Synthesis K. Kiyokawa et al. Special Topic

Oxidative Cyclization of β,γ-Unsaturated Carboxylic Acids Using Hypervalent Iodine Reagents: An Efficient Synthesis of 4-Substituted Furan-2-ones

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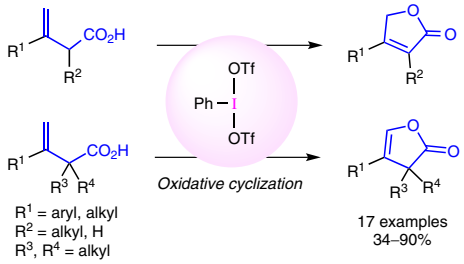
Published as part of the Special Topic *Modern Strategies with Iodine in Synthesis*

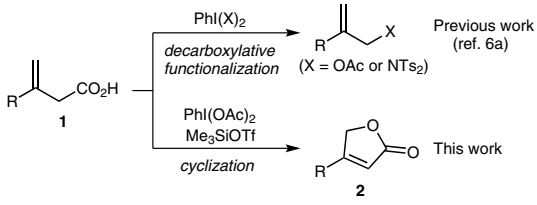


Received: 16.02.2017
Accepted after revision: 09.03.2017
Published online: 30.03.2017
DOI: 10.1055/s-0036-1588987; Art ID: ss-2017-c0096-st

Abstract The oxidative cyclization of β-substituted β,γ-unsaturated carboxylic acids using a hypervalent iodine reagent to provide 4-substituted furan-2-one products, is reported. In this cyclization, the use of a highly electrophilic $PhI(OTf)_2$, which is in situ prepared from $PhI(OAc)_2$ and Me_3SiOTf, is crucial. Depending on the substitution pattern at the α-position of the substrates, furan-2(5*H*)-ones or furan-2(3*H*)-ones are produced. Thus, the present method offers a useful tool for accessing various types of 4-substituted furan-2-ones that are important structural motifs in the field of organic chemistry and medicinal chemistry.

Key words hypervalent iodine, oxidation, cyclization, β,γ-unsaturated carboxylic acids, furanones

Furan-2(5*H*)-one derivatives are an important class of compounds that are frequently found in natural products and biologically active molecules.[1] Therefore, the development of simple and efficient methods for the synthesis of furan-2(5*H*)-one derivatives from readily available starting materials is an important research topic in the field of organic chemistry as well as medicinal chemistry.[2] An intramolecular cyclization is a fundamental transformation for the construction of furan-2(5*H*)-one scaffolds, and, indeed, several useful methods have been developed to date.[3] However, although the oxidative 5-*endo* cyclization of β,γ-unsaturated carboxylic acids is one of the most straightforward methods for preparing the furan-2(5*H*)-one motif, only a limited number of examples of the use of this approach have been reported.[4] Wirth et al. recently reported that a hypervalent iodine reagent was effective for this type of oxidative cyclization with the rearrangement of 4-arylbut-3-enoic acids, affording 4-arylfuran-2(5*H*)-ones, albeit the substrate scope was limited.[5] Meanwhile, our group reported on the decarboxylative functionalization of β-substituted β,γ-unsaturated carboxylic acids **1** via the use of hypervalent iodine reagents (Scheme 1).[6] During the course of the study, we observed that oxidative cyclization proceeded smoothly when Me_3SiOTf was added to the reaction mixture, providing 4-substituted furan-2(5*H*)-ones **2**, which are particularly important structural motifs in medicinal chemistry (Scheme 1). This preliminary result prompted us to further investigate this oxidative cyclization to expand the synthetic utility of the method. We herein report the oxidative cyclization of β-substituted β,γ-unsaturated carboxylic acids using a hypervalent iodine reagent, enabling easy access to a variety of 4-substituted furan-2-ones.

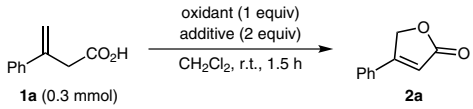


Scheme 1 Oxidative functionalization of β,γ-unsaturated carboxylic acids using hypervalent iodine reagents

Our initial experiments intended to optimize the reaction conditions for the oxidative cyclization were performed with 3-phenylbut-3-enoic acid (**1a**) as a model substrate. When the reactions were carried out using $PhI(OAc)_2$ and $PhI(OCOCF_3)_2$ as oxidants in dichloromethane at room temperature, no cyclized product was formed (Table 1, entries 1 and 2). Meanwhile, the highly electrophilic Koser's reagent, PhI(OH)(OTs), was found to provide the furan-2(5*H*)-one **2a** in a moderate yield (entry 3). Encouraged by this result, we next examined the activation of hypervalent iodine reagents with Me_3SiOTf, to generate the highly electrophilic $PhI(OTf)_2$.[7] A brief screening of hypervalent iodine reagents revealed that the use of $PhI(OAc)_2$ with two equivalents of Me_3SiOTf provided **2a** in the highest yield (88% iso-

lated yield) (entries 4–6). Decreasing the amount of Me_3SiOTf to one equivalent reduced the yield of **2a** slightly, and further decrease of the reagent resulted in an even lower yield (entries 7 and 8). In addition, the oxidative cyclization also proceeded by the use of TfOH instead of Me_3SiOTf, but yields were somewhat lower than those obtained with Me_3SiOTf (entries 9 and 10).[8] It should be noted that no cyclized products were formed when iodine oxidants that function as an iodonium source, such as bis(pyridine)iodonium tetrafluoroborate (IPy_2BF_4) and *N*-iodosuccinimide (NIS), were used (entries 11 and 12). Solvent screening indicated that a halogenated solvent was effective for the reaction (entry 13). The use of MeCN resulted in low yield, and reactions conducted in toluene and THF did not provide **2a** at all (entries 14–16).

Table 1 Optimization of Reaction Conditions[a]

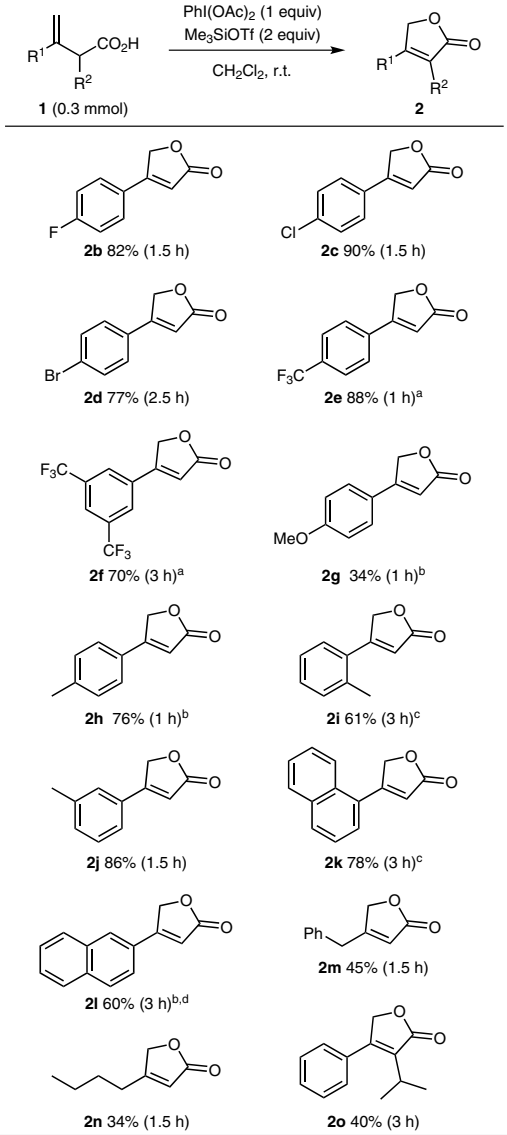


1a (0.3 mmol) **2a**

Entry	Oxidant	Additive	Solvent	Yield (%)[b]
1	$PhI(OAc)_2$	none	CH_2Cl_2	0
2	$PhI(OCOCF_3)_2$	none	CH_2Cl_2	0
3	PhI(OH)(OTs)	none	CH_2Cl_2	42
4	$PhI(OAc)_2$	Me_3SiOTf	CH_2Cl_2	92 (88)[c]
5	$PhI(OCOCF_3)_2$	Me_3SiOTf	CH_2Cl_2	62
6	PhIO	Me_3SiOTf	CH_2Cl_2	51
7[d]	$PhI(OAc)_2$	Me_3SiOTf	CH_2Cl_2	87
8[e]	$PhI(OAc)_2$	Me_3SiOTf	CH_2Cl_2	65
9	$PhI(OAc)_2$	TfOH	CH_2Cl_2	76
10[f]	$PhI(OAc)_2$	TfOH	CH_2Cl_2	72
11	IPy_2BF_4	none	CH_2Cl_2	0
12	NIS	none	CH_2Cl_2	0
13[g]	$PhI(OAc)_2$	Me_3SiOTf	$ClCH_2CH_2Cl$	88
14[g]	$PhI(OAc)_2$	Me_3SiOTf	MeCN	40
15[g]	$PhI(OAc)_2$	Me_3SiOTf	toluene	0
16[g]	$PhI(OAc)_2$	Me_3SiOTf	THF	0

[a] Standard reaction conditions: **1a** (0.3 mmol), oxidant (0.3 mmol), additive (0.6 mmol), CH_2Cl_2 (3 mL), r.t., 1.5 h.
[b] Determined by ^1H NMR analysis of the crude product using 1,1,2,2-tetrachloroethane as an internal standard.
[c] Isolated yield in parentheses.
[d] Me_3SiOTf (1 equiv) was used.
[e] Me_3SiOTf (0.5 equiv) was used.
[f] TfOH (1 equiv) was used.
[g] Reaction was run for 1 h.

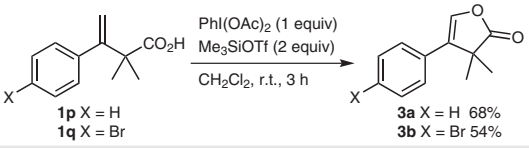
With the optimized reaction conditions identified (Table 1, entry 4), the substrate scope for the oxidative cyclization was investigated next (Scheme 2). Various types of β-substituted β,γ-unsaturated carboxylic acids were found to be applicable and were efficiently converted into the corresponding 4-substituted furan-2(5*H*)-ones. Halogen substituents, such as fluoro **2b**, chloro **2c**, and bromo **2d** groups, on the aromatic ring at the β-position were well tolerated and had only a minor effect on product yield. Because substrates bearing a highly electron-withdrawing trifluoromethyl group were less reactive, these reactions were conducted at 80 °C in 1,2-dichloroethane, furnishing furanone products **2e** and **2f** in high yields. On the other hand, under standard reaction conditions, carboxylic acids containing



Scheme 2 Scope of β,γ-unsaturated carboxylic acids. Unless otherwise noted, the following reaction conditions were employed: **1** (0.3 mmol), $PhI(OAc)_2$ (0.3 mmol), Me_3SiOTf (0.6 mmol), CH_2Cl_2 (3 mL), r.t. Reaction time is shown in parentheses. Yields are isolated yields. [a] The reaction was conducted at 80 °C in $ClCH_2CH_2Cl$. [b] 2,6-Di-*tert*-butylpyridine (DTBP) (2 equiv) was added. [c] $PhI(OAc)_2$ (1.5 equiv), Me_3SiOTf (3 equiv), and DTBP (3 equiv) were used. [d] The reaction was conducted at 60 °C in $ClCH_2CH_2Cl$.

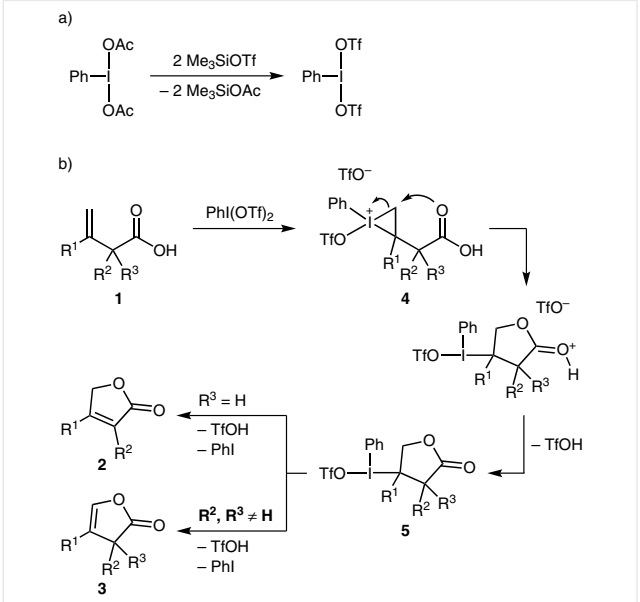
an electron-donating methoxy group on the aromatic ring gave a very low yield of **2g**, along with the formation of unidentified by-products probably because the substrate underwent decomposition in the presence of the in situ generated TfOH.[9] To avoid this type of side reaction, we examined the use of a base to trap the TfOH. After screening a number of bases, 2,6-di-*tert*-butylpyridine (DTBP) was found to increase the yield of **2g**, albeit the yield was relatively low. Employing DTBP also improved the yield of **2h** and **2i** containing *p*- and *o*-tolyl substituents, respectively. Meanwhile, *m*-tolyl group at the β-position had a negligible effect on reactivity, furnishing **2j** in high yield under the standard reaction conditions. Fused-ring systems **2k** and **2l** including 1- and 2-naphthyl groups were also well tolerated. In addition to substrates with aromatic substituents, this oxidative cyclization could also be expanded to substrates with β-aliphatic substituents, such as benzyl **2m** and *n*-butyl **2n** groups. Notably, benzylic and allylic C–H bonds were well tolerated under the oxidative reaction conditions. Furthermore, the cyclization of a carboxylic acid with an α-substituent proceeded successfully to afford the 3,4-disubstituted furan-2(5*H*)-one **2o**.

To expand the utility of this method, the use of α,α-disubstituted acids in the reaction was examined next (Scheme 3). It is noteworthy that 3-aryl-2,2-dimethylbut-3-enoic acids **1p** and **1q** underwent oxidative cyclization on treatment with $PhI(OTf)_2$ in dichloromethane at room temperature, furnishing the corresponding furan-2(3*H*)-one products, which are difficult to access by other methods.



Scheme 3 Oxidative cyclization of α,α-disubstituted substrates

A plausible reaction pathway is shown in Scheme 4. According to previous reports,[7] the highly electrophilic $PhI(OTf)_2$ is generated in situ by a ligand exchange between $PhI(OAc)_2$ and Me_3SiOTf (Scheme 4, a). In addition, the oxidative cyclization proceeded effectively with one equivalent of Me_3SiOTf (Table 1, entry 7), indicating that PhI(OAc)(OTf) and $[PhIOIPh](OTf)_2$ (the Zefirov's reagent) would also function as active iodine reagents.[10] The resulting $PhI(OTf)_2$ then participates in the activation of the alkene moiety of acid **1** via the formation of a cyclic iodonium intermediate **4**, which would subsequently undergo an intramolecular cyclization rather than decarboxylation, thus constructing a γ-lactone framework (Scheme 4, b). Finally, the elimination of iodobenzene as well as TfOH from intermediate **5** affords the furanone product. Substrates containing a proton at the α-position provide furan-2(5*H*)-ones **2**, while, in the case of α,α-disubstituted substrates, furan-2(3*H*)-ones **3** are formed.



Scheme 4 Plausible reaction pathway

In conclusion, we have developed the oxidative cyclization of β-substituted β,γ-unsaturated carboxylic acids using a highly electrophilic $PhI(OTf)_2$. The use of $PhI(OTf)_2$ was found to be crucial for achieving this oxidative cyclization to occur in preference to decarboxylation.[6] The present method provides valuable furan-2(5*H*)-one and furan-2(3*H*)-one derivatives, some of which are difficult to synthesize by other methods, thus offering a new, straightforward approach to the preparation of furanones.

New compounds were characterized by ^1H, ^{13}C, and ^{19}F NMR, IR, MS, and HRMS. ^1H, ^{13}C, and ^{19}F NMR spectra were recorded on a Jeol JMTC-400/54/SS spectrometer (^1H NMR, 400 MHz; ^{13}C NMR, 100 MHz; ^{19}F NMR, 377 MHz). ^1H NMR chemical shifts were determined relative to Me_4Si (0.0 ppm) as an internal standard. ^{13}C NMR chemical shifts were determined relative to $CDCl_3$ (77.0 ppm). ^{19}F NMR chemical shifts were determined relative to C_6F_6 (–164.9 ppm) as an external standard. IR spectra were recorded on a Shimadzu IRAffinity-1 FT-IR spectrophotometer. Mass spectra were obtained on a Shimadzu GCMS-QP2010 and a Jeol JMS-DX303HF mass spectrometer. High-resolution mass spectra were obtained on a Jeol JMS-DX303HF mass spectrometer. Melting points were determined on a Stanford Research Systems MPA100 OptiMelt Automated Melting Point System. All reactions were carried out under N_2. Products were purified by chromatography on silica gel BW-300 (Fuji Silysia Chemical Ltd.). Analytical TLC was performed on precoated silica gel glass plates (Merck silica gel 60 F_{254}). Compounds were visualized with UV lamp or treatment with an ethanolic solution of phosphomolybdic acid followed by heating. Anhyd CH_2Cl_2 was used as obtained. β,γ-Unsaturated carboxylic acids were prepared according to literature procedures.[6] All other solvents and reagents were purchased and used as obtained.

Furan-2(5*H*)-ones 2 and Furan-2(3*H*)-ones 3; General Procedure

A heat-gun-dried two-necked reaction flask containing a magnetic stir bar was charged with $PhI(OAc)_2$ (0.30 mmol), CH_2Cl_2 (3 mL), and Me_3SiOTf (0.60 mmol), and the reaction mixture was stirred for 10 min. To the mixture, carboxylic acid **1** (0.30 mmol) was added. The resulting solution was stirred at r.t. for the appropriate time. The reaction was quenched with aq 1 M $Na_2S_2O_3$ (5 mL). The mixture was extracted with CH_2Cl_2 (3 × 10 mL), and the combined organic layers were dried (Na_2SO_4). The solution was concentrated under reduced pressure to give the crude product, which was analyzed by ^1H NMR spectroscopy using 1,1,2,2-tetrachloroethane as an internal standard. Purification was performed by flash column chromatography on silica gel (hexane/EtOAc).

4-Phenylfuran-2(5*H*)-one (2a)

According to the general procedure, the reaction using $PhI(OAc)_2$ (96.9 mg, 0.30 mmol), Me_3SiOTf (109 μL, 0.60 mmol), and 3-phenylbut-3-enoic acid (48.4 mg, 0.30 mmol) in CH_2Cl_2 (3 mL) was conducted at r.t. for 1.5 h. Purification by flash column chromatography on silica gel (hexane/EtOAc) gave the product as a white solid; yield: 42.0 mg (88%). The analytical and spectral data for this compound were in excellent agreement with the reported data.[11]

4-(4-Fluorophenyl)furan-2(5*H*)-one (2b)

According to the general procedure, the reaction using $PhI(OAc)_2$ (96.9 mg, 0.30 mmol), Me_3SiOTf (109 μL, 0.60 mmol), and 3-(4-fluorophenyl)but-3-enoic acid (53.7 mg, 0.30 mmol) in CH_2Cl_2 (3 mL) was conducted at r.t. for 1.5 h. Purification by flash column chromatography on silica gel (hexane/EtOAc) gave the product as a white solid; yield: 44.4 mg (82%); mp 155.3–155.7 °C.

IR (ATR): 1732, 1510, 1159, 835 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.56–7.48 (m, 2 H), 7.22–7.10 (m, 2 H), 6.34 (t, *J* = 1.6 Hz, 1 H), 5.21 (d, *J* = 1.6 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.7, 164.6 (d, $J_{C,F}$ = 252.8 Hz), 162.6, 128.6 (d, $J_{C,F}$ = 9.0 Hz), 126.0 (d, $J_{C,F}$ = 3.3 Hz), 116.6 (d, $J_{C,F}$ = 22.3 Hz), 112.8 (d, $J_{C,F}$ = 1.6 Hz), 70.9.

^{19}F NMR (377 MHz, $CDCl_3$): δ = –109.8

MS (EI): *m*/*z* (%) = 178 (M^+, 66), 149 (100), 121 (76), 120 (100), 101 (49), 75 (22).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{10}H_7FO_2$: 178.0430; found: 178.0429.

4-(4-Chlorophenyl)furan-2(5*H*)-one (2c)

According to the general procedure, the reaction using $PhI(OAc)_2$ (96.4 mg, 0.30 mmol), Me_3SiOTf (109 μL, 0.60 mmol), and 3-(4-chlorophenyl)but-3-enoic acid (58.7 mg, 0.30 mmol) in CH_2Cl_2 (3 mL) was conducted at r.t. for 1.5 h. Purification by flash column chromatography on silica gel (hexane/EtOAc) gave the product as a yellow solid; yield: 52.5 mg (90%). The analytical and spectral data for this compound were in excellent agreement with the reported data.[3d]

4-(4-Bromophenyl)furan-2(5*H*)-one (2d)

According to the general procedure, the reaction using $PhI(OAc)_2$ (96.7 mg, 0.30 mmol), Me_3SiOTf (109 μL, 0.60 mmol), and 3-(4-bromophenyl)but-3-enoic acid (73.6 mg, 0.31 mmol) in CH_2Cl_2 (3 mL) was conducted at r.t. for 2.5 h. Purification by flash column chromatography on silica gel (hexane/EtOAc) gave the product as a yellow solid, yield: 50.9 mg (77%). The analytical and spectral data for this compound were in excellent agreement with the reported data.[11]

4-[4-(Trifluoromethyl)phenyl]furan-2(5*H*)-one (2e)

According to the general procedure, the reaction using $PhI(OAc)_2$ (96.7 mg, 0.30 mmol), Me_3SiOTf (109 μL, 0.60 mmol), and 3-[4-(trifluoromethyl)phenyl]but-3-enoic acid (68.6 mg, 0.30 mmol) in 1,2-dichloroethane (3 mL) was conducted at 80 °C for 1 h. Purification by flash column chromatography on silica gel (hexane/EtOAc) gave the product as a white solid; yield: 59.7 mg (88%); mp 168.9–169.3 °C.

IR (ATR): 1757, 1323 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.75 (d, *J* = 8.0 Hz, 2 H), 7.64 (d, *J* = 8.0 Hz, 2 H), 6.50 (t, *J* = 2.0 Hz, 1 H), 5.26 (d, *J* = 2.0 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.1, 162.1, 133.1 (q, $J_{C,F}$ = 32.9 Hz), 132.9, 126.8, 126.3 (q, $J_{C,F}$ = 3.3 Hz), 123.4 (q, $J_{C,F}$ = 270.8 Hz), 115.3, 70.8.

^{19}F NMR (377 MHz, $CDCl_3$): δ = –66.3.

MS (EI): *m*/*z* (%) = 228 (M^+, 60), 199 (79), 171 (44), 170 (47), 151 (100), 120 (32), 115 (28), 102 (45), 75 (37), 69 (56), 63 (30), 62 (24), 51 (34), 50 (30).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{11}H_7F_3O_2$: 228.0398; found: 228.0398.

4-[3,5-Bis(trifluoromethyl)phenyl]furan-2(5*H*)-one (2f)

According to the general procedure, the reaction using $PhI(OAc)_2$ (96.2 mg, 0.30 mmol), Me_3SiOTf (110 μL, 0.60 mmol), and 3-[3,5-bis(trifluoromethyl)phenyl]but-3-enoic acid (89.4 mg, 0.30 mmol) in 1,2-dichloroethane (3 mL) was conducted at 80 °C for 3 h. Purification by flash column chromatography on silica gel (hexane/EtOAc) gave the product as a white solid; yield: 62.2 mg (70%); mp 138.5–139.1 °C.

IR (ATR): 1802, 1775, 1275, 1111, 1063 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.07–7.90 (m, 3 H), 6.60 (t, *J* = 2.0 Hz, 1 H), 5.30 (d, *J* = 2.0 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.3, 160.2, 133.1 (q, $J_{C,F}$ = 33.0 Hz), 131.8, 126.3, 125.0–124.8 (m), 122.7 (q, $J_{C,F}$ = 271.8 Hz), 116.8, 70.6.

^{19}F NMR (377 MHz, $CDCl_3$): δ = –66.2.

MS (EI): *m*/*z* (%) = 296 (M^+, 22), 277 (21), 267 (100), 239 (36), 238 (29), 219 (41), 169 (24), 69 (35).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{12}H_6F_6O_2$: 296.0272; found: 296.0275.

4-(4-Methoxyphenyl)furan-2(5*H*)-one (2g)

According to the general procedure, the reaction using $PhI(OAc)_2$ (96.5 mg, 0.30 mmol), Me_3SiOTf (109 μL, 0.60 mmol), 2,6-di-*tert*-butylpyridine (113.4 mg, 0.59 mmol), and 3-(4-methoxyphenyl)but-3-enoic acid (57.4 mg, 0.30 mmol) in CH_2Cl_2 (3 mL) was conducted at r.t. for 1 h. Purification by flash column chromatography on silica gel (hexane/EtOAc) gave the product as a yellow solid; yield: 19.2 mg (34%). The analytical and spectral data for this compound were in excellent agreement with the reported data.[12]

4-(4-Tolyl)furan-2(5*H*)-one (2h)

According to the general procedure, the reaction using $PhI(OAc)_2$ (96.6 mg, 0.30 mmol), Me_3SiOTf (109 μL, 0.60 mmol), 2,6-di-*tert*-butylpyridine (121.8 mg, 0.64 mmol), and 3-(4-tolyl)but-3-enoic acid (52.6 mg, 0.30 mmol) in CH_2Cl_2 (3 mL) was conducted at r.t. for 1 h. Purification by flash column chromatography on silica gel (hexane/EtOAc) gave the product as a white solid; yield: 43.7 mg (76%). The analytical and spectral data for this compound were in excellent agreement with the reported data.[12]

4-(2-Tolyl)furan-2(5*H*)-one (2i)

According to the general procedure, the reaction using $PhI(OAc)_2$ (145.1 mg, 0.45 mmol), Me_3SiOTf (164 µL, 0.90 mmol), 2,6-di-*tert*-butylpyridine (170.2 mg, 0.89 mmol), and 3-(2-tolyl)but-3-enoic acid (52.5 mg, 0.30 mmol) in CH_2Cl_2 (3 mL) was conducted at r.t. for 3 h. Purification by flash column chromatography on silica gel (hexane/EtOAc) gave the product as a white solid; yield: 31.7 mg (61%). The analytical and spectral data for this compound were in excellent agreement with the reported data.[12]

4-(3-Tolyl)furan-2(5*H*)-one (2j)

According to the general procedure, the reaction using $PhI(OAc)_2$ (96.6 mg, 0.30 mmol), Me_3SiOTf (109 µL, 0.60 mmol), and 3-(3-tolyl)but-3-enoic acid (51.8 mg, 0.29 mmol) in CH_2Cl_2 (3 mL) was conducted at r.t. for 1.5 h. Purification by flash column chromatography on silica gel (hexane/EtOAc) gave the product as a yellow solid; yield: 44.2 mg (86%). The analytical and spectral data for this compound were in excellent agreement with the reported data.[12]

4-(1-Naphthyl)furan-2(5*H*)-one (2k)

According to the general procedure, the reaction using $PhI(OAc)_2$ (144.3 mg, 0.45 mmol), Me_3SiOTf (165 µL, 0.90 mmol), 2,6-di-*tert*-butylpyridine (174.5 mg, 0.91 mmol), and 3-(1-naphthyl)but-3-enoic acid (63.6 mg, 0.30 mmol) in CH_2Cl_2 (3 mL) was conducted at r.t. for 3 h. Purification by flash column chromatography on silica gel (hexane/EtOAc) gave the product as a yellow solid; yield: 49.1 mg (78%). The analytical and spectral data for this compound were in excellent agreement with the reported data.[3d]

4-(2-Naphthyl)furan-2(5*H*)-one (2l)

According to the general procedure, the reaction using $PhI(OAc)_2$ (96.6 mg, 0.30 mmol), Me_3SiOTf (109 µL, 0.60 mmol), 2,6-di-*tert*-butylpyridine (112.8 mg, 0.59 mmol), and 3-(2-naphthyl)but-3-enoic acid (63.7 mg, 0.30 mmol) in 1,2-dichloroethane (3 mL) was conducted at 60 °C for 3 h. Purification by flash column chromatography on silica gel (hexane/EtOAc) gave the product as a yellow solid; yield: 38.1 mg (60%). The analytical and spectral data for this compound were in excellent agreement with the reported data.[3d]

4-Benzylfuran-2(5*H*)-one (2m)

According to the general procedure, the reaction using $PhI(OAc)_2$ (96.9 mg, 0.30 mmol), Me_3SiOTf (109 µL, 0.60 mmol), and 3-benzylbut-3-enoic acid (52.9 mg, 0.30 mmol) in CH_2Cl_2 (3 mL) was conducted at r.t. for 1.5 h. Purification by flash column chromatography on silica gel (hexane/EtOAc) gave the product as a yellow viscous liquid; yield: 23.3 mg (45%). The analytical and spectral data for this compound were in excellent agreement with the reported data.[13]

4-(*n*-Butyl)furan-2(5*H*)-one (2n)

According to the general procedure, the reaction using $PhI(OAc)_2$ (97.2 mg, 0.30 mmol), Me_3SiOTf (109 µL, 0.60 mmol), and 3-methylideneheptanoic acid (40.1 mg, 0.28 mmol) in CH_2Cl_2 (3 mL) was conducted at r.t. for 1.5 h. Purification by flash column chromatography on silica gel (hexane/EtOAc) gave the product as a yellow viscous liquid; yield: 13.3 mg (34%). The analytical and spectral data for this compound were in excellent agreement with the reported data.[14]

3-Isopropyl-4-phenylfuran-2(5*H*)-one (2o)

According to the general procedure, the reaction using $PhI(OAc)_2$ (94.4 mg, 0.29 mmol), Me_3SiOTf (105 µL, 0.58 mmol), and 2-isopropyl-3-phenylbut-3-enoic acid (59.5 mg, 0.29 mmol) in CH_2Cl_2 (3 mL) was conducted at r.t. for 3 h. Purification by flash column chromatography on silica gel (hexane/EtOAc) gave the product as a yellow viscous liquid; yield: 23.2 mg (40%).

IR (ATR): 1746, 1649 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.55–7.40 (m, 3 H), 7.40–7.30 (m, 2 H), 4.94 (s, 2 H), 3.07 (sept, *J* = 7.2 Hz, 1 H), 1.30 (d, *J* = 7.2 Hz, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.4, 155.3, 132.4, 131.6, 129.8, 129.0, 127.4, 70.6, 25.1, 20.1.

MS (EI): *m*/*z* (%) = 202 (M^+, 91), 201 (81), 157 (63), 143 (69), 142 (38), 141 (49), 131 (28), 130 (22), 129 (69), 128 (100), 127 (28), 117 (20), 115 (61), 105 (49), 91 (56), 77 (44), 51 (28).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{13}H_{14}O_2$: 202.0994; found: 202.0992.

3,3-Dimethyl-4-phenylfuran-2(3*H*)-one (3a)

According to the general procedure, the reaction using $PhI(OAc)_2$ (96.8 mg, 0.30 mmol), Me_3SiOTf (110 µL, 0.60 mmol), and 2,2-dimethyl-3-phenylbut-3-enoic acid (55.8 mg, 0.29 mmol) in CH_2Cl_2 (3 mL) was conducted at r.t. for 3 h. Purification by flash column chromatography on silica gel (hexane/EtOAc) gave the product as a yellow solid; yield: 37.5 mg (68%); mp 68.7–69.6 °C.

IR (ATR): 1798, 1622 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.40–7.30 (m, 5 H), 7.05 (s, 1 H), 1.51 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 182.5, 136.2, 131.1, 129.5, 128.8, 128.0, 126.3, 45.0, 23.9.

MS (EI): *m*/*z* (%) = 188 (M^+, 88), 160 (61), 145 (95), 142 (20), 132 (48), 131 (89), 130 (25), 129 (42), 128 (40), 127 (25), 118 (21), 117 (100), 116 (88), 115 (100), 91 (100), 89 (39), 78 (22), 77 (46), 65 (35), 63 (50), 53 (21), 51 (46), 50 (21).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{12}H_{12}O_2$: 188.0837; found: 188.0835.

4-(4-Bromophenyl)-3,3-dimethylfuran-2(3*H*)-one (3b)

According to the general procedure, the reaction using $PhI(OAc)_2$ (96.2 mg, 0.30 mmol), Me_3SiOTf (109 µL, 0.60 mmol), and 3-(4-bromophenyl)-2,2-dimethylbut-3-enoic acid (79.9 mg, 0.30 mmol) in CH_2Cl_2 (3 mL) was conducted at r.t. for 3 h. Purification by flash column chromatography on silica gel (hexane/EtOAc) gave the product as a white solid; yield: 42.9 mg (54%); mp 89.8–90.6 °C.

IR (ATR): 1782, 1634 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.50 (d, *J* = 8.4 Hz, 2 H), 7.22 (d, *J* = 8.4 Hz, 2 H), 7.07 (s, 1 H), 1.49 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 182.2, 136.6, 132.0, 130.0, 128.5, 127.8, 122.0, 44.9, 23.8.

MS (EI): *m*/*z* (%) = 266 (M^+, 58), 268 (59), 240 (29), 238 (31), 159 (100), 144 (26), 131 (97), 130 (46), 129 (37), 128 (20), 116 (35), 115 (71), 91 (26).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{12}H_{11}BrO_2$: 265.9942; found: 265.9944.

Acknowledgment

This work was supported by JSPS KAKENHI Grant Number JP16K17868.

Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0036-1588987.

References

(1) (a) Kupchan, S. M.; Court, W. A.; Dailey, R. G. Jr.; Gilmore, C. J.; Bryan, R. F. *J. Am. Chem. Soc.* **1972**, *94*, 7194. (b) Pelter, A.; Ward, R. S.; Rao, E. V.; Raju, N. R. *J. Chem. Soc., Perkin Trans. 1* **1981**, 2491. (c) De Guzman, F. S.; Schmitz, F. J. *J. Nat. Prod.* **1990**, *53*, 926. (d) Bezuidenhoudt, B. C. B.; Swanepoel, A.; Brandt, E. V.; Ferreira, D. *J. Chem. Soc., Perkin Trans. 1* **1990**, 2599. (e) Miao, S.; Andersen, R. J. *J. Org. Chem.* **1991**, *56*, 6275. (f) Miles, D. H.; Chittawong, V.; Lho, D.-S.; Payne, A. M.; de la Cruz, A. A.; Gomez, E. D.; Weeks, J. A.; Atwood, J. L. *J. Nat. Prod.* **1991**, *54*, 286. (g) Nohara, T.; Kinjo, J.; Furusawa, J.; Sakai, Y.; Inoue, M.; Shirataki, Y.; Ishibashi, Y.; Yokoe, I.; Komatsu, M. *Phytochemistry* **1993**, *33*, 1207. (h) Cerri, A.; Mauri, P.; Mauro, M.; Melloni, P. *J. Heterocycl. Chem.* **1993**, *30*, 1581. (i) Evidente, A.; Sparapano, L. *J. Nat. Prod.* **1994**, *57*, 1720. (j) Figadère, B. *Acc. Chem. Res.* **1995**, *28*, 359. (k) Midland, S. L.; Keen, N. T.; Sims, J. J. *J. Org. Chem.* **1995**, *60*, 1118. (l) Honda, T.; Mizutani, H.; Kanai, K. *J. Org. Chem.* **1996**, *61*, 9374. (m) Gunasekera, S. P.; McCarthy, P. J.; Kelly-Borges, M.; Lobkovsky, E.; Clardy, J. *J. Am. Chem. Soc.* **1996**, *118*, 8759. (n) Smith, C. J.; Hettich, R. L.; Jompa, J.; Tahir, A.; Buchanan, M. V.; Ireland, C. M. *J. Org. Chem.* **1998**, *63*, 4147. (o) Ortega, M. J.; Zubía, E.; Ocaña, J. M.; Naranjo, S.; Salvá, J. *Tetrahedron* **2000**, *56*, 3963. (p) Bellina, F.; Anselmi, C.; Viel, S.; Mannina, L.; Rossi, R. *Tetrahedron* **2001**, *57*, 9997. (q) Ueda, J.; Tezuka, Y.; Banskota, A. H.; Tran, Q. L.; Tran, Q. K.; Saiki, I.; Kadota, S. *J. Nat. Prod.* **2003**, *66*, 1427. (r) Braña, M. F.; García, M. L.; López, B.; de Pascual-Teresa, B.; Ramos, A.; Pozuelo, J. M.; Domínguez, M. T. *Org. Biomol. Chem.* **2004**, *2*, 1864. (s) Keyzers, R. A.; Davies-Coleman, M. T. *Chem. Soc. Rev.* **2005**, *34*, 355. (t) Ohsaki, A.; Kobayashi, Y.; Yoneda, K.; Kishida, A.; Ishiyama, H. *J. Nat. Prod.* **2007**, *70*, 2003. (u) Zhang, H.; Conte, M. M.; Huang, X.-C.; Khalil, Z.; Capon, R. J. *Org. Biomol. Chem.* **2012**, *10*, 2656.

(2) For reviews, see: (a) Rao, Y. S. *Chem. Rev.* **1976**, *76*, 625. (b) Avetisyan, A. A.; Dangyan, M. T. *Russ. Chem. Rev.* **1977**, *46*, 643. For selected examples, see: (c) Wu, J.; Zhu, Q.; Wang, L.; Fathi, R.; Yang, Z. *J. Org. Chem.* **2003**, *68*, 670. (d) Boukouvalas, J.; Loach, R. P. *J. Org. Chem.* **2008**, *73*, 8109. (e) Hyde, A. M.; Buchwald, S. L. *Org. Lett.* **2009**, *11*, 2663. (f) Matsuo, K.; Shindo, M. *Org. Lett.* **2010**, *12*, 5346. (g) Lee, D.; Newman, S. G.; Taylor, M. S. *Org. Lett.* **2009**, *11*, 5486. (h) Cheng, J.; Chen, P.; Liu, G. *Org. Chem. Front.* **2014**, *1*, 289. (i) Mao, W.; Zhu, C. *Org. Lett.* **2015**, *17*, 5710.

(3) For selected examples, see: (a) Danieli, N.; Mazur, Y.; Sondheimer, F. *J. Am. Chem. Soc.* **1962**, *84*, 875. (b) Danieli, N.; Mazur, Y.; Sondheimer, F. *Tetrahedron* **1966**, *22*, 3189. (c) Krauser, S. F.; Watterson, A. C. Jr. *J. Org. Chem.* **1978**, *43*, 3400. (d) Kagabu, S.; Shimizu, Y.; Ito, C.; Moriya, K. *Synthesis* **1992**, 830. (e) Renard, M.; Ghosez, L. A. *Tetrahedron* **2001**, *57*, 2597. (f) Bassetti, M.; D'Annibale, A.; Fanfoni, A.; Minissi, F. *Org. Lett.* **2005**, *7*, 1805. (g) Liu, Y.; Song, F.; Guo, S. *J. Am. Chem. Soc.* **2006**, *128*, 11332. (h) Tejedor, D.; Santos-Expośito, A.; García-Tellado, F. *Synlett* **2006**, 1607. (i) Alfonsi, M.; Arcadi, A.; Chiarini, M.; Marinelli, F. *J. Org. Chem.* **2007**, *72*, 9510. (j) Li, S.; Miao, B.; Yuan, W.; Ma, S. *Org. Lett.* **2013**, *15*, 977.

(4) (a) Kasahara, A.; Izumi, T.; Sato, K.; Maemura, M.; Hayasaka, T. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 1899. (b) Browne, D. M.; Niyomura, O.; Wirth, T. *Org. Lett.* **2007**, *9*, 3169. (c) Bajracharya, G. B.; Koranne, P. S.; Nadaf, R. N.; Gabr, R. K. M.; Takenaka, K.; Takizawa, S.; Sasai, H. *Chem. Commun.* **2010**, *46*, 9064. (d) Kawamata, Y.; Hashimoto, T.; Maruoka, K. *J. Am. Chem. Soc.* **2016**, *138*, 5206.

(5) Singh, F. V.; Rehbein, J.; Wirth, T. *ChemistryOpen* **2012**, *1*, 245.

(6) (a) Kiyokawa, K.; Yahata, S.; Kojima, T.; Minakata, S. *Org. Lett.* **2014**, *16*, 4646. For iodine-catalyzed decarboxylative amidation, see: (b) Kiyokawa, K.; Kojima, T.; Hishikawa, Y.; Minakata, S. *Chem. Eur. J.* **2015**, *21*, 15548.

(7) (a) Zefirov, N. S.; Safronov, S. O.; Kaznacheev, A. A.; Zhdankin, V. V. *Zh. Org. Khim.* **1989**, *25*, 1807. (b) Lutz, K. E.; Thomson, R. J. *Angew. Chem. Int. Ed.* **2011**, *50*, 4437. (c) Farid, U.; Wirth, T. *Angew. Chem. Int. Ed.* **2012**, *51*, 3462.

(8) (a) Zefirov, N. S.; Zhdankin, V. V.; Dan'kov, Y. V.; Koz'min, A. S. *J. Org. Chem. USSR* **1984**, *20*, 401; *Zh. Org. Khim.* **1984**, *20*, 446. (b) Zefirov, N. S.; Zhdankin, V. V.; Dan'kov, Y. V.; Sorokin, V. D.; Semerikov, V. N.; Koz'min, A. S.; Caple, R.; Berglund, B. A. *Tetrahedron Lett.* **1986**, *27*, 3971.

(9) Upon treatment with TfOH in CH_2Cl_2, methoxy-substituted substrate **1g** completely isomerized into the corresponding α,β-unsaturated carboxylic acid, which decomposed into a complex mixture under the standard cyclization conditions.

(10) Izquierdo, S.; Essafi, S.; del Rosal, I.; Vidossich, P.; Pleixats, R.; Vallribera, A.; Ujaque, G.; Lledós, A.; Shafir, A. *J. Am. Chem. Soc.* **2016**, *138*, 12747.

(11) Gronnier, C.; Kramer, S.; Odabachian, Y.; Gagosz, F. *J. Am. Chem. Soc.* **2012**, *134*, 828.

(12) Hu, Y.; Ding, Q.; Ye, S.; Peng, Y.; Wu, J. *Tetrahedron* **2011**, *67*, 7258.

(13) Carter, N. B.; Mabon, R.; Richecœur, A. M. E.; Sweeney, J. B. *Tetrahedron* **2002**, *58*, 9117.

(14) Pelletier, S. W.; Djarmati, Z.; Lajšić, S. D.; Mićović, I. V.; Yang, D. T. C. *Tetrahedron* **1975**, *31*, 1659.