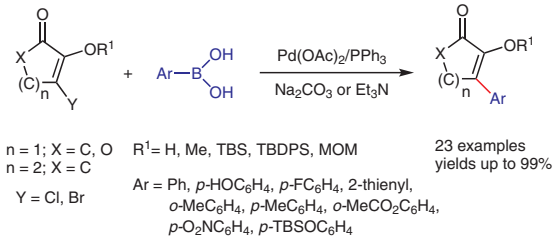
Synthesis E. Lopušanskaja et al. Paper

Synthesis of Cyclic 3-Aryl-Substituted 1,2-Dicarbonyl Compounds via Suzuki Cross-Coupling Reactions

Eleana Lopušanskaja
Anne Paju
Ivar Järving
Margus Lopp*

Department of Chemistry, Tallinn University of Technology, Akadeemia tee 15, Tallinn, Estonia
margus.lopp@ttu.ee



Received: 17.12.2017
Accepted after revision: 19.01.2018
Published online: 12.02.2018
DOI: 10.1055/s-0036-1591543; Art ID: ss-2017-t0823-op

Abstract A method for the synthesis of cyclic 3-aryl- and heteroaryl-substituted 1,2-dicarbonyl compounds with different ring sizes by using a Suzuki cross-coupling reaction between 3-halo-1,2-dicarbonyl compounds and arylboronic acids is developed. The 3-halo-1,2-dicarbonyl substrates are easily available from 1,2-dicarbonyl compounds. The method is versatile, affording good to high yields of the target compounds.

Key words Suzuki cross-coupling, dicarbonyl compounds, halodiketones, arylation, palladium catalysis

Cyclic 3-substituted 1,2-dicarbonyl compounds are simple multifunctional structures the synthetic potential of which has not been fully exploited, although there are many examples of the successful use of these molecules in organic synthesis. For example, α-alkylation,[1a] α′-allylation,[1b] Michael addition,[1c] and Claisen rearrangement[2] using this structural unit have been reported. In addition, there are examples of asymmetric alkylations of these structural units,[3] and asymmetric oxidation to afford γ-lactone carboxylic acids.[4]

Cyclic 3-alkyl-substituted 1,2-dicarbonyl compounds have been used in the synthesis of natural compounds such as milbemycin β_3, trichodiene, (–)-terpestacin and (+)-confertin.[5] The cyclic 3-aryl-substituted 1,2-dicarbonyl structural motif is present in several biologically active compounds, including the aldose reductase inhibitor WF-3681[6] and the anti-inflammatory agent DFP (Figure 1).[7] Several butyrolactones exhibit cytotoxic activity against some tumor cells,[8a,8b] and antiplasmodial activity.[8c] In addition, aryl derivatives of ascorbic acid (vitamin C) show anti-inflammatory[9a] and HIV-1 integrase inhibition.[9b] We have used 3-aryl-substituted 1,2-dicarbonyl compounds in the synthesis of 2-aryl-γ-lactone acids and 4′-aryl-substituted nucleoside analogues.[10]

There are several possible ways of synthesizing 3-aryl-substituted cyclopentane-1,2-diones (Figure 1) and cyclohexane-1,2-diones. For example, 3-phenyl-1,2-cyclopentanedione was synthesized starting from 3-phenyl-2-cyclopenten-1-one by epoxidation and subsequent epoxyketone rearrangement,[11a] from 3-phenyl-1,2,4-cyclopentanetrione by reduction of the 2-phenyl-3,5,5-triethoxy-2-cyclopenten-1-one intermediate,[11b] and by the heterogeneous platinum catalytic aerobic oxidation of 3-phenylcyclopentane-1,2-diols.[11c]

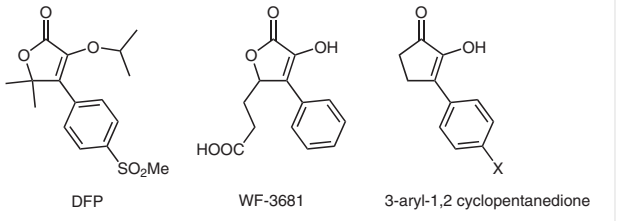


Figure 1 Examples of cyclic 3-aryl-substituted 1,2-dicarbonyl compounds

Various aryl-substituted cyclopentane-1,2-diones were synthesized by the Stetter reaction between substituted benzaldehydes and 1-acetoxy-3-butene-2-one followed by cyclization. However, for the preparation of 1-acetoxy-3-butene-2-one, a toxic Hg salt was used[10,12] making this approach unattractive for preparative synthesis. Also, for the arylation of 1,2-diketones, photolysis of 2-arenesulfonyl-2-cycloalkenones was used to synthesize 3-aryl/heteroarylcycloalkene-1,2-diones.[13] Furthermore, for the synthesis of 3-phenyl-1,2-cyclohexanedione, methods involving conjugate addition of lithium dicuprate reagents to the enol tosylate

of a 1,2-diketone,[14a] reaction of 2-phenylcyclohexanone with iodine/copper(II) acetate[14b] and Swern oxidation of 2-hydroxy-5-phenylcyclohexanone[14c] were used. For different 3-aryl-substituted cyclohexanediones an efficient Heck arylation procedure using aryl bromides in reactions with 1,2-cyclohexanedione[15a] or 2,3-epoxycyclohexanone[15b] were applied.

There are also many synthetic procedures for the synthesis of 4-aryl-substituted 2,3-dihydrofurandiones. Of these, the more general are the aldol reactions of pyruvic acid derivatives with aromatic aldehydes using different catalysts.[9a,16] Also, there are examples of using the oxidative cyclization of α,β-unsaturated methyl ketones,[17a] the Wittig rearrangement/alkylative cyclization sequence,[17b] reactions of the dianion of 2,4-oxazolidinedione with α-haloketones[17c] and Suzuki cross-coupling reactions of cyclic 3-bromoisotetronic acids with substituted arylboronic acids.[18]

Considering the increasing need for 3-substituted 1,2-diones, we previously developed methods for the synthesis of 3-alkyl- and 3-alkynyl-substituted 1,2-diketones by using bromodiketones as substrates for Negishi[19a] and Sonogashira[19b] cross-coupling reactions.

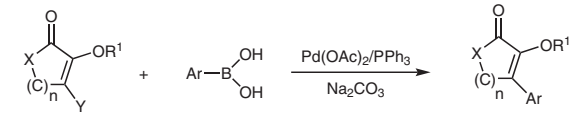
In the present study, we completed our investigations by synthesizing 3-substituted 1,2-diones via Suzuki cross-coupling reactions[20] of halodiketones **1**, **2** and **3** with arylboronic acids **4** to afford 3-aryl- and 3-heteroaryl-substituted 1,2-diketones **5**, **6** and **7**.

The substrates for the coupling reactions, 3-bromo-1,2-cyclopentanedione (**1-Br**), 3-bromo-1,2-cyclohexanedione (**2-Br**) and their OTBS-protected derivatives, were prepared from cyclopentane-1,2-dione and 1,2-cyclohexanedione using NBS as described in our previous publication.[19b] 3-Chloro-1,2-cyclopentanedione (**1-Cl**) was prepared analogously using NCS. **1-Br**, **1-Cl** and **2-Br** methoxy-protected derivatives were prepared according to the reported procedure,[21] whilst hydroxy-protected 4-bromo-3-hydroxy-2-furanones **3** were prepared from 3-hydroxyfuran-2(5*H*)-one[22] by bromination with NBS followed by different protecting group manipulations (see the Supporting Information).

We started our investigations with the more stable Me- and MOM-protected 3-halo-cyclopentane-1,2-diones **1**, **2** and **3** and phenylboronic acids **4** by using standard conditions.[18] The obtained results of the Suzuki cross-coupling reactions yielding the corresponding coupling products **5**, **6** and **7** are presented in Table 1.

The reaction of methyl-protected 3-bromocyclopentane-1,2-dione (**1-Br-*b***) with phenylboronic acid (**4a**) under standard reaction conditions [$Pd(OAc)_2$ as the catalyst (5 mol%), PPh_3 (10 mol%), Na_2CO_3 as the base in THF/H_2O mixture (4:1) at 60 °C overnight] afforded the coupling product **5a-*b*** in 84% isolated yield (Table 1, entry 1). Also, the reactions of boronic acids **4b–e** with methyl-protected 3-bromocyclopentane-1,2-dione (**1-Br-*b***) gave good

Table 1 Synthesis of Cyclopentane- and Cyclohexane-3-Aryl-Substituted 1,2-Diketones by Suzuki Cross-Coupling[a]



1 n = 1; X = C; **2** n = 2; X = C; **3** n = 1, X = O; Y = Cl, Br

R^1 = H (***a***), Me (***b***), MOM (***d***)

4 Ar = Ph (**a**), *p*-HOC_6H_4 (**b**), *p*-FC_6H_4 (**c**), 2-thienyl (**d**), *o*-MeC_6H_4 (**e**), *p*-MeC_6H_4 (**f**), *o*-$MeCO_2C_6H_4$ (**g**), *p*-$O_2NC_6H_4$ (**h**)

5 n = 1; X = C; **6** n = 2; X = C; **7** n = 1; X = O

Entry	Substrate	R^1	$ArB(OH)_2$	$Pd(OAc)_2$(mol %)	Product (Yield %)[b]
1	**1-Br**	***b***	**4a**	5	**5a-*b*** (84)
2	**1-Br**	***b***	**4b**	5	**5b-*b*** (70)
3	**1-Br**	***b***	**4c**	5	**5c-*b*** (90)
4	**1-Br**	***b***	**4d**	5	**5d-*b*** (92)
5	**1-Br**	***b***	**4e**	5	**5e-*b*** (79)
6	**1-Br**	***a***	**4a**	5	**5a-*a*** (14)
7	**1-Cl**	***b***	**4a**	5	**5a-*b*** (51)
8	**1-Cl**	***b***	**4a**	10	**5a-*b*** (96)
9[c]	**1-Br**	***b***	**4a**	5	**5a-*b*** (95)
10	**2-Br**	***b***	**4a**	5	**6a-*b*** (96)
11	**2-Br**	***b***	**4f**	5	**6f-*b*** (82)
12	**2-Br**	***b***	**4g**	5	**6g-*b*** (36)
13	**2-Br**	***b***	**4g**	10	**6g-*b*** (50)
14[c]	**2-Br**	***b***	**4f**	5	**6f-*b*** (88)
15	**3-Br**	***b***	**4c**	5	**7c-*b*** (82)
16	**3-Br**	***d***	**4d**	5	**7d-*d*** (99)
17	**3-Br**	***d***	**4g**	5	**7g-*d*** (25)
18	**3-Br**	***d***	**4h**	5	**7h-*d*** (68)
19[c]	**3-Br**	***d***	**4d**	5	**7d-*d*** (66)

[a] *Reagents and conditions*: substrate **1**, **2** or **3** (0.5 mmol), $ArB(OH)_2$ **4** (0.75 mmol), $Pd(OAc)_2$ (6 mg, 5 mol% or 12 mg, 10 mol%), PPh_3 (13 mg, 10 mol% or 26 mg, 20 mol%), Na_2CO_3 (106 mg, 1.0 mmol), THF/H_2O (4:1, 5 mL), 60 °C, overnight.

[b] Yield of isolated product.

[c] *Reagents and conditions*: substrate **1-Br**, **2-Br** or **3-Br** (0.5 mmol), $ArB(OH)_2$ **4** (0.75 mmol), $Pd(OAc)_2$ (6 mg, 5 mol%), PPh_3 (13 mg, 10 mol%), Et_3N (1.5 mmol), H_2O (1.5 mL), r.t., under air, overnight.

to excellent yields (70–92%) of the 3-aryl-substituted cyclopentane-1,2-dione coupling products **5b–e** (entries 2–5). Protection of the enol OH in the substrate is recommended because the reaction of unprotected **1-Br-*a*** with phenylboronic acid (**4a**) afforded the coupling product **5a-*a*** in a low 14% yield (entry 6). When we compared the reactivity of Me-protected 3-chloro-cyclopentanedione (**1-Cl-*b***) and the corresponding bromo derivative, we found that it was slightly less reactive than **1-Br-*b***, affording the coupling product **5a-*b*** in 51% yield (entry 7). A two-fold amount of the catalyst (10 mol%) was needed to obtain an excellent coupling yield (96%) with the 3-chloro-substituted sub-

strate (entry 8). Thus, we continued our studies with 3-bromo-substituted substrates **2-Br** and **3-Br**. We also checked the possibility of using water as a solvent for the reaction.[23] By slightly changing the reaction conditions—running the reaction at room temperature and allowing free access of air—the coupling product **5a-*b*** was obtained in an excellent 95% yield (entry 9).

With cyclohexane substrate **2-Br-*b***, a similar result to that of the reaction of **1-Br-*b*** with boronic acid (**4a**) was obtained, with the yield of **6a-*b*** being 96% (Table 1, entry 10). The more complex and sterically demanding boronic acid **4g** was less reactive (36% yield, entry 12) requiring 10 mol% of the catalyst to increase the yield to 50% (entry 13). Again, in aqueous solution, the reaction of boronic acid **4f** with **2-Br-*b*** afforded a slightly higher yield of **6f-*b*** than in the THF/water mixture (88% vs 82%, entries 14 and 11).

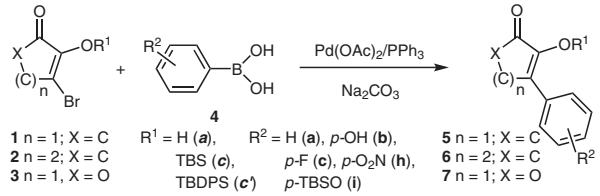
The 4-bromofurandiones **3-Br** showed good reactivity with different boronic acids, affording the coupling products **7** in good to high yields (Table 1, entries 15, 16, 18 and 19). The more labile MOM protecting group was utilized in the substrate instead of the Me group because of the lower stability of the furanone ring compared with the carbocycles, and such that removal of the protecting group in later transformations would be tolerated. Again, the boronic acid **4g** was less reactive, resulting in compound **7g** with a low yield of 25% (entry 17), most probably because of steric factors. However, the furanone substrate **3-Br-*d*** gave a lower yield in water than in the THF/water solvent (66% vs 99%), probably because of the tendency of lactone units to hydrolyze in water.

To obtain the coupling products with even more easily removable protecting groups, we investigated the coupling of different boronic acids **4** with silyl-protected substrates **1-Br-c**, **2-Br-c**, **3-Br-c** and **3-Br-c′**. The results are presented in Table 2.

The reaction of unsubstituted boronic acid **4a** with **1-Br-*c*** afforded the coupling product **5a-*c*** in good yield, which, however, was less than that for corresponding Me-protected substrate **1-Br-b** (68% vs 84%, compare Table 2, entry 1 and Table 1, entry 1).

A more drastic drop in the yield was observed when the reaction was carried out in water (65% vs 95%; compare Table 2, entry 2 and Table 1, entry 9), which may be connected with the stability of the substrate in water. The problem of the stability of the silyl-protecting group in the reaction was clearly seen in the case of the reaction of boronic acid **4b** with a free phenolic OH group and substrate **1-Br-*c***: both the deprotected and protected coupling products **5b-*a*** and **5b-*c*** were obtained (Table 2, entry 3). This means that the phenolic OH was acidic enough to cause partial deprotection during the reaction. From our results with the free enol OH group in compound **1-Br-*a*** (see Table 1, entry 6), we know that it is a poor substrate for coupling. We suggest that the deprotection of the substrate during the reaction might be the reason for the low yield.

Table 2 Optimization of the Conditions for Silyl-Protected Products[a]



1 n = 1; X = C
2 n = 2; X = C
3 n = 1, X = O

R^1 = H (***a***), TBS (***c***), TBDPS (***c′***)

R^2 = H (**a**), *p*-OH (**b**), *p*-F (**c**), *p*-O_2N (**h**), *p*-TBSO (**i**)

5 n = 1; X = C
6 n = 2; X = C
7 n = 1; X = O

Entry	Substrate	R^1	$ArB(OH)_2$	Solvent	Product (Yield %)[b]
1	**1-Br**	***c***	**4a**	THF/H_2O (4:1)	**5a-*c*** (68)
2[c]	**1-Br**	***c***	**4a**	H_2O	**5a-*c*** (65)
3	**1-Br**	***c***	**4b**	THF/H_2O (4:1)	**5b-*a*** (26); **5b-*c*** (23)
4[d]	**1-Br**	***c***	**4i**	toluene/H_2O (10:1)	**5i-*c*** (67)
5	**2-Br**	***c***	**4a**	THF/H_2O (4:1)	**6a-*c*** (86)
6	**2-Br**	***c***	**4c**	THF/H_2O (4:1)	**6c-*c*** (87)
7	**2-Br**	***c***	**4h**	THF/H_2O (4:1)	**6h-*a*** (60); **6h-*c*** (32)
8	**2-Br**	***c***	**4h**	THF/H_2O (10:1)	**6h-*a*** (25); **6h-*c*** (33)
9[d]	**2-Br**	***c***	**4h**	toluene/H_2O (10:1)	**6h-*c*** (69)
10	**3-Br**	***c***	**4a**	THF/H_2O (4:1)	**7a-*a*** (51)
11	**3-Br**	***c′***	**4a**	THF/H_2O (4:1)	**7a-*a*** (68)

[a] *Reagents and conditions*: substrate **1**, **2** or **3** (0.5 mmol), $ArB(OH)_2$ **4** (0.75 mmol), $Pd(OAc)_2$ (6 mg, 5 mol%), PPh_3 (13 mg, 10 mol%), Na_2CO_3 (106 mg, 1.0 mmol), solvent (5 mL), 60 °C, overnight.
[b] Yield of isolated product.
[c] *Reagents and conditions*: substrate **1-Br**, **2-Br** or **3-Br** (0.5 mmol), $ArB(OH)_2$ **4** (0.75 mmol), $Pd(OAc)_2$ (6 mg, 5 mol%), PPh_3 (13 mg, 10 mol%), Et_3N (1.5 mmol), H_2O (1.5 mL), r.t., under air, overnight.
[d] Reaction at 100 °C, overnight.

Reactions of phenylboronic and *p*-fluorophenylboronic acids with the TBS-protected cyclohexane substrate **2-Br-*c*** afforded the coupling products **6a-*c*** and **6c-*c*** in good yields of 86% (Table 2, entries 5 and 6). The use of *p*-nitrophenylboronic acid was more complicated: under the standard reaction conditions a mixture of deprotected and protected **6h-*a*** and **6h-*c*** (60:32) was obtained (entry 7). Reducing the amount of water to 10:1 led to a decrease in the yield of the process, affording deprotected and protected products **6h-*a*** and **6h-*c*** in a ratio of 25:33, with an overall reduction in the yield of unprotected **6h-*a*** (entry 8). After changing THF to toluene and increasing the temperature to 100 °C, finally only the protected product **6h-*c*** was obtained in 69% yield (entry 9). Also, under these conditions, by using TBS-protected **1-Br-*c*** and **4i**,[24] the disilylated coupling product **5i-*c*** was obtained in 67% yield (entry 4).

The 4-bromofurandione with a TBS protecting group afforded only the deprotected coupling compound **7a-*a*** in 51% yield (Table 2, entry 10). Changing the TBS moiety to the more stable TBDPS group resulted in an increased yield of 68% (entry 11). In the reaction of **3-Br-*c'*** and boronic acid **4a** in aqueous medium, the unprotected product **7a-*a*** was formed in only trace amount. So, in the case of furanones, silyl protection of the substrate is not tolerated under the Suzuki cross-coupling reaction conditions.

In conclusion, we have demonstrated that various cyclic 3-aryl-substituted 1,2-dicarbonyl compounds can be easily obtained by Suzuki cross-coupling reactions of 3-chloro- and 3-bromo-1,2-diketones **1-Cl**, **1-Br**, **2-Br** and **3-Br** with arylboronic acids **4** possessing different substituents. The reaction can be carried out in different solvents, including water, and tolerates a variety of protecting groups. The present protocol for the preparation of different types of 3-aryl-substituted 1,2-dicarbonyl compounds **5**, **6** and **7** is an addition to our previously developed procedures for the synthesis of 3-alkyl- and 3-alkynyl-substituted 1,2-cycloalkanediones,[19] and completes the series, allowing cross-coupling reactions to be utilized in a simple and general route for the preparation of a wide range of 3-substituted 1,2-dicarbonyl compounds.

All reactions sensitive to oxygen or moisture were conducted under an argon atmosphere in oven-dried glassware. Purchased chemicals and solvents were used as received. THF was degassed before use. Precoated silica gel 60 F_{254} plates (TLC Silicagel Merck) were used for TLC. Column chromatography was performed on a preparative purification system with 40–63 µm silica gel (Thomar). Melting points were obtained using a Boëtius (Nagema) instrument and are uncorrected. IR spectra were recorded on a Bruker PMA 50 spectrometer. ^{1}H and ^{13}C NMR spectra were recorded in deuterated solvents on a Bruker Avance USLA 400 spectrometer. Deuterated solvent peaks were used as references. 2D FT methods were used for the full assignment of ^{1}H and ^{13}C NMR chemical shifts. Mass spectra were measured on a Shimadzu GCMS - QP2010 spectrometer using EI (70 eV). High-resolution mass spectrometry was performed using an Agilent Technologies 6540 UHD Accurate-Mass Q-TOF LC/MS spectrometer with AJ-ESI ionization..

Coupling of Halodiketones 1–3 with Arylboronic Acids 4; General Procedure A

The reaction was conducted overnight at 60 °C under an argon atmosphere in THF/H_2O (4:1, 5 mL) by using of **1**, **2** or **3** (0.5 mmol), $ArB(OH)_2$ **4** (0.75 mmol), Na_2CO_3 (1.0 mmol), $Pd(OAc)_2$ (5 mol%) and PPh_3 (10 mol%). After cooling to r.t., the mixture was diluted with H_2O and extracted with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4 or $MgSO_4$, filtered and then evaporated to dryness. The crude residue was purified by column chromatography (generally using petroleum ether/EtOAc) to afford the pure product.

2-Methoxy-3-phenylcyclopent-2-en-1-one (5a-*b*)

Following general procedure A gave product **5a-*b*** as a yellow solid.

Yield: 78 mg (84%); mp 45–47 °C.

IR (KBr): 2853, 1695, 1603, 1357, 768 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.95–7.82 (m, 2 H), 7.49–7.34 (m, 3 H), 4.05 (s, 3 H), 2.91–2.80 (m, 2 H), 2.56–2.44 (m, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 203.7, 152.4, 147.9, 134.1, 129.9, 128.6, 127.5, 58.3, 32.7, 23.8.

MS (EI, 70 eV): *m*/*z* (%) = 188 (100) [M]$^+$, 145 (46), 129 (23), 115 (63), 103 (82), 89 (40), 77 (33), 63 (23).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{13}O_2$: 189.0910; found: 189.0915.

3-(4-Hydroxyphenyl)-2-methoxycyclopent-2-en-1-one (5b-*b*)

Following general procedure A gave product **5b-*b*** as a white solid.

Yield: 72 mg (70%); mp 166–170 °C.

IR (KBr): 3095, 1658, 1570, 1243, 817 cm^{-1}.

^{1}H NMR (400 MHz, MeOD): δ = 7.82 (d, *J* = 8.8 Hz, 2 H), 6.84 (d, *J* = 8.9 Hz, 2 H), 6.61 (s, 1 H), 3.92 (s, 3 H), 2.90–2.80 (m, 2 H), 2.49–2.40 (m, 2 H).

^{13}C NMR (101 MHz, MeOD): δ = 206.1, 160.9, 152.7, 130.7, 126.5, 116.8, 116.4, 58.5, 33.2, 24.7.

MS (EI, 70 eV): *m*/*z* (%) = 204 (61) [M]$^+$, 187 (11), 161 (13), 148 (11), 133 (22), 119 (100), 105 (22), 91 (23), 77 (27), 65 (18), 51 (21).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{13}O_3$: 205.0859; found: 205.0865.

3-(4-Fluorophenyl)-2-methoxycyclopent-2-en-1-one (5c-*b*)

Following general procedure A gave product **5c-*b*** as a yellow solid.

Yield: 106 mg (90%); mp 85–88 °C.

IR (KBr): 3064, 2949, 1703, 1602, 1510, 1447, 1226, 820 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.93–7.86 (m, 2 H), 7.15–7.07 (m, 2 H), 4.05 (s, 3 H), 2.87–2.80 (m, 2 H), 2.54–2.47 (m, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 203.5, 163.5 (FC_{arom} d, *J* = 251.3 Hz), 152.0 (d, *J* = 1.9 Hz), 146.5, 130.4 (C_{arom} d, *J* = 3.5 Hz), 129.6 (*o*-CH_{arom} d, *J* = 8.4 Hz), 115.7 (*m*-CH_{arom} d, *J* = 21.4 Hz), 58.2, 32.6, 23.8.

MS (EI, 70 eV): *m*/*z* (%) = 206 (99) [M]$^+$, 177 (21), 163 (38), 147 (20), 133 (52), 121 (100), 107 (47), 101 (38), 96 (14), 75 (18), 57 (20).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{12}FO_2$: 207.0816; found: 207.0821.

2-Methoxy-3-(thiophen-2-yl)cyclopent-2-en-1-one (5d-*b*)

Following general procedure A gave product **5d-*b*** as a greenish solid.

Yield: 90 mg (92%); mp 63–65 °C.

IR (KBr): 3064, 2923, 1679, 1611, 1441, 1359, 1119, 1059, 960, 818, 730 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.53 (dd, *J* = 5.1, 1.1 Hz, 1 H), 7.44 (dd, *J* = 3.7, 1.1 Hz, 1 H), 7.13 (dd, *J* = 5.1, 3.7 Hz, 1 H), 4.11 (s, 3 H), 2.94–2.81 (m, 2 H), 2.59–2.48 (m, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 201.7, 149.7, 143.5, 136.7, 130.0, 127.5, 127.4, 58.1, 33.0, 23.6.

MS (EI, 70 eV): *m*/*z* (%) = 194 (89) [M]$^+$, 165 (16), 151 (11), 137 (26), 123 (27), 109 (100), 95 (13), 77 (10).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{10}H_{11}O_2S$: 195.0474; found: 195.0476.

2-Methoxy-3-(*o*-tolyl)cyclopent-2-en-1-one (5e-*b*)

Following general procedure A gave product **5e-*b*** as a white solid.

Yield: 80 mg (79%); mp 44–46 °C.

IR (KBr): 2946, 1701, 1625, 1445, 1348, 1139, 1105, 783 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.32–7.16 (m, 4 H), 3.65 (s, 3 H), 2.77–2.69 (m, 2 H), 2.58–2.50 (m, 2 H), 2.29 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 203.2, 152.3, 148.6, 135.7, 135.5, 130.4, 128.7, 127.4, 125.8, 58.4, 33.2, 27.9, 20.1.

MS (EI, 70 eV): *m*/*z* (%) = 202 (51) $[M]^+$, 187 (100), 159 (14), 145 (44), 128 (32), 115 (67), 103 (23), 91 (34), 77 (27).

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{13}H_{15}O_2$: 203.1067; found: 203.1069.

2-Hydroxy-3-phenylcyclopent-2-en-1-one (5a-*a*)

Following general procedure A gave product **5a-*a*** as a white solid.

Yield: 12 mg (14%).

IR (KBr): 3394, 3282, 2918, 1681, 1633, 1495, 1449, 1391, 1323, 1286, 1218, 1136, 1047, 988, 889, 765, 691, 623 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 9.88 (s, 1 H), 7.99–7.85 (m, 2 H), 7.45 (dd, *J* = 8.3, 6.8 Hz, 2 H), 7.41–7.31 (m, 1 H), 2.82–2.72 (m, 2 H), 2.48–2.39 (m, 2 H).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 202.8, 149.8, 136.9, 134.7, 128.7, 128.5, 127.0, 31.1, 22.7.

MS (EI, 70 eV): *m*/*z* (%) = 174 (100) $[M]^+$, 145 (25), 131 (20), 117 (63), 103 (50), 89 (29), 77 (33), 63 (20), 51 (24).

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{11}H_{11}O_2$: 175.0754; found: 175.0752.

2-Methoxy-3-phenylcyclohex-2-en-1-one (6a-*b*)

Following general procedure A gave product **6a-*b*** as a yellow liquid.

Yield: 97 mg (96%).

IR (KBr): 2934, 2834, 1676, 1603, 1493, 1442, 1351, 1329, 1306, 1278, 1234, 1203, 1140, 1090, 991, 893, 763, 697 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.56–7.46 (m, 2 H), 7.44–7.28 (m, 3 H), 3.52 (s, 3 H), 2.76 (t, *J* = 6.0 Hz, 2 H), 2.57 (dd, *J* = 7.4, 6.1 Hz, 2 H), 2.09 (dt, *J* = 12.4, 6.2 Hz, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 196.0, 149.1, 144.0, 137.5, 128.7, 128.3, 128.0, 60.0, 38.9, 31.0, 22.7.

MS (EI, 70 eV): *m*/*z* (%) = 202 (100) $[M]^+$, 187 (21), 156 (21), 145 (31), 129 (50), 117 (73), 103 (81), 91 (45), 77 (60), 63 (22), 51 (36).

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{13}H_{15}O_2$: 203.1067; found: 203.1075.

2-Methoxy-3-(*p*-tolyl)cyclohex-2-en-1-one (6f-*b*)

Following general procedure A gave product **6f-*b*** as a brown oil.

Yield: 89 mg (82%); mp 44–46 °C.

IR (KBr): 2931, 1676, 1604, 1510, 1436, 1350, 1186, 1141, 994, 815 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.48–7.39 (m, 2 H), 7.23–7.15 (m, 2 H), 3.51 (s, 3 H), 2.75 (t, *J* = 6.0 Hz, 2 H), 2.61–2.50 (m, 2 H), 2.37 (s, 3 H), 2.07 (dt, *J* = 12.2, 6.3 Hz, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 196.0, 149.0, 144.0, 138.8, 134.5, 129.0, 128.0, 59.9, 38.8, 30.9, 22.6, 21.4.

MS (EI, 70 eV): *m*/*z* (%) = 216 (37) $[M]^+$, 201 (100), 155 (12), 145 (22), 131 (54), 115 (40), 91 (30), 77 (9).

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{14}H_{17}O_2$: 217.1223; found: 217.1226.

2-Methoxy-3-(*o*-methoxycarbonylphenyl)cyclohex-2-en-1-one (6g-*b*)

Following general procedure A gave product **6g-*b*** as a yellow solid.

Yield: 65 mg (50%); mp 55–58 °C.

IR (KBr): 2950, 1723, 1681, 1626, 1435, 1351, 1292, 1260, 1136, 1097, 1075, 994, 894, 760, 709 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.00 (ddd, *J* = 7.9, 1.4, 0.5 Hz, 1 H), 7.54 (td, *J* = 7.6, 1.4 Hz, 1 H), 7.40 (td, *J* = 7.7, 1.3 Hz, 1 H), 7.20 (ddd, *J* = 7.7, 1.3, 0.5 Hz, 1 H), 3.85 (s, 3 H), 3.39 (s, 3 H), 2.61 (dt, *J* = 10.7, 6.4 Hz, 4 H), 2.14 (quin, *J* = 6.0 Hz, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 195.4, 166.9, 147.6, 147.3, 139.7, 132.3, 130.6, 128.4, 128.2, 127.9, 59.6, 52.2, 38.9, 32.4, 22.9.

MS (EI, 70 eV): *m*/*z* (%) = 260 (73) $[M]^+$, 229 (21), 186 (82), 168 (16), 157 (22), 141 (18), 129 (100), 115 (43), 102 (25), 77 (18), 55 (21).

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{15}H_{17}O_4$: 261.1121; found: 261.1126.

4-(4-Fluorophenyl)-3-methoxyfuran-2(5*H*)-one (7c-*b*)

Following general procedure A gave product **7c-*b*** as a white solid.

Yield: 84 mg (82%); mp 164–167 °C.

IR (KBr): 2963, 1739, 1651, 1593, 1513, 1447, 1355, 1229, 1149, 1071, 970, 836 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.86–7.74 (m, 2 H), 7.32–7.19 (m, 2 H), 5.19 (s, 2 H), 4.29 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.8, 163.4 (FC_{arom} d, *J* = 251.8 Hz), 139.7 (d, *J* = 2.2 Hz), 132.8, 128.8 (*o*-CH_{arom} d, *J* = 8.2 Hz), 126.3 (C_{arom} d, *J* = 3.5 Hz), 116.2 (*m*-CH_{arom} d, *J* = 21.7 Hz), 67.2, 58.6.

MS (EI, 70 eV): *m*/*z* (%) = 208 (100) $[M]^+$, 179 (29), 162 (21), 151 (23), 136 (79), 121 (95), 109 (89), 75 (27).

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{11}H_{10}O_3F$: 209.0608; found: 209.0609.

3-(Methoxymethoxy)-4-(thiophen-2-yl)furan-2(5*H*)-one (7d-*d*)

Following general procedure A gave product **7d-*d*** as a yellow solid.

Yield: 112 mg (99%); mp 54–56 °C.

IR (KBr): 3106, 2936, 1752, 1655, 1516, 1428, 1360, 1162, 1128, 925, 838, 715 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.55 (dd, *J* = 5.1, 1.1 Hz, 1 H), 7.31–7.22 (m, 1 H), 7.13 (dd, *J* = 5.1, 3.7 Hz, 1 H), 5.58 (s, 2 H), 5.09 (s, 2 H), 3.53 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.2, 135.1, 132.4, 131.3, 129.7, 127.6, 126.7, 95.6, 67.3, 57.7.

MS (EI, 70 eV): *m*/*z* (%) = 226 (7) $[M]^+$, 196 (14), 168 (8), 109 (28), 65 (6), 45 (100).

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{10}H_{11}O_4S$: 227.0373; found: 227.0380.

3-(Methoxymethoxy)-4-(*o*-methoxycarbonylphenyl)furan-2(5*H*)-one (7g-*d*)

Following general procedure A gave product **7g-*d*** as a yellow liquid.

Yield: 35 mg (25%).

IR (KBr): 2955, 1730, 1598, 1574, 1436, 1349, 1265, 1159, 1092, 940, 765, 710 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.01 (dd, *J* = 7.8, 1.4 Hz, 1 H), 7.59 (td, *J* = 7.6, 1.4 Hz, 1 H), 7.50 (td, *J* = 7.7, 1.4 Hz, 1 H), 7.34 (dd, *J* = 7.6, 1.3 Hz, 1 H), 5.05 (s, 2 H), 4.99 (s, 2 H), 3.86 (s, 3 H), 3.17 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.8, 166.8, 139.9, 137.7, 132.3, 131.0, 130.9, 130.3, 129.6, 129.5, 95.5, 69.9, 56.7, 52.6.

MS (EI, 70 eV): *m*/*z* (%) = 278 (0.3) $[M]^+$, 246 (1), 233 (3), 189 (17), 161 (12), 129 (13), 45 (100).

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{14}H_{15}O_6$: 279.0863; found: 279.0865.

3-(Methoxymethoxy)-4-(4-nitrophenyl)furan-2(5*H*)-one (7h-*d*)

Following general procedure A gave product **7h-*d*** as a yellow solid.

Yield: 90 mg (68%); mp 135–137 °C.

IR (KBr): 2928, 1753, 1644, 1596, 1513, 1460, 1341, 1153, 1062, 944, 886, 754 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 8.39–8.32 (m, 2 H), 8.05–7.96 (m, 2 H), 5.53 (s, 2 H), 5.37 (s, 2 H), 3.37 (s, 3 H).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 167.9, 147.5, 138.8, 135.5, 134.6, 128.0, 124.0, 95.3, 67.6, 56.9.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{12}H_{12}NO_6$: 266.0659; found: 266.0659.

2-[(*tert*-Butyldimethylsilyl)oxy]-3-phenylcyclopent-2-en-1-one (5a-*c*)

Following general procedure A gave product **5a-*c*** as a white solid.

Yield: 98 mg (68%); mp 84–86 °C.

IR (KBr): 2927, 1702, 1607, 1374, 1247, 1146, 843, 761, 650 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.95–7.90 (m, 2 H), 7.45–7.34 (m, 3 H), 2.89–2.84 (m, 2 H), 2.51–2.46 (m, 2 H), 0.97 (s, 9 H), 0.25 (s, 6 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 203.4, 149.4, 144.9, 134.6, 129.4, 128.4, 127.5, 31.6, 26.0, 23.9, 18.7, –3.4.

MS (EI, 70 eV): *m*/*z* (%) = 231 (100) $[M - 57]^+$, 216 (5), 201 (10), 128 (8), 115 (7), 75 (14).

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{17}H_{25}O_2Si$: 289.1618; found: 289.1624.

2-Hydroxy-3-(4-hydroxyphenyl)cyclopent-2-en-1-one (5b-*a*)

Following general procedure A gave product **5b-*a*** as a brown solid.

Yield: 25 mg (26%); mp 236–241 °C.

IR (KBr): 3319, 2923, 2468, 1656, 1598, 1516, 1430, 1386, 1280, 1214, 1175, 1139, 1117, 957, 845, 821, 560 cm^{-1}.

^1H NMR (400 MHz, MeOD): δ = 7.97–7.76 (m, 2 H), 6.91–6.76 (m, 2 H), 2.89–2.74 (m, 2 H), 2.51–2.29 (m, 2 H).

^{13}C NMR (101 MHz, MeOD): δ = 204.8, 159.8, 149.2, 141.4, 130.5, 127.6, 116.2, 32.2, 24.3.

MS (EI, 70 eV): *m*/*z* (%) = 190 (100) $[M]^+$,161 (15), 145 (12), 133 (42), 119 (56), 105 (23), 91 (28), 77 (24), 65 (18), 51 (23).

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{11}H_{11}O_3$: 191.0703; found: 191.0707.

2-[(*tert*-Butyldimethylsilyl)oxy]-3-(4-hydroxyphenyl)cyclopent-2-en-1-one (5b-*c*)

Following general procedure A gave product **5b-*c*** as a white solid.

Yield: 36 mg (23%); mp 169–171 °C.

IR (KBr): 3394, 3283, 2918, 1682, 1632, 1495, 1441, 1392, 1323, 1286, 1218, 1136, 1047, 988, 889, 765, 691, 623 cm^{-1}.

^1H NMR (400 MHz, MeOD): δ = 7.87–7.79 (m, 2 H), 6.86–6.79 (m, 2 H), 2.86–2.80 (m, 2 H), 2.46–2.39 (m, 2 H), 0.97 (s, 9 H), 0.21 (s, 6 H).

^{13}C NMR (101 MHz, MeOD): δ = 205.4, 160.4, 149.2, 148.3, 130.6, 127.0, 116.1, 32.3, 26.4, 24.8, 19.5, –3.4.

MS (EI, 70 eV): *m*/*z* (%) = 289 (2) $[M]^+$ = 304, 247 (100), 232 (4), 217 (7), 131 (3), 115 (5), 75 (16).

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{17}H_{25}O_3Si$: 305.1567; found: 305.1558.

2-[(*tert*-Butyldimethylsilyl)oxy]-3-phenylcyclohex-2-en-1-one (6a-*c*)

Following general procedure A gave product **6a-*c*** as a white solid.

Yield: 130 mg (86%); mp 41–43 °C.

IR (KBr): 2928, 1670, 1572, 1415, 1249, 1168, 852, 674 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.48–7.41 (m, 2 H), 7.39–7.31 (m, 2 H), 7.31–7.24 (m, 1 H), 2.73 (t, *J* = 6.0 Hz, 2 H), 2.60–2.50 (m, 2 H), 2.13–2.02 (m, 2 H), 0.66 (s, 9 H), 0.00 (s, 6 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 195.8, 144.2, 138.6, 138.4, 128.6, 128.0, 38.5, 31.2, 25.6, 22.9, 18.7, –4.1.

MS (EI, 70 eV): *m*/*z* (%) = 245 (100) $[M – 57]^+$, 167 (4), 141 (4), 128 (4), 115 (5), 103 (3), 91 (6), 75 (26), 57 (4).

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{18}H_{26}O_2Si$: 303.1775; found: 303.1778.

2-[(*tert*-Butyldimethylsilyl)oxy]-3-(4-fluorophenyl)cyclohex-2-en-1-one (6c-*c*)

Following general procedure A gave product **6c-*c*** as a white solid.

Yield: 139 mg (87%); mp 36–38 °C.

IR (KBr): 2928, 1672, 1600, 1509, 1470, 1537, 1223, 1162, 836, 785 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.50–7.39 (m, 2 H), 7.08–7.00 (m, 2 H), 2.70 (t, *J* = 6.0 Hz, 2 H), 2.58–2.51 (m, 2 H), 2.07 (dt, *J* = 12.2, 6.3 Hz, 2 H), 0.68 (s, 9 H), 0.01 (s, 6 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 195.7, 162.4 (FC_{arom} d, *J* = 247.8 Hz), 144.4, 137.0, 134.5 (C_{arom} d, *J* = 3.4 Hz), 130.5 (o-CH_{arom} d, *J* = 8.0 Hz), 115.0 (m-CH_{arom} d, *J* = 21.4 Hz), 38.4, 31.1, 25.7, 22.8, 18.7, -4.1.

MS (EI, 70 eV): *m*/*z* (%) = 263 (100) $[M – 57]^+$, 233 (3), 159 (4), 133 (5), 109 (8), 75 (29).

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{18}H_{26}O_2SiF$: 321.1681; found: 321.1688.

2-Hydroxy-3-(4-nitrophenyl)cyclohex-2-en-1-one (6h-*a*)

Following general procedure A gave a brown solid (78 mg), from which **6h-*a*** (70 mg, 60%) and the impurity 4,4′-dinitro-1,1′-biphenyl (8 mg) were obtained.

IR (KBr): 3406, 3358, 2930, 1647, 1592, 1510, 1494, 1378, 1340, 1289, 1229, 1189, 1163, 1110, 850, 698 cm^{-1}.

^{1}H NMR (400 MHz, MeOD): δ = 8.22–8.17 (m, 2 H), 7.98–7.91 (m, 2 H), 2.79 (t, *J* = 5.9 Hz, 2 H), 2.60 (dd, *J* = 7.3, 6.0 Hz, 2 H), 2.10 (quin, *J* = 6.4 Hz, 2 H).

^{13}C NMR (101 MHz, MeOD): δ = 197.0, 148.0, 146.8, 146.2, 130.4, 126.2, 124.0, 37.5, 29.6, 23.8.

MS (EI, 70 eV): *m*/*z* (%) = 233 (100) [M]$^+$, 216 (52), 205 (35), 186 (55), 158 (21), 129 (24), 115 (63), 102 (37), 91 (38), 77 (47), 63 (27), 51 (33).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{12}O_4N$: 234.0761; found: 234.0761.

2-[(*tert*-Butyldimethylsilyl)oxy]-3-(4-nitrophenyl)cyclohex-2-en-1-one (6h-*c*)

Following general procedure A gave a yellow solid (66 mg), from which **6h-*c*** (55 mg, 32%) and the impurity 4,4′-dinitro-1,1′-biphenyl (11 mg) were obtained. See below for the physical and spectroscopic properties of product **6h-*c*** obtained via general procedure C.

3-Hydroxy-4-phenylfuran-2(5*H*)-one (7a-*a*)

Following general procedure A gave **7a-*a*** as a white solid.

Yield: 60 mg (68%); mp 202–205 °C.

IR (KBr): 3302, 2939, 2457, 1722, 1499, 1453, 1400, 1324, 1167, 759, 687 cm^{-1}.

^{1}H NMR (400 MHz, MeOD): δ = 7.78–7.66 (m, 2 H), 7.47–7.37 (m, 2 H), 7.36–7.24 (m, 1 H), 5.09 (s, 2 H).

^{13}C NMR (101 MHz, MeOD): δ = 172.3, 138.8, 132.2, 129.9, 129.7, 127.5, 127.4, 69.2.

MS (EI, 70 eV): *m*/*z* (%) = 176 (23) [M]$^+$, 131 (23), 103 (100), 91 (7), 77 (18), 65 (5), 63 (6), 51 (15).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{10}H_9O_3$: 177.0546; found: 177.0544.

Coupling of Halodiketones 1–3 with Arylboronic Acids 4 under Aqueous Conditions; General Procedure B

The reaction was conducted at r.t. for 3 h under an air atmosphere in H_2O (1.5 mL) by using **1**, **2** or **3** (0.5 mmol), $ArB(OH)_2$ (0.75 mmol), Et_3N (1.5 mmol), $Pd(OAc)_2$ (5 mol%) and PPh_3 (10 mol%). The mixture was diluted with H_2O and extracted with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4 or $MgSO_4$, filtered and then evaporated to dryness. The crude residue was purified by column chromatography (generally using petroleum ether/EtOAc) to afford the pure product.

2-Methoxy-3-phenylcyclopent-2-en-1-one (5a-*b*)

Following general procedure B on 0.35 mmol scale gave **5a-*b*** as a yellow solid.

Yield: 63 mg (95%).

The physical and spectroscopic properties correspond to the data given above (following general procedure A).

2-Methoxy-3-(*p*-tolyl)cyclohex-2-en-1-one (6f-*b*)

Following general procedure A on 0.37 mmol scale gave **6f-*b*** as a brown oil.

Yield: 70 mg (88%).

The physical and spectroscopic properties correspond to the data given above (following general procedure A).

3-(Methoxymethoxy)-4-(thiophen-2-yl)furan-2(5*H*)-one (7d-*d*)

Following general procedure B gave **7d-*d*** as a yellow solid.

Yield: 75 mg (66%).

The physical and spectroscopic properties correspond to the data given above (following general procedure A).

2-[(*tert*-Butyldimethylsilyl)oxy]-3-phenylcyclopent-2-en-1-one (5a-*c*)

Following general procedure B gave **5a-*c*** as a white solid.

Yield: 93 mg (65%).

The physical and spectroscopic properties correspond to the data given above (following general procedure A).

Coupling of Halodiketones 1 and 2 with Arylboronic Acids 4 (Silyl-Protected Compounds); General Procedure C

The reaction was conducted overnight at 100 °C under an argon atmosphere in toluene/H_2O (10:1, 5 mL) by using of **1** or **2** (0.5 mmol), $ArB(OH)_2$ (0.75 mmol), Na_2CO_3 (1.0 mmol), $Pd(OAc)_2$ (5 mol%) and PPh_3 (10 mol%). After cooling to r.t., the mixture was diluted with H_2O and extracted with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4 or $MgSO_4$, filtered and then evaporated to dryness. The crude residue was purified by column chromatography (generally using petroleum ether/EtOAc) to afford the pure product.

2-[(*tert*-Butyldimethylsilyl)oxy]-3-{4-[(*tert*-butyldimethylsilyl)oxy]phenyl}cyclopent-2-en-1-one (5i-*c*)

Following general procedure C gave **5i-*c*** as a white solid.

Yield: 141 mg (67%); mp 117–118 °C.

IR (KBr): 2957, 2929, 2858, 1707, 1605, 1512, 1373, 1276, 1146, 1108, 916, 845, 782 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87–7.80 (m, 2 H), 6.92–6.83 (m, 2 H), 2.87–2.78 (m, 2 H), 2.49–2.42 (m, 2 H), 0.99 (s, 9 H), 0.97 (s, 9 H), 0.25 (s, 6 H), 0.22 (s, 6 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 203.0, 157.0, 148.3, 145.2, 129.1, 128.0, 120.1, 31.6, 26.1, 25.8, 23.9, 18.7, 18.4, –3.4, –4.2.

MS (EI, 70 eV): *m*/*z* (%) = 418 (0.3) [M]$^+$, 403 (2), 387 (1), 361 (100), 289 (3), 152 (8), 73 (21).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{23}H_{39}O_3Si_2$: 419.2432; found: 419.2425.

2-[(*tert*-Butyldimethylsilyl)oxy]-3-(4-nitrophenyl)cyclohex-2-en-1-one (6h-*c*)

Following general procedure C gave a yellow solid (123 mg), from which **6h-*c*** (119 mg, 69%) and the impurity 4,4′-dinitro-1,1′′-biphenyl (4 mg) were obtained.

IR (KBr): 2927, 1679, 1593, 1517, 1470, 1371, 1343, 1249, 842, 782 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.25–8.17 (m, 2 H), 7.68–7.58 (m, 2 H), 2.73 (t, *J* = 5.9 Hz, 2 H), 2.59 (dd, *J* = 7.4, 5.9 Hz, 2 H), 2.12 (quin, *J* = 6.2 Hz, 2 H), 0.66 (s, 9 H), 0.04 (s, 6 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 195.4, 147.1, 145.5, 145.3, 134.6, 129.6, 123.3, 38.4, 30.6, 25.6, 22.8, 18.7, –3.9.

MS (EI, 70 eV): *m*/*z* (%) = 290 (100) [M – 57]$^+$, 244 (21), 115 (3), 75 (12).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{26}O_4NSi$: 348.1626; found: 348.1613.

Funding Information

This work has been supported by the Estonian Ministry of Education and Research grants IUT 19-32 and IUT23-7 and the Centre of Excellence in Molecular Cell Engineering (No. 2014-2020.4.01.15-0013).

Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0036-1591543.

References

(1) (a) Wang, Z.; Reinus, B. J.; Dong, G. *J. Am. Chem. Soc.* **2012**, *134*, 13954. (b) Tanyeli, C.; Özdemirhan, D. *Tetrahedron* **2005**, *61*, 8212. (c) Utaka, M.; Fujii, Y.; Takeda, A. *Chem. Lett.* **1985**, 1123.
(2) Enholm, E. J.; Moran, K. M.; Whitley, P. E.; Battiste, M. A. *J. Am. Chem. Soc.* **1998**, *120*, 3807.
(3) Trost, B. M.; Schoeder, G. M. *J. Am. Chem. Soc.* **2000**, *122*, 3785.
(4) (a) Paju, A.; Kanger, T.; Pehk, T.; Lindmaa, R.; Müürisepp, A.-M.; Lopp, M. *Tetrahedron: Asymmetry* **2003**, *14*, 1565. (b) Paju, A.; Oja, K.; Matkevitš, K.; Lumi, P.; Järving, I.; Pehk, T.; Lopp, M. *Heterocycles* **2014**, *88*, 981.
(5) (a) Schow, S. R.; Bloom, J. D.; Thompson, A. S.; Winzenberg, K. N.; Smith, A. B. *J. Am. Chem. Soc.* **1986**, *108*, 2662. (b) Kraus, G. A.; Thomas, P. J. *J. Org. Chem.* **1986**, *51*, 503. (c) Trost, B. M.; Dong, G.; Vance, J. A. *Chem. Eur. J.* **2010**, *16*, 6265. (d) Quinkert, G.; Schmalz, H. G.; Walzer, E.; Gross, S.; Kowalczyk-Przewloka, T.; Schierloh, C.; Dürner, G.; Bats, J. W.; Kessler, H. *Liebigs Ann. Chem.* **1988**, *4*, 283.
(6) Namiki, T.; Nishikawa, M.; Itoh, Y.; Uchida, I.; Hasimoto, M. *J. Antibiot.* **1987**, *40*, 1400.
(7) Leblanc, Y.; Roy, P.; Boyce, S.; Brideau, C.; Chan, C. C.; Charleson, S.; Gordon, R.; Grimm, E.; Guay, J.; Leger, S.; Li, C. S.; Riendeau, D.; Visco, D.; Wang, Z.; Webb, J.; Xu, L. J.; Prasit, P. *Bioorg. Med. Chem. Lett.* **1999**, *9*, 2207.
(8) (a) Rao, K. V.; Sadhukhan, A. K.; Veerender, M.; Ravikumar, V.; Mohan, E. V. S.; Dhanvantri, S. D.; Sitaramkumar, M.; Moses Babu, J.; Vyas, K.; Om Reddy, G. *Chem. Pharm. Bull.* **2000**, *48*, 559. (b) Ye, Y.-Q.; Xia, C.-F.; Yang, J.-X.; Yang, Y.-C.; Gao, X.-M.; Du, G.; Yang, H.-Y.; Li, X.-M.; Hu, Q.-F. *Heterocycles* **2014**, *89*, 2177. (c) Haritakun, R.; Rachtawee, P.; Chanthaket, R.; Boonyuen, N.; Isaka, M. *Chem. Pharm. Bull.* **2010**, *58*, 1545.
(9) (a) Weber, V.; Coudert, P.; Rubat, C.; Duroux, E.; Vallee-Goyet, D.; Gardette, D.; Bria, M.; Albuisson, E.; Leal, F.; Gramain, J.-C.; Couqueleta, J.; Madesclairea, M. *Bioorg. Med. Chem.* **2002**, *10*, 1647. (b) Bailly, F.; Queffelec, C.; Mbemba, G.; Mouscadet, J.-F.; Pommery, N.; Pommery, J.; Henichart, J.-P.; Cotelle, P. *Eur. J. Med. Chem.* **2008**, *43*, 1222.
(10) (a) Jõgi, A.; Paju, A.; Pehk, T.; Kailas, T.; Müürisepp, A.-M.; Kanger, T.; Lopp, M. *Synthesis* **2006**, 3031. (b) Jõgi, A.; Paju, A.; Pehk, T.; Kailas, T.; Müürisepp, A.-M.; Lopp, M. *Tetrahedron* **2009**, *65*, 2959.
(11) (a) House, H. O.; Wasson, R. L. *J. Am. Chem. Soc.* **1957**, *79*, 1488. (b) Brussel, W. V.; Vandewalle, M. *Synthesis* **1976**, 39. (c) Reile, I.; Kalle, S.; Werner, F.; Järving, I.; Kudrjashova, M.; Paju, A.; Lopp, M. *Tetrahedron* **2014**, *70*, 3608.
(12) Stetter, H.; Schlenker, W. *Tetrahedron Lett.* **1980**, *21*, 3479.
(13) (a) Feigenbaum, A.; Pete, J. P.; Scholler, D. *J. Org. Chem.* **1984**, *49*, 2355. (b) Tomari, K.; Machiya, K.; Ichimoto, I.; Ueda, H. *Biol. Chem.* **1980**, *44*, 2135. (c) Poquet, A. L.; Feigenbaum, A.; Pete, J. P. *Tetrahedron Lett.* **1986**, *27*, 2975.
(14) (a) Charonnat, J. A.; Mitchell, A. L.; Keogh, B. P. *Tetrahedron Lett.* **1990**, *31*, 315. (b) Horiuchi, A.; Kiyomiya, H.; Takahashi, M.; Suzuki, Y. *Synthesis* **1989**, 785. (c) Kawada, K.; Gross, R. S.; Watt, D. S. *Synth. Commun.* **1989**, *19*, 777.
(15) (a) Garg, N.; Larhed, M.; Hallberg, A. *J. Org. Chem.* **1998**, *63*, 4158. (b) Svennebring, A.; Garg, N.; Nilsson, P.; Hallberg, A.; Larhed, M. *J. Org. Chem.* **2005**, *70*, 4720.
(16) (a) Lee, D.; Newman, S. G.; Taylor, M. S. *Org. Lett.* **2009**, *11*, 5486. (b) Zhang, B.; Jiang, Z.; Zhou, X.; Lu, S.; Li, J.; Liu, Y.; Li, C. *Angew. Chem. Int. Ed.* **2012**, *51*, 13159.
(17) (a) Zhou, Z.; Walleser, P. M.; Tius, M. A. *Chem. Commun.* **2015**, *51*, 10858. (b) Everett, R. K.; Wolfe, J. P. *Org. Lett.* **2013**, *15*, 2926. (c) Zask, A. *J. Org. Chem.* **1992**, *57*, 4558.
(18) Chen, H. S.; Ma, X. P.; Li, Z. M.; Wang, Q. R.; Tao, F. G. *Chin. Chem. Lett.* **2008**, *19*, 1309.
(19) (a) Paju, A.; Kostomarova, D.; Matkevitš, K.; Laos, M.; Pehk, T.; Kanger, T.; Lopp, M. *Tetrahedron* **2015**, *71*, 9313. (b) Paju, A.; Kanger, T.; Mürisepp, A.-M.; Aid, T.; Pehk, T.; Lopp, M. *Tetrahedron* **2014**, *70*, 5843.
(20) (a) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457. (b) Kotha, S.; Lahiri, K.; Kasinath, D. *Tetrahedron* **2002**, *58*, 9633.
(21) Sha, C. K.; Ho, W. Y. *J. Chin. Chem. Soc.* **1999**, *46*, 469.
(22) Tamiri, T.; Ben Ari, J.; Zitrin, S.; Mandelbaum, A. *Int. J. Mass Spectrom.* **2003**, *228*, 191.
(23) Liang, Q.; Xing, P.; Huang, Z.; Dong, J.; Sharpless, K. B.; Li, X.; Jiang, B. *Org. Lett.* **2015**, *17*, 1942.
(24) Yang, C.; Edsall, R. Jr.; Harris, H. A.; Zhang, X.; Manas, E. S.; Mewshaw, R. E. *Bioorg. Med. Chem.* **2004**, *12*, 2553.