210 (^{81}Br), 248.00485 (^{79}Br).

Anal. calcd for $C_9H_{13}BrO_3$ (249.104): C, 43.40; H, 5.26. Found: C, 42.74; H, 4.87.

Ethyl 2-[3,3-Dibromodihydrofuran-2(3*H*)-ylidene]propionate (6a)
Yield: 0.023 g (12%); slightly yellowish oil.

IR (neat): 2981 (w), 2931 (w), 2902 (w), 1713 (s), 1636 (m), 1443 (w), 1371 (w), 1318 (w), 1290 (m), 1279 (m), 1204 (m), 1174 (m), 1141 (s), 1103 (s), 1030 (w), 1001 (w), 738 (w) cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz): δ = 1.31 (t, *J* = 7.2 Hz, 3 H, CH_3), 2.21 (s, 3 H, CH_3), 3.27 (t, *J* = 6.3 Hz, 2 H, CH_2), 4.22 (q, *J* = 7.2 Hz, 2 H, OCH_2CH_3), 4.32 (t, *J* = 6.3 Hz, 2 H, OCH_2).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.2, 14.6 (CH_3), 50.4 (CBr_2), 51.7 (CH_2), 60.5 (OCH_2), 68.7 (C-5), 103.2 (C=CO), 162.1 (OC=C), 167.2 (O=CO).

MS (EI, 70 eV): *m*/*z* (%) = 328 (M^+ [^{81}Br, ^{79}Br], 11), 326 (M^+ [2 × ^{79}Br], 2), 285 (4), 283 (16), 281 (4), 249 (54), 247 (54), 221 (59), 219 (56), 205 (3), 204 (10), 203 (12), 202 (10), 201 (6), 177 (2), 175 (14), 173 (5), 169 (21), 167 (7), 165 (6), 141 (28), 139 (77), 129 (16), 123 (16), 108 (3), 95 (18), 83 (100), 66 (54).

HRMS (ESI): *m*/*z* calcd for $C_9H_{12}Br_2O_3$ [M^+]: 329.91127 (2 × ^{81}Br), 327.91327 (^{81}Br, ^{79}Br), 325.91532 (2 × ^{79}Br); found: 329.90904 (2 × ^{81}Br), 327.91240 (^{81}Br, ^{79}Br), 325.91549 (2 × ^{79}Br).

Ethyl 2-[3-Bromodihydrofuran-2(3*H*)-ylidene]butyrate (3g)
Ethyl 2-[dihydrofuran-2(3*H*)-ylidene]butyrate (**2g**; 1.000 g, 5.43 mmol) and NBS (1.063 g, 5.97 mmol) in CCl_4 (30 mL), gave **3g** after chromatography (*n*-hexane–EtOAc, 100:1→1:1).

Yield: 1.140 g (80%); yellow oil.

IR (neat): 2975 (s), 2936 (m), 2905 (w), 2877 (w), 1696 (s), 1639 (s), 1448 (m), 1371 (m), 1307 (s), 1253 (s), 1212 (m), 1185 (s), 1105 (s), 1055 (m), 1032 (s), 990 (w), 951 (w), 877 (w), 780 (w) cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz): δ = 0.99 (t, *J* = 7.4 Hz, 3 H, CH_3), 1.32 (t, *J* = 7.2 Hz, 3 H, CH_3), 2.29–2.38 (m, 2 H, CH_2), 2.42–2.49 (m, 2 H, CH_2), 4.18–4.27 (m, 2 H, OCH_2CH_3), 4.41–4.50 (m, 2 H, OCH_2), 5.81 (m, 1 H, CHBr).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 12.7, 13.9 (CH_3), 19.2, 36.3 (CH_2), 45.1 (CHBr), 59.6 (OCH_2), 68.8 (C-5), 106.3 (*C*=CO), 166.8 (O=CO), 166.9 (O*C*=C).

MS (EI, 70 eV): *m*/*z* (%) = 264 (M^+ [^{81}Br], 21), 262 (M^+ [^{79}Br], 23), 249 (3), 247 (3), 219 (14), 217 (15), 203 (5), 201 (4), 191 (5), 189 (5), 183 (100), 155 (57), 137 (50), 109 (21), 81 (15), 70 (50).

Anal. calcd for $C_{10}H_{15}BrO_3$ (263.131): C, 45.65; H, 5.75. Found: C, 45.05; H, 5.55.

2-Alkylidenetetrahydrofurans 3h and 6b

Tetrahydro[2,3′]bifuranyliden-2′-one (**2h**; 0.200 g, 1.30 mmol) and NBS (0.277 g, 1.56 mmol) in CCl_4 (10 mL) gave **3h** and **6b** after chromatography (*n*-hexane–EtOAc, 20:1→1:1).

3-Bromotetrahydro[2,3′]bifuranyliden-2′-one (3h)

Yield: 0.229 g (76%); slightly yellowish solid.

IR (KBr): 2910 (w), 1737 (s), 1683 (s), 1366 (m), 1254 (s), 1222 (m), 1184 (m), 1166 (m), 1080 (m), 1051 (s), 1029 (s), 993 (w), 931 (w), 670 (w) cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz): δ = 2.46–2.52 (m, 2 H, CH_2), 2.75–3.02 (m, 2 H, CH_2), 4.31–4.39 (m, 2 H, OCH_2), 4.47–4.58 (m, 2 H, OCH_2), 5.82–5.84 (m, 1 H, CHBr).

^{13}C NMR ($CDCl_3$, 150 MHz): δ = 25.0, 36.1 (CH_2), 41.8 (CHBr), 65.3 (OCH_2), 70.4 (C-5), 95.7 (*C*=CO), 166.3 (O=CO), 171.1 (O*C*=C).

MS (EI, 70 eV): *m*/*z* (%) = 234 (M^+ [^{81}Br], 92), 232 (M^+ [^{79}Br], 86), 153 (100), 125 (14), 123 (20), 107 (32), 97 (23), 95 (39), 85 (14), 81 (23), 79 (34), 70 (35), 68 (40).

HRMS (EI, 70 eV): *m*/*z* calcd for $C_8H_9BrO_3$: 231.9735; found: 231.9735 ± 2 ppm.

3,3-Dibromotetrahydro-[2,3′]bifuranyliden-2′-one (6b)

Yield: 0.089 g (22%); slightly yellowish solid.

IR (KBr): 2908 (w), 1738 (s), 1663 (s), 1224 (w), 1197 (w), 1149 (s), 1134 (m), 1070 (w), 1029 (m), 991 (w), 728 (w) cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz): δ = 3.26 (t, *J* = 6.5 Hz, 2 H, CH_2), 3.33 (t, *J* = 7.5 Hz, 2 H, CH_2), 4.40 (t, *J* = 7.5 Hz, 2 H, OCH_2), 4.49 (t, *J* = 6.5 Hz, 2 H, OCH_2).

^{13}C NMR ($CDCl_3$, 150 MHz): δ = 26.2, 50.3 (CH_2), 51.0 (CBr_2), 65.7 (OCH_2), 70.5 (C-5), 98.2 (*C*=CO), 163.0 (O=CO), 170.3 (O*C*=C).

MS (EI, 70 eV): *m*/*z* (%) = 314 (M^+ [2 × ^{81}Br], 2), 312 (M^+ [^{81}Br, ^{79}Br], 6), 310 (M^+ [2 × ^{79}Br], 3), 234 (10), 233 (29), 232 (14), 231 (33), 189 (96), 188 (56), 187 (100), 186 (29), 185 (8), 184 (8), 180 (6), 178 (7), 177 (12), 175 (20), 173 (6), 153 (14), 150 (13), 148 (9), 123 (7), 121 (5), 112 (5), 107 (12), 95 (14), 81 (10), 79 (15), 77 (10), 68 (13), 66 (16).

HRMS (EI, 70 eV): *m*/*z* calcd for $C_8H_8BrO_3$: 309.8840; found: 309.8840 ± 2 ppm.

Synthesis of Furans; General Procedure

To a THF solution (10 mL/mmol) of starting material **3**, **5**, or **6** (1 equiv) was added DBU (2 equiv) and the solution was stirred for 12 h at 20 °C. The solvent was removed in vacuo and the residue was purified by chromatography (*n*-hexane–EtOAc) to give furan **7**. Visualization of the spots on TLC plates was not possible by UV; they were visualized with a dye (MeOH–AcOH–anisaldehyde, 85:14:1).

Isopropyl (Furan-2-yl)acetate (7a)[7b]

Substrate **3a** (0.080 g, 0.32 mmol) and DBU (0.10 mL, 0.64 mmol) in THF (3 mL) gave **7a** after chromatography (*n*-hexane–EtOAc, 100:1→10:1) as a colorless oil (0.036 g, 67%).

Methyl (3-Methylfuran-2-yl)acetate (7b)[7b]

Substrate **3b** (0.100 g, 0.425 mmol) and DBU (0.13 mL, 0.85 mmol) in THF (3 mL) gave **7b** after chromatography (*n*-hexane–EtOAc, 100:1→50:1) as a colorless oil (0.049 g, 75%).

Ethyl (3-Ethylfuran-2-yl)acetate (7c)[7b]

Substrate **3c** (0.080 g, 0.304 mmol) and DBU (0.09 mL, 0.61 mmol) in THF (3 mL) gave **7c** after chromatography (*n*-hexane–EtOAc, 100:1→50:1) as a colorless oil (0.035 g, 64%).

Ethyl (3-Propylfuran-2-yl)acetate (7d)[7b]

Substrate **3d** (0.100 g, 0.36 mmol) and DBU (0.11 mL, 0.72 mmol) in THF (4 mL) gave **7d** after chromatography (*n*-hexane–EtOAc, 100:1→50:1) as a slightly yellowish oil (0.039 g, 55%).

Ethyl (3-Butylfuran-2-yl)acetate (7e)[7b]

Substrate **3e** (0.150 g, 0.52 mmol) and DBU (0.15 mL, 1.0 mmol) in THF (5 mL), gave **7e** after chromatography (*n*-hexane–EtOAc, 100:1→50:1) as a slightly yellowish oil (0.058 g, 53%).

Ethyl (2-Furan-2-yl)propionate (7f)

Substrate **3f** (0.100 g, 0.40 mmol) and DBU (0.12 mL, 0.80 mmol) in THF (5 mL) gave **7f** after chromatography (*n*-hexane–EtOAc, 100:1→10:1).

Yield: 0.035 g (52%); colorless oil.

IR (neat): 2986 (m), 2937 (w), 1738 (s), 1648 (w), 1505 (w), 1457 (m), 1376 (w), 1322 (m), 1255 (m), 1203 (s), 1169 (s), 1096 (m), 1070 (m), 1017 (m), 927 (w), 793 (w), 738 (s) cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz): δ = 1.25 (t, *J* = 7.2 Hz, 3 H, CH_3), 1.52 (d, *J* = 7.3 Hz, 3 H, CH_3), 3.81 (q, *J* = 7.3 Hz, 1 H, CH), 4.13 (q, *J* = 7.2 Hz, 2 H, OCH_2), 6.17 (dt, *J* = 3.2, 0.8 Hz, 1 H, CH), 6.32 (dd, *J* = 3.2, 1.8 Hz, 1 H, CH), 7.34 (dd, *J* = 1.8, 0.8 Hz, 1 H, CH).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.1, 15.8 (CH_3), 39.5 (CH), 61.0 (OCH_2), 105.9, 110.2. 141.7 (CH), 153.4 (C), 172.6 (O=CO).

MS (EI, 70 eV): *m*/*z* (%) = 168 (M^+, 13), 121 (2), 105 (2), 95 (100), 81 (2), 68 (13).

HRMS (ESI): *m*/*z* calcd for $C_9H_{12}O_3$ $[M + 1]^+$: 169.08647; found: 169.08574.

Ethyl (2-Furan-2-yl)butyrate (7g)

Substrate **3g** (0.090 g, 0.34 mmol) and DBU (0.10 mL, 0.48 mmol) in THF (5 mL) gave **7g** after chromatography (*n*-hexane–EtOAc, 100:1→30:1).

Yield: 0.041 g (66%); colorless oil.

IR (neat): 2972 (w), 2934 (w), 1738 (s), 1650 (w), 1503 (w), 1459 (m), 1392 (w), 1376 (w), 1337 (w), 1296 (w), 1257 (m), 1231 (w), 1197 (m), 1160 (s), 1092 (w), 1018 (m), 737 (m) cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz): δ = 0.94 (t, *J* = 7.2 Hz, 3 H, CH_3), 1.25 (t, *J* = 7.2 Hz, 3 H, CH_3), 1.87–2.08 (m, 2 H, CH_2), 3.60 (t, *J* = 7.8 Hz, 1 H, CH), 4.17 (dq, *J* = 7.2, 1.0 Hz, 2 H, OCH_2), 6.19 (dt, *J* = 3.2, 0.8 Hz, 1 H, CH), 6.32 (dd, *J* = 3.0, 1.8 Hz, 1 H, CH), 7.34 (dd, *J* = 1.8, 0.8 Hz, 1 H, CH).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 11.9, 14.2 (CH_3), 24.4 (CH_2), 47.1 (CH), 60.9 (OCH_2), 106.6, 110.3, 141.7 (CH), 152.4 (C), 172.1 (O=CO).

MS (EI, 70 eV): *m*/*z* (%) = 182 (M^+, 100), 168 (7), 153 (58), 139 (53), 125 (12), 108 (42), 91 (8), 80 (19).

Anal. calcd for $C_{10}H_{14}O_3$ (182.219): C, 65.92; H, 7.74. Found: C, 66.03; H, 7.12.

4′,5′-Dihydro-3′*H*-[2,3′]bifuranyl-2′-one (7h)[7b]
Substrate **3h** (0.100 g, 0.43 mmol) and DBU (0.13 mL, 0.86 mmol) in THF (5 mL) gave **7h** after chromatography (*n*-hexane–EtOAc, 50:1→5:1) as a slightly yellowish oil (0.041 g, 63%).

Ethyl Bromo(3-ethylfuran-2-yl)acetate (7i)
Substrate **5c** (0.080 g, 0.234 mmol) and DBU (0.07 mL, 0.468 mmol) in THF (3 mL) gave **7i** after chromatography (*n*-hexane–EtOAc, 100:1→5:1).

Yield: 0.037 g (61%); yellowish oil.

IR (neat): 2976 (m), 2936 (m), 2879 (w), 1743 (s), 1696 (m), 1656 (w), 1631 (w), 1506 (w), 1459 (m), 1419 (m), 1376 (m), 1261 (s), 1150 (s), 1072 (s), 1019 (s), 950 (w), 889 (w), 866 (w), 759 (w) cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz): δ = 1.18 (t, *J* = 7.5 Hz, 3 H, CH_3), 1.25 (t, *J* = 7.2 Hz, 3 H, CH_3), 2.48 (q, *J* = 7.5 Hz, 2 H, CH_2), 4.26 (q, *J* = 7.2 Hz, 2 H, OCH_2), 5.18 (s, 1 H, CHBr), 6.28 (d, *J* = 1.8 Hz, 1 H, CH), 7.29 (d, *J* = 1.8 Hz, 1 H, CH).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.1, 14.9 (CH_3), 17.7 (CH_2), 62.4 (CHBr), 65.1 (OCH_2), 111.6 (CH), 125.6 (C), 142.1 (CH), 145.2 (C), 171.9 (O=CO).

MS (EI, 70 eV): *m*/*z* (%) = 246 ([M – Me]$^+$, 1), 198 (10), 180 (1), 167 (1), 141 (1), 139 (1), 137 (1), 125 (100), 111 (4), 110 (10), 109 (13), 108 (10), 106 (2), 97 (2), 95 (4), 81 (5), 68 (9).

HRMS (ESI): *m*/*z* calcd for $C_{10}H_{13}BrO_3$ [M – Br]$^+$: 181.08647; found: 181.08578.

Ethyl 2-(3-Bromofuran-2-yl)propionate (7j)
Substrate **6a** (0.300 g, 0.915 mmol) and DBU (0.27 mL, 1.83 mmol) in THF (10 mL) gave **7j** after chromatography (*n*-hexane–EtOAc, 100:1→30:1).

Yield: 0.171 g (76%); slightly yellowish oil.

IR (neat): 2987 (m), 2939 (w), 1739 (s), 1700 (w), 1650 (w), 1506 (w), 1455 (m), 1378 (w), 1318 (m), 1191 (s), 1145 (m), 1098 (m), 1070 (m), 1022 (m), 973 (w), 739 (m) cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz): δ = 1.23 (t, *J* = 7.2 Hz, 3 H, CH_3), 1.51 (d, *J* = 7.2 Hz, 3 H, CH_3), 3.94 (q, *J* = 7.2 Hz, 1 H, CH), 4.17(q, *J* = 7.2 Hz, 2 H, OCH_2), 6.39 (d, *J* = 1.8 Hz, 1 H, CH), 7.32 (d, *J* = 1.8 Hz, 1 H, CH).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.0, 14.8 (CH_3), 37.6 (CH), 61.1 (OCH_2), 97.1 (C), 113.7, 141.9 (CH), 149.8 (C), 171.3 (O=CO).

MS (EI, 70 eV): *m*/*z* (%) = 248 (M^+ [^{81}Br], 12), 246 (M^+ [^{79}Br], 12), 175 (97), 173 (100), 161 (1), 157 (8), 143 (29), 121 (6), 119 (18), 116 (9), 110 (21), 101 (5), 94 (21), 83 (14), 66 (23).

3-Bromo-4′,5′-dihydro-3′*H*-[2,3′]bifuranyl-2′-one (7k)
Substrate **6b** (0.070 g, 0.224 mmol) and DBU (0.07 mL, 0.449 mmol) in THF (3 mL) gave **7k** after chromatography (*n*-hexane–EtOAc, 50:1→3:1).

Yield: 0.043 g (83%); slightly yellowish oil.

IR (neat): 2957 (w), 2922 (m), 1771 (s), 1628 (w), 1507 (w), 1454 (w), 1376 (m), 1218 (w), 1158 (m), 1143 (m), 1102 (w), 1048 (w), 1022 (m), 983 (m), 949 (w), 878 (w), 742 (w) cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz): δ = 2.59–2.65 (m, 2 H, CH_2), 4.06 (t, *J* = 9.8 Hz, 1 H, CH), 4.33–4.42 (m, 1 H, OCH_2), 4.52–4.59 (m, 1 H, OCH_2), 6.44 (d, *J* = 2.1 Hz, 1 H, CH), 7.35 (d, *J* = 2.1 Hz, 1 H, CH).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 28.0 (CH_2), 38.1 (CH), 66.9 (OCH_2), 99.4 (CBr), 114.2 (CH), 142.7 (OCH), 146.5 (C), 173.8 (O=CO).

MS (EI, 70 eV): *m*/*z* (%) = 232 (M^+ [^{81}Br], 40), 230 (M^+ [^{79}Br], 40), 188 (69), 186 (67), 174 (11), 172 (12), 161 (14), 159 (22), 157 (6), 145 (3), 143 (2), 107 (47), 79 (100), 77 (86), 66 (25).

HRMS (FT-ICR): *m*/*z* calcd for $C_8H_7BrO_3$ [M + 1]$^+$: 232.96363 (^{81}Br), 230.96568 (^{79}Br); found: 232.96319 (^{81}Br), 230.96515 (^{79}Br).

Ethyl (3-Ethylfuran-2-yl)phenylacetate (8)
To a solution of (*Z*)-**5c** (0.300 g, 0.88 mmol) in 1,4-dioxane (5 mL), K_3PO_4 (1.117 g, 5.26 mmol), phenylboronic acid (0.654 g, 5.3 mmol), and $Pd(PPh_3)_4$ (0.051 g, 0.044 mmol) were added at 20 °C under an argon atmosphere. The reaction mixture was stirred under reflux for 6 h. The reaction mixture was allowed to cool to 20 °C and Et_2O (10 mL) was added. The precipitate was filtered, washed with Et_2O, and the filtrate was concentrated in vacuo. The residue was purified by chromatography (*n*-hexane–EtOAc, 100:1→20:1) to give **8**.

Yield: 0.135 g (60%); colorless oil.

IR (neat): 2969 (m), 2932 (w), 1742 (s), 1500 (w), 1457 (m), 1369 (w), 1302 (w), 1281 (w), 1261 (m), 1230 (m), 1190 (m), 1153 (s), 1115 (w), 1093 (m), 1071 (w), 1028 (m), 730 (m), 699 (m) cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz): δ = 1.03 (t, *J* = 7.5 Hz, 3 H, CH_3), 1.17 (t, *J* = 7.2 Hz, 3 H, OCH_2CH_3), 2.31 (q, *J* = 7.5 Hz, 2 H, CH_2), 4.13 (q, *J* = 7.2 Hz, 2 H, OCH_2CH_3), 4.96 (s, 1 H, C*H*Ph), 6.19 (d, *J* = 1.8 Hz, 1 H, CH), 7.18–7.29 (m, 6 H, Ph, CH).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.1, 14.8 (CH_3), 18.0 (CH_2), 49.3 (*C*HPh), 61.4 (OCH_2), 111.3 (CH), 123.3 (Ph-C), 127.3, 128.4, 128.6 (Ph-CH), 136.6 (Ph-C), 141.5 (CH), 145.1 (C), 170.6 (O=CO).

MS (EI, 70 eV): *m*/*z* (%) = 258 (M^+, 8), 185 (100), 170 (4), 155 (2), 95 (1).

HRMS (EI, 70 eV): *m*/*z* calcd for $C_{16}H_{18}O_3$ [M^+]: 258.1256; found: 258.1256 ± 2 ppm.

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References

(1) 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.; Joergensen, 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. (g) For cyclopropanations, see: Kirmse, W.; Rode, K. *Chem. Ber.* **1987**, *120*, 847. (h) For hydrogenations, see: Ohta, T.; Miyake, T.; Seido, N.; Kumobayashi, H.; Takaya, H. *J. Org. Chem.* **1995**, *60*, 357; see also ref. 2.

(2) 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.

(3) (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.

(4) 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.

(5) (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) Bellur, E.; Langer, P. *Synlett* **2004**, 2172. (d) Bellur, E.; Langer, P. *J. Org. Chem.* **2005**, *70*, 3819.

(6) (a) Bellur, E.; Langer, P. *Synlett* **2004**, 2169. (b) Bellur, E.; Langer, P. *Eur. J. Org. Chem.* **2005**, 4815.

(7) For the synthesis of furans by a '[3+2]-cyclization/ oxidation' strategy, see: (a) Bellur, E.; Freifeld, I.; Langer, P. *Tetrahedron Lett.* **2005**, *46*, 2185. (b) For the synthesis of 4-methoxy-2-alkylidenetetrahydrofurans and subsequent elimination to give furans, see: Bellur, E.; Görls, H.; Langer, P. *Eur. J. Org. Chem.* **2005**, 2074. (c) See also: Langer, P.; Krummel, T. *Chem. Eur. J.* **2001**, *7*, 1720.

(8) For related compounds, see: (a) Mylari, B. L.; Zembrowski, W. J.; Beyer, T. A.; Aldinger, C. E.; Siegel, T. W. *J. Med. Chem.* **1992**, *35*, 2155. (b) Kaiser, C.; Spagnuolo, C. J.; Adams, T. C.; Audia, V. H.; Dupont, A. C. *J. Med. Chem.* **1992**, *35*, 4415.

(9) (a) *Römpp Lexikon Naturstoffe*; Steglich, W.; Fugmann, B.; Lang-Fugmann, S., Eds.; Thieme: Stuttgart, **1997**. (b) For furan natural products, see: Bach, T.; Krüger, L. *Eur. J. Org. Chem.* **1999**, 2045; see also ref. 1–11 therein.

(10) For reviews of furan syntheses, see: (a) Friedrichsen, W. In *Comprehensive Heterocyclic Chemistry*, Vol. 2; Katritzky, A. R.; Rees, C. W.; Scriven, E. F. V., Eds.; Elsevier: New York, **1996**, 359–363; and references cited therein. (b) König, B. In *Science of Synthesis*, Vol. 9; Thieme: Stuttgart, **2001**, 183–285. (c) Marshall, J. A.; Robinson, E. D. *J. Org. Chem.* **1990**, *55*, 3450. (d) Marshall, J. A.; Wang, X. *J. Org. Chem.* **1991**, *56*, 960. (e) Marshall, J. A.; Wang, X. *J. Org. Chem.* **1992**, *57*, 3387. (f) Marshall, J. A.; DuBay, W. J. *J. Org. Chem.* **1993**, *58*, 3602. (g) Aso, M.; Ojida, A.; Yang, G.; Cha, O.-J.; Osawa, E.; Kanematsu, K. *J. Org. Chem.* **1993**, *58*, 3960. (h) Marshall, J. A.; Bartley, G. S. *J. Org. Chem.* **1994**, *59*, 7169. (i) Marshall, J. A.; Sehon, C. A. *J. Org. Chem.* **1995**, *60*, 5966. (j) Hashmi, A. S. K.; Ruppero, T. L.; Knöfel, T.; Bats, J. W. *J. Org. Chem.* **1997**, *62*, 7295. (k) Gabriele, B.; Salerno, G.; De Pascali, F.; Costa, M.; Chiusoli, G. P. *J. Org. Chem.* **1999**, *64*, 7693. (l) Lee, C. F.; Liu, C. Y.; Song, H. C.; Luo, S. J.; Tseng, J. C.; Tso, H. H.; Luh, T. Y. *Chem. Commun.* **2002**, 2824. (m) Sperry, J. B.; Whitehead, C. R.; Ghiviriga, I.; Walczak, R. M.; Wright, D. L. *J. Org. Chem.* **2004**, *69*, 3726. (n) Katritzky, A. R.; Hür, D.; Kirichenko, K.; Yu, J.; Steel, P. J. *Arkivoc* **2004**, *(ii)*, 109. (o) Burke, M. D.; Berger, E. M.; Schreiber, S. L. *J. Am. Chem. Soc.* **2004**, *126*, 14095.

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

(12) Karpov, A. S.; Merkul, E.; Oeser, T.; Müller, T. J. J. *Chem. Commun.* **2005**, *20*, 2581.