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Highly efficient palladium-catalyzed Suzuki–Miyaura reactions of potassium aryltrifluoroborates with 5-iodo-1,3-dioxin-4-ones in water: an approach to α-aryl-β-ketoesters

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ABSTRACT

The high efficient palladium-catalyzed Suzuki–Miyaura reactions of potassium aryltrifluoroborates **3** with 5-iodo-1,3-dioxin-4-ones **2a**–**b** in water as only solvent in the presence of *n*-Bu_4NOH as base is reported. The respective 5-aryl-1,3-dioxin-4-ones **4a**–**n** were obtained in good to excellent yields. The catalyst system provides high efficiency at low load using electronically diverse coupling partners. The obtained 2,2,6-trimethyl-5-aryl-1,3-dioxin-4-ones were transformed into corresponding α-aryl-β-ketoesters **6** by reaction with an alcohol in the absence of solvent.

1. Introduction

Water is the most abundant molecule on Earth and the universal solvent in which the chemistry of most life processes occurs. Interest in water as a solvent was invigorated in the 1990s with the introduction of the concept of *Green Chemistry*.[1] In this context, water, being cheap, safe, non-toxic, and environmentally benign, was soon recognized as perhaps the ultimate 'green' solvent.[2] In view of the potential rewards of replacing hazardous organic solvents with water, researchers took up the academic challenge of developing new synthetic methods that are compatible with the aqueous medium. Another important aspect is the development of chemical reactions in water that can achieve the desired chemical transformations without the need for the protection–deprotection of reactive functional groups or for generation of anhydrous conditions. This fact is particularly important in industrial scale-up processes to replace the use of hazardous and flammable organic solvents. The combination of these aspects is highly challenging and will provide even more benefits for chemical synthesis.

Transition-metal-mediated cross-coupling reactions have revolutionized organic synthesis, and their development transformed the creation of carbon–carbon bonds.[3,4] The palladium-catalyzed coupling of organoboranes with organic halides or triflates under basic conditions (Suzuki–Miyaura coupling) provides a highly versatile and powerful method for the construction of new carbon–carbon bonds.[5,6] This reaction is one of the most frequently applied transition-metal-catalyzed reactions both in academic institutions and in the pharmaceutical industry, and these processes are routinely used in fields ranging from materials science[7] to natural product synthesis[8] and medicinal chemistry.[9] The Suzuki–Miyaura cross-coupling is particularly valued because boron compounds present many important advantages in relation to other organometallic compounds, including ease of accessibility and ultimate product isolation, minimal toxicity, and other important environmental factors.

Diverse organoboronic components have been utilized effectively for Suzuki–Miyaura coupling reactions. However, in recent years, potassium organotrifluoroborate salts (RBF_3K) have received a great deal of attention with regard to their application in organic synthesis[10] and have emerged as some of the most important organometallic reagents for Suzuki–Miyaura cross-coupling reactions due to its important features. These compounds are crystalline solids that are very stable to air and moisture and are easily

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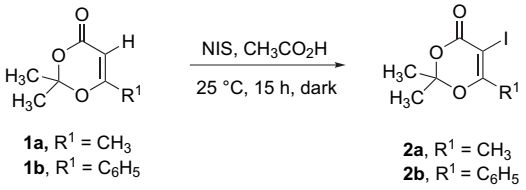
prepared by the addition of inexpensive KHF_2 to a variety of organoboronic intermediates or starting from the easily accessible organolithium[10] or Grignard reagents.[10,11] In addition, the organotrifluoroborate salts are more reactive in Suzuki–Miyaura reactions compared with their boronic acid or boronate ester analogs, and have high compatibility with aqueous media.[6c] Leadbeater and coworkers studied the Suzuki reaction extensively and found that it is possible to perform couplings of aryl halides in neat water using microwave heating at low concentration of palladium as catalyst.[12]

2. Results and discussion

As part of our ongoing research interest in the chemistry of potassium organotrifluoroborate salts,[13] 5-halo-1,3-dioxin-4-ones, and their potential use as intermediates in organic synthesis, we report herein a new and highly efficient method for the synthesis of 5-aryl-1,3-dioxin-4-ones by the Suzuki–Miyaura palladium-catalyzed cross-coupling reaction of 5-iodo-1,3-dioxin-4-ones and potassium aryltrifluoroborate salts in water as solvent.

1,3-Dioxin-4-ones are important building blocks in organic synthesis as direct precursors of 1,3-dicarbonilic compounds.[14] The functionalization of position 5 of the 1,3-dioxin-4-ones with an electrophile leads to products with a potential use as pharmaceuticals and agrochemical intermediates.[15] Thus, the iodination of the readily available 1,3-dioxin-4-ones **1a**–**b** with *N*-iodosuccinimide (NIS) in acetic acid furnishes 5-iodo-1,3-dioxin-4-ones **2a**–**b** in 68–85% isolated yield[15b] as depicted in Scheme 1.



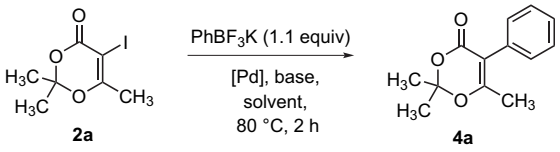
Scheme 1. Synthesis of 5-iodo-1,3-dioxin-4-ones **2a**–**b**.

The preparation of the potassium aryltrifluoroborates **3** was achieved starting from Grignard reagents.[10,11] The addition of trimethylborate to the organomagnesium bromide at −30 °C and treatment with aqueous KHF_2, followed by recrystallization from acetone–Et_2O, was used to prepare the requisite potassium aryltrifluoroborates **3**. Salts of type **3** are air- and water-stable solids that can be stored for extended periods of time at room temperature with no further precautions.[10]

Our initial studies were focused on the development of an optimum set of reaction conditions for the palladium-catalyzed cross-coupling reaction of potassium aryltrifluoroborates with 5-iodo-1,3-dioxin-4-one **2**. For this purpose, several reaction conditions were evaluated, as depicted in Table 1.

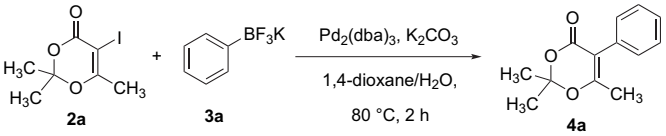
The cross-coupling of **2a** was optimized by using potassium phenyltrifluoroborate (**3a**) as the nucleophile, using several palladium catalysts ($Pd(PPh_3)_4$, $Pd(AcO)_2$, $Pd_2(dba)_3$, and $PdCl_2$), a variety of different bases (e.g., Et_3N, Hunig's base, *i*-Pr_2NH, Li_2CO_3, Na_2CO_3, K_2CO_3, Cs_2CO_3, *n*-Bu_4NOH, and K_3PO_4), and different solvent systems (MeOH, EtOH, *i*-PrOH, THF, DME, and 1,4-dioxane) under both anhydrous and aqueous conditions. Among the examined solvents, the mixture of 1,4-dioxane–H_2O (2:1) (3 mL) and $Pd_2(dba)_3$ (1 mol %) as catalyst provided the best results. In this mixture, not all potassium aryltrifluoroborates and bases were completely soluble, but over time and with applied heat (80 °C) the reaction mixtures homogenized. In the presence of 1 mol % of $Pd_2(dba)_3$ and 1.5 equiv of K_2CO_3 at 80 °C for 2 h, this solvent system furnished the 2,2,6-trimethyl-5-phenyl-1,3-dioxin-4-one **4a** in 80% isolated yield (Scheme 2).

Table 1
Optimization of conditions for the cross-coupling reaction



Entry	Catalyst[a]	Base[b]	Solvent	Yield[c] (%)
1	$PdCl_2$	K_2CO_3	1,4-Dioxane–H_2O[d]	57
2	$Pd(AcO)_2$	K_2CO_3	1,4-Dioxane–H_2O[d]	59
3	$Pd(Ph_3P)_4$	K_2CO_3	1,4-Dioxane–H_2O[d]	65
4	$Pd_2(dba)_3$	K_2CO_3	1,4-Dioxane–H_2O[d]	80
5	$Pd_2(dba)_3$	Cs_2CO_3	1,4-Dioxane–H_2O[d]	59
6	$Pd_2(dba)_3$	*n*-Bu_4NOH	1,4-Dioxane–H_2O[d]	72
7	$Pd_2(dba)_3$	*n*-Bu_4NOH	H_2O	89
8	$Pd_2(dba)_3$	Et_3N	CH_3OH	43
9	$Pd_2(dba)_3$	*i*-Pr_2NH	CH_3OH	47
10	$Pd_2(dba)_3$	*i*-Pr_2NH	CH_3OH	53

[a] 1.0 mol % of palladium catalyst.
[b] 1.5 equiv of base.
[c] Isolated yield of pure product.
[d] 1,4-Dioxane–H_2O, ratio: 2:1.

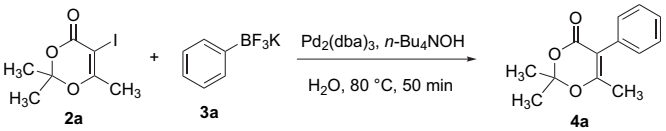


Scheme 2. Synthesis of 2,2,6-trimethyl-5-phenyl-1,3-dioxin-4-one (**4a**).

The reaction demonstrated sensitivity to oxygen and because of this it was necessary to degas the solvent and the base prior to performing the reaction; otherwise, the isolated yield decreased. This cross-coupling reaction takes place with 1,4-dioxane–H_2O (2:1) as the solvent, unlike the commonly used palladium-mediated processes, which employ alcoholic aqueous solvents. Curiously, alcohol–H_2O mixtures did not provide the desired product in satisfactory yields.

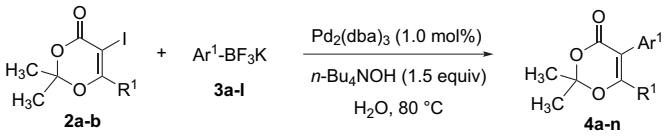
The use of Cs_2CO_3 and *n*-Bu_4NOH as base also provided good results (Table 1, entries 5–7). In light of these results, we decided to evaluate the behavior of the reaction in the presence of 1.5 equiv of base by using only water as the solvent due to the fact that the use of water as solvent is environmentally sound. The effect of base and solvent system on yield was noteworthy. Much to our surprise, when the cross-coupling reaction was performed in water as the solvent in the presence of 1.5 equiv of *n*-Bu_4NOH, an appreciable improvement in the yield was observed, and the desired product (**4a**) was obtained in 89%. Larger excesses of base (3.0 equiv) gave no improvement in the yield.

We evaluated the influence of the organotrifluoroborates counter ion by starting from the tetra-*n*-butylammonium phenyltrifluoroborate salt and found no significant influence on the reaction behavior with respect to yield. Considering that the tetra-*n*-butylammonium aryltrifluoroborate salt must be further prepared and isolated, its use is not experimentally advantageous. This salt is generated in situ by a mixture of potassium aryltrifluoroborate with *n*-Bu_4NOH in aqueous medium.[16] Among the several reaction conditions tested, one in particular is notable (Table 1, entry 7): The treatment of the potassium



Scheme 3. Optimized conditions for the cross-coupling reaction.

Table 2
Cross-coupling reactions of 5-iodo-1,3-dioxin-4-ones **2a–b** with potassium aryltrifluoroborates **3a–n**



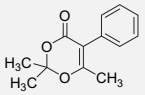
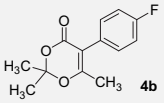
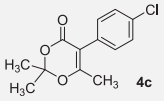
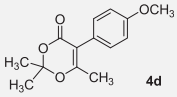
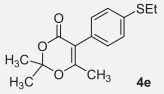
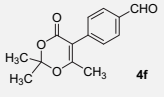
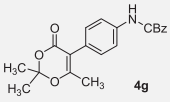
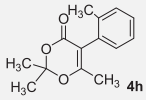
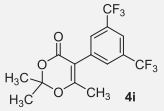
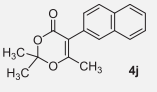
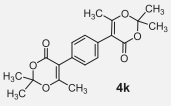
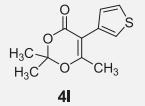
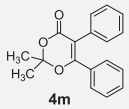
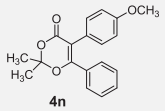
Entry	Ar^1–BF_3K (**3**)[a]	Reaction time (min)	Product (**4**)	Yield[b] (%)
1	$C_6H_5BF_3K$ (**3a**)	50	 **4a**	89
2	4-$FC_6H_4BF_3K$ (**3b**)	55	 **4b**	77
3	4-$ClC_6H_4BF_3K$ (**3c**)	55	 **4c**	79
4	4-$CH_3OC_6H_4BF_3K$ (**3d**)	40	 **4d**	94
5	4-$EtSC_6H_4BF_3K$ (**3e**)	40	 **4e**	91
6	4-$CHOC_6H_4BF_3K$ (**3f**)	70	 **4f**	73
7	4-$CBzNHC_6H_4BF_3K$ (**3g**)	50	 **4g**	82
8	2-$CH_3C_6H_4BF_3K$ (**3h**)	60	 **4h**	78
9	3,4-$(CF_3)_2C_6H_3BF_3K$ (**3i**)	80	 **4i**	67
10	2-$C_{10}H_7BF_3K$ (**3j**)	50	 **4j**	83
11	1,4-$(BF_3K)_2C_6H_4$ (**3k**)	75	 **4k**	76
12	3-C_4H_3S-BF_3K (**3l**)	55	 **4l**	73

Table 2 (*continued*)

Entry	Ar^1–BF_3K (**3**)[a]	Reaction time (min)	Product (**4**)	Yield[b] (%)
13	$C_6H_5BF_3K$ (**3a**)	60	 **4m**	62
14	4-$CH_3OC_6H_4BF_3K$ (**3d**)	50	 **4n**	75

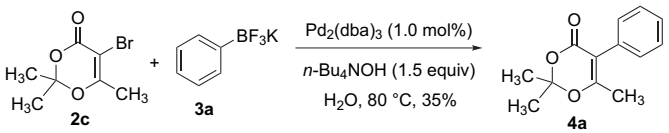
[a] 1.1 equiv of the Ar^1–BF_3K.
[b] Isolated yield of pure product.

phenyltrifluoroborate **3a** (1.1 equiv) with *n*-Bu_4NOH (1.5 equiv) in degassed water (3 mL) under inert atmosphere for 2 min, followed by the addition of $Pd_2(dba)_3$ (1.0 mol %) and 2,2,6-trimethyl-5-iodo-1,3-dioxin-2-one **2** (1.0 equiv) and vigorous stirring for 50 min at 80 °C, afforded the 2,2,6-trimethyl-5-phenyl-1,3-dioxin-2-one (**4a**) in 89% yield after column chromatography (Scheme 3).

These optimal conditions were subsequently applied to the cross-coupling reaction of **2a–b** with different potassium aryltrifluoroborates **3b–l**. As outlined in Table 2, the reaction proceeded with satisfactory yields in all cases. All reactions were monitored by TLC until consumption of **2a** or **2b** was complete. In this methodology, the reaction was tolerant of a variety of functional groups, including ethers, thioethers, aldehyde, and carbamate groups, despite the aqueous and basic conditions. Moreover, potassium aryltrifluoroborates bearing both electron-withdrawing and electron-donating groups react with **2a–b**, affording the desired products in good yields.

ortho-Substituted substrates (Table 2, entry 8) react to provide the coupling products in satisfactory yields. Even in the case of the hindered potassium 2-methyl-phenyltrifluroborate (**3h**), good yield of the desired product **4h** was obtained. The reaction could be scaled up to 1 g of the 5-iodo-1,3-dioxin-4-ones without alteration of the reaction time and yield. Furthermore, analysis of the ^1H NMR and ^{13}C NMR spectra showed that all 5-aryl-1,3-dioxin-4-ones **4a–n** presented data in full agreement with their assigned structures.

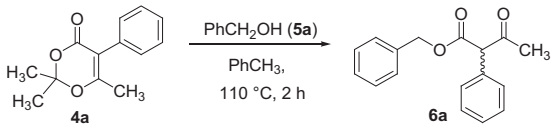
We studied the cross-coupling reaction of 5-bromo-1,3-dioxin-4-one **2c** with potassium aryltrifluoroborate. For this purpose the 2,2,6-trimethyl-5-bromo-1,3-dioxin-4-one was prepared from the 1,3-dioxin-4-one **1a** according to the literature procedures[15] and was submitted to the cross-coupling reaction with potassium phenyltrifluoroborate **3a**. By using the reactions conditions found for the iodide **2a**, the 5-aryl-1,3-dioxin-4-one **4a** was obtained in only 35% isolated yield (Scheme 4). This result is due to the fact the C–Br bond is stronger than the C–I bond and in this way vinyl iodides are more reactive as electrophile compared to vinyl bromides.



Scheme 4. Cross-coupling reaction of the 5-bromo-1,3-dioxin-4-one **2c**.

β-Ketoesters are important building blocks in synthetic organic chemistry, especially in the preparation of heterocyclic compounds.[17] However, classical methodologies for the preparation of β-ketoesters may require harsh reaction conditions and the use of strong bases.

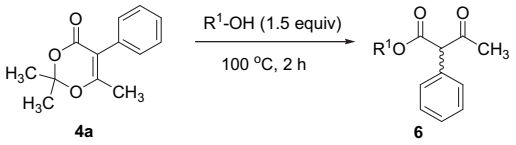
In order to test the potential use of the 5-aryl-1,3-dioxin-4-ones **4** as direct precursors of β-ketoesters, we were interested in the ring opening of the 5-aryl-1,3-dioxin-4-ones in the presence of an alcohol.[15b] For this purpose, the 2,2,6-trimethyl-5-phenyl-1,3-dioxin-4-one **4a** was heated with benzylic alcohol (**5a**) (1.5 equiv) in toluene at 110 °C for 2 h (Scheme 5). The reaction proceeds only with moderate yield (64%). In light of this result, we tested different solvents, reaction times, and elevated temperatures in this reaction; however, in all cases, the yield was never above to 70%.

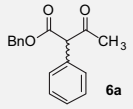
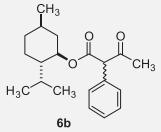
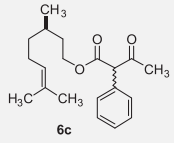
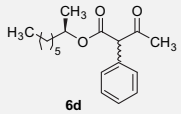
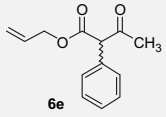


Scheme 5. Synthesis of β-ketoester **6a**.

Next we performed the reaction by simple mixture of the 2,2,6-trimethyl-5-phenyl-1,3-dioxin-4-one **4a** and benzylic alcohol (1.5 equiv) and stirring for 2 h at 100 °C without solvent. Much to our surprise, the respective β-ketoester **6a** was obtained in 93% isolated yield via column chromatography. This very simple condition was extended to a series of different alcohols as depicted in Table 3. The β-ketoesters **6** were obtained in 1:1 ratio of stereoisomers (Table 3).

Table 3
Reaction of the 5-aryl-1,3-dioxin-4-one **4a** with alcohol



Entry	Product (**6**)	Yield[a] (%)
1	 **6a**	93
2	 **6b**	82
3	 **6c**	84
4	 **6d**	88
5	 **6e**	85

[a] Isolated yield of pure product.

The crystal structure of 5-(4-fluorophenyl)-2,2,6-trimethyl-1,3-dioxin-4-one (**4b**) is representative of the class of **4a**–**n** compounds (Fig. 1). Compound **4b** was carefully crystallized from dry methanol to afford the desired crystal. The compound crystallizes as a discrete monoclinic system.[18]

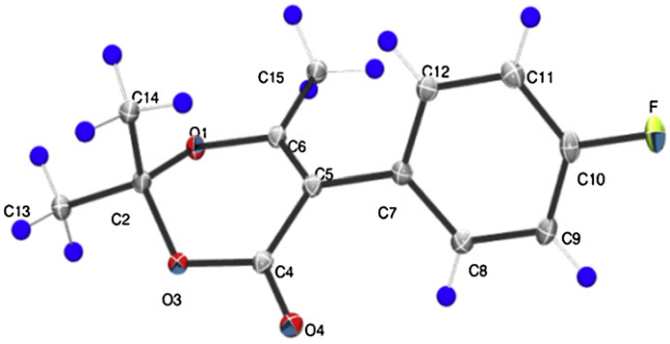


Figure 1. Crystal structure of 5-(4-fluorophenyl)-2,2,6-trimethyl-1,3-dioxin-4-one (**4b**).

3. Conclusion

In summary, we have shown that a range of functionalized potassium aryltrifluoroborates can readily react with 5-iodo-1,3-dioxin-4-ones in water as solvent in the presence of *n*-Bu_4NOH as base. Remarkable functional group compatibility was observed in the starting potassium aryltrifluoroborate, including the presence of a Cl, CF_3, CHO, $N(H)CO_2Bn$, and SC_2H_5. The cross-coupling products were obtained in very good yields and were transformed into corresponding β-ketoesters by reaction with an alcohol in the absence of solvent. This methodology is advantageous relative to many other organometallic-compound-based cross-coupling reactions because of the ready availability, high stability, very low toxicity, mildly nucleophilic character, and unique compatibility with aqueous media of the potassium organotrifluoroborate salts.

4. Experimental

4.1. General

All air-sensitive and/or water-sensitive reactions were carried out under nitrogen atmosphere with dry solvents under anhydrous conditions. Standard syringe techniques were applied for transfer of dry solvents and some air-sensitive reagents. The reactions were monitored by TLC carried out on Merk silica gel (60 F_{254}) by using UV light as visualizant agent and 5% vanillin in 10% H_2SO_4 and heat as developing agents. Baker silica gel (particle size 0.040–0.063 mm) was used for flash chromatography. Toluene was distilled from CaH_2 and stored over sodium-wire. Dry THF was distilled from sodium benzophenone ketyl prior to use. EtOH was dried, distilled from CaH_2, and stored over MS 4 Å. Et_3N was distilled from KOH pellets. NMR spectra were recorded with Bruker DPX 300 (300 MHz) instrument using $CDCl_3$ as solvent and calibrated using tetramethylsilane as internal standard. Chemical shifts are reported in δ parts per million relative to $(CH_3)_4Si$ for ^1H and $CDCl_3$ for ^{13}C NMR. Coupling constants (J) are reported in hertz. Infrared (IR) spectra were obtained from $CHCl_3$ solutions, using a Varian 3100 FT-IR spectrophotometer and wavelengths are reported in cm^{-1}. Mass spectra (MS) were measured on a Shimadzu GC-MS-QP5050A mass spectrometer. The HRMS spectra were measured on a Bruker Daltonics Micro TOF (direct inlet probe).

4.2. Typical procedure for the synthesis of 5-iodo-1,3-dioxin-4-ones (2)[15b]

The preparation of the 2,2,6-trimethyl-5-iodo-1,3-dioxin-4-one (**2a**) is representative. A solution of 2,2,6-trimethyl-1,3-dioxin-4-one **1a** (1.42 g; 10 mmol) and *N*-iodosuccinimide (NIS or NBS for **2c**) (2.92 g; 13 mmol) in acetic acid (25 mL) was stirred for 15 h at room

temperature in the dark. The reaction mixture was diluted with water (30 mL) and extracted with ethyl acetate (3×30 mL). The organic layer was washed with water (20 mL) and dried over $MgSO_4$. The residue obtained after evaporation of the solvent was chromatographed on silica gel (hexane–AcOEt 10:1) to give the 2,2,6-trimethyl-5-iodo-1,3-dioxin-4-one **2a** as pale yellow prisms (1.77 g; 6.8 mmol; 68%); mp 62–63 °C (from Et_2O–hexane).

*4.2.1. 2,2,6-Trimethyl-5-iodo-1,3-dioxin-4-one (**2a**)*[15b]. Mp 62–63 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.70 (s, 6H), 2.31 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.1, 25.0, 62.4, 106.6, 158.1, 169.5. GC–MS: *m*/*z* (relative intensity): 268 (10) [M^+], 210 (62), 167 (58), 142 (75), 127 (15), 43 (100).

*4.2.2. 2,2-Dimethyl-5-iodo-6-phenyl-1,3-dioxin-4-one (**2b**)*[15b]. Yellow prisms. Mp 72–73 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.67 (s, 6H), 7.30–7.47 (m, 3H), 7.8 (d, *J*=8.1 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.5, 70.1, 106.8, 126.3, 128.8, 131.0, 132.1, 161.7, 165.0. GC–MS: *m*/*z* (relative intensity): 330 (13) [M^+], 272 (74), 229 (53), 127 (19), 43 (100).

*4.2.3. 2,2,6-Trimethyl-5-bromo-1,3-dioxin-4-one (**2c**)*[15b]. Pale yellow oil (1.83 g; 8.3 mmol; 83%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.64 (s, 6H), 2.16 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.3, 25.0, 90.0, 106.5, 157.2, 166.5. GC–MS: *m*/*z* (relative intensity): 220 (10) [M^+], 162 (75), 119 (44), 43 (100).

4.3. General procedure for the cross-coupling reaction of potassium aryltrifluoroborates with 5-iodo-1,3-dioxin-4-ones (2a–b)

The synthesis of 2,2,6-trimethyl-5-phenyl-1,3-dioxin-4-one (**4a**) is representative. To a solution of potassium phenyltrifluoroborate (**3a**) (202 mg, 1.1 mmol; 1.1 equiv) in degassed water (3 mL) was added 50% aqueous solution of *n*-Bu_4NOH (0.8 mL; 394 mg, 1.5 mmol; 1.5 equiv). The mixture was vigorously stirred for 2 min under a nitrogen atmosphere. Next, $Pd_2(dba)_3$ (9.1 mg; 1.0 mol%) was added, followed by 2,2,6-trimethyl-5-iodo-1,3-dioxin-2-one (**2a**) (268 mg; 1.0 mmol; 1.0 equiv). The reaction was heated at 80 °C and vigorously stirred for 50 min. After TLC analysis the reaction mixture was cooled to room temperature and was then transferred to an extraction funnel with ethyl acetate (30 mL), and the organic phase was removed. The aqueous phase was extracted with ethyl acetate (3×15 mL), and the combined organic phases were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude 2,2,6-trimethyl-5-phenyl-1,3-dioxin-4-one was purified by flash chromatography (hexanes–EtOAc, 10:1) to afford the product **4a** in 89% yield (193 mg) as a white solid. Mp 51–52 °C.

*4.3.1. 5-Phenyl-2,2,6-trimethyl-4H-1,3-dioxin-4-one (**4a**).* Following the general procedure. 89% yield. White solid, mp 51–52 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.79 (s, 6H), 1.96 (s, 3H), 7.27–7.33 (m, 2H), 7.35–7.42 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.4, 24.9, 105.1, 108.0, 127.4, 128.0, 130.3, 132.2, 161.0, 164.8. GC–MS: *m*/*z* (relative intensity): 218 (4) [M^+], 160 (68), 118 (100), 90 (24), 43 (78). HRMS (ESI, positive) *m*/*z* calcd for $C_{13}H_{14}O_3$: 219.1021 $(M+H)^+$; found: 219.1008 $(M+H)^+$. IR ($CHCl_3$ solution, cm^{-1}): 3015, 2937, 1717, 1632, 1397, 1275, 1219, 1012, 772.

*4.3.2. 5-(4-Fluorophenyl)-2,2,6-trimethyl-4H-1,3-dioxin-4-one (**4b**).* Yellow solid, mp 81–82 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.75 (s, 6H), 1.92 (s, 3H), 7.05 (t, *J*=8.7 Hz, 2H), 7.23 (d, *J*=8.7 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.5, 25.1, 105.4, 107.2, 115.3, 128.3, 132.3, 161.2, 162.3 (d, *J*=240.1 Hz), 165.3. ^{19}F NMR (282 MHz, $CDCl_3$) δ −37.5 (s) (Ar-F). GC–MS: *m*/*z* (relative intensity): 236 (5) [M^+], 178 (61), 136 (87), 108 (21), 43 (100). HRMS (ESI, positive) *m*/*z* calcd for $C_{13}H_{13}O_3F$: 237.0927 $(M+H)^+$; found: 237.0923 $(M+H)^+$. IR ($CHCl_3$ solution, cm^{-1}): 3025, 2940, 1717, 1683, 1512, 1395, 1275, 1203, 1011, 774.

*4.3.3. 5-(4-Chlorophenyl)-2,2,6-trimethyl-4H-1,3-dioxin-4-one (**4c**).* Yellow solid, mp 69–70 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.73 (s, 6H), 1.93 (s, 3H), 7.19 (d, *J*=8.4 Hz, 2H), 7.31 (d, *J*=8.4 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.6, 25.2, 105.5, 107.1, 128.5, 130.9, 132.0, 133.7, 161.0, 165.4. GC–MS: *m*/*z* (relative intensity): 252 (6) [M^+], 184 (51), 152 (62), 124 (10), 43 (100). HRMS (ESI, positive) *m*/*z* calcd for $C_{13}H_{13}ClO_3$: 253.0632 $(M+H)^+$; found: 253.0659 $(M+H)^+$. IR ($CHCl_3$ solution, cm^{-1}): 3015, 2941, 1718, 1632, 1513, 1391, 1275, 1009, 773.

*4.3.4. 5-(4-Methoxyphenyl)-2,2,6-trimethyl-4H-1,3-dioxin-4-one (**4d**).* White solid, mp 83–84 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.78 (s, 6H), 1.95 (s, 3H), 3.83 (s, 3H), 6.93 (d, *J*=8.6 Hz, 2H), 7.19 (d, *J*=8.6 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.3, 24.9, 55.0, 104.9, 107.5, 113.5, 124.3, 131.4, 158.8, 161.3, 164.5. GC–MS: *m*/*z* (relative intensity): 248 (2) [M^+], 190 (100), 148 (77), 134 (20), 120 (24), 91 (12), 43 (60). HRMS (ESI, positive) *m*/*z* calcd for $C_{14}H_{16}O_4$: 249.1127 $(M+H)^+$; found: 249.1124 $(M+H)^+$. IR ($CHCl_3$ solution, cm^{-1}): 3015, 2939, 1712, 1633, 1609, 1514, 1247, 1219, 1020, 771.

*4.3.5. 5-[4-(Ethylthio)phenyl]-2,2,6-trimethyl-4H-1,3-dioxin-4-one (**4e**).* Yellow solid, mp 55–56 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.32 (t, *J*=7.3 Hz, 3H), 1.77 (s, 6H), 1.94 (s, 3H), 2.96 (q, *J*=7.3 Hz, 2H), 7.17 (d, *J*=8.4 Hz, 2H), 7.31 (d, *J*=8.4 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.3, 18.6, 25.1, 27.3, 105.3, 107.6, 128.4, 129.7, 131.0, 136.4, 161.2, 165.1. GC–MS: *m*/*z* (relative intensity): 278 (4) [M^+], 194 (30), 151 (100), 123 (46), 43 (25). HRMS (ESI, positive) *m*/*z* calcd for $C_{15}H_{18}SO_3$, 279.1055 $(M+H)^+$; found: 279.1067 $(M+H)^+$. IR ($CHCl_3$ solution, cm^{-1}): 3016, 2942, 1717, 1632, 1597, 1390, 1250, 1202, 1008, 772.

*4.3.6. 4-(2,2,6-Trimethyl-4-oxo-4H-1,3-dioxin-5-yl)benzaldehyde (**4f**).* White solid, mp 107–108 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.79 (s, 6H), 2.00 (s, 3H), 7.47 (d, *J*=7.8 Hz, 2H), 7.90 (d, *J*=7.8 Hz, 2H), 10.0 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.8, 25.2, 105.7, 107.4, 129.5, 131.3, 135.4, 139.0, 160.6, 165.9, 191.8. GC–MS: *m*/*z* (relative intensity): 246 (2) [M^+], 120 (100), 91 (45), 43 (97). HRMS (ESI, positive) *m*/*z* calcd for $C_{14}H_{14}O_4$: 247.0971 $(M+H)^+$; found: 247.0983 $(M+H)^+$. IR ($CHCl_3$ solution, cm^{-1}): 3026, 2951, 1715, 1703, 1627, 1606, 1397, 1276, 1204, 1011, 779.

*4.3.7. Benzyl 4-(2,2,6-trimethyl-4-oxo-4H-1,3-dioxin-5-yl)phenylcarbamate (**4g**).* White solid, mp 136–137 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.75 (s, 6H), 1.93 (s, 3H), 5.20 (s, 2H), 6.87 (s, 1H), 7.18 (d, *J*=8.4 Hz, 2H), 7.31–7.40 (m, 7H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.6, 25.1, 66.9, 105.3 107.6, 118.5, 127.3, 128.2, 128.3, 128.6, 131.2, 136.1, 137.4, 153.4, 161.4, 165.1. GC–MS: *m*/*z* (relative intensity): 367 (2) [M^+], 283 (5), 196 (13), 132 (31), 91 (100), 43 (57). HRMS (ESI, positive) *m*/*z* calcd for $C_{21}H_{21}NO_5$: 368.1498 $(M+H)^+$; found: 368.1504 $(M+H)^+$. IR ($CHCl_3$ solution, cm^{-1}): 3431, 3015, 2947, 1718, 1701, 1613, 1523, 1275, 1204, 1054, 774.

*4.3.8. 5-o-Tolyl-2,2,6-trimethyl-4H-1,3-dioxin-4-one (**4h**).* White solid, mp 75–76 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.79 (s, 6H), 1.81 (s, 3H), 2.23 (s, 3H), 7.10 (d, *J*=8.1 Hz, 1H), 7.17–7.25 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.2, 19.9, 25.1, 25.5, 105.4, 107.3, 125.9, 128.3, 130.2, 130.9, 131.9, 137.8, 160.8, 165.2. GC–MS: *m*/*z* (relative intensity): 232 (2) [M^+], 174 (86), 156 (46), 128 (43), 104 (30), 77 (15), 43 (100). HRMS (ESI, positive) *m*/*z* calcd for $C_{14}H_{16}O_3$: 233.1178 $(M+H)^+$; found: 233.1197 $(M+H)^+$. IR ($CHCl_3$ solution, cm^{-1}): 3015, 2939, 1716, 1633, 1396, 1272, 1219, 1011, 771.

*4.3.9. 5-[3,5-Bis-(trifluoromethyl)phenyl]-2,2,6-trimethyl-4H-1,3-dioxin-4-one (**4i**).* White solid, mp 97–98 °C. ^{1}H NMR (300 MHz,

$CDCl_3$) δ 1.76 (s, 6H), 1.96 (s, 3H), 7.74 (s, 2H), 7.83 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.7, 25.2, 105.8, 106.2, 121.5, 125.0, 128.5, 131.6 (q, J=37.5 Hz), 134.7, 160.2, 166.5. ^{19}F NMR (282 MHz, $CDCl_3$) δ 13.8 (s, CF_3). GC–MS: m/z (relative intensity): 354 (3) [M^+], 296 (37), 254 (46), 43 (100). HRMS (ESI, positive) m/z calcd for $C_{15}H_{12}O_3F_6$: 355.0769 $(M+H)^+$; found: 355.0775 $(M+H)^+$. IR ($CHCl_3$ solution, cm^{-1}): 3026, 2936, 1719, 1632, 1405, 1280, 1141, 777.

*4.3.10. 5-(Naphthalen-2-yl)-2,2,6-trimethyl-4H-1,3-dioxin-4-one (**4j**).* White solid, mp 119–120 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 1.79 (s, 6H), 2.04 (s, 3H), 7.38 (dd, J=8.4, 1.8 Hz, 1H), 7.44–7.49 (m, 2H), 7.72 (s, 1H), 7.79–7.85 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.6, 25.1, 105.3, 108.1, 126.0, 126.1, 127.5, 127.8, 127.9, 128.2, 129.6, 129.8, 132.6, 133.0, 161.2, 165.3. GC–MS: m/z (relative intensity): 268 (2) [M^+], 184 (27), 141 (100), 115 (23), 43 (27). HRMS (ESI, positive) m/z calcd for $C_{17}H_{16}O_3$, 269.1178 $(M+H)^+$; found: 269.1186 $(M+H)^+$. IR ($CHCl_3$ solution, cm^{-1}): 3015, 2938, 1716, 1628, 1398, 1277, 1203, 1026, 772.

*4.3.11. 5,5′-(1,4-Phenylene)-bis-(2,2,6-trimethyl-4H-1,3-dioxin-4-one) (**4k**).* White solid, mp 171–172 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 1.77 (s, 12H), 2.14 (6H), 7.34 (s, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.9, 25.8, 101.2, 107.8, 130.1, 158.7, 167.2. GC–MS: m/z (relative intensity): 358 (1) [M^+], 217 (32), 141 (21), 43 (100). HRMS (ESI, positive) m/z calcd for $C_{20}H_{22}O_6$: 359.1495 $(M+H)^+$; found: 359.1499 $(M+H)^+$. IR ($CHCl_3$ solution, cm^{-1}): 3016, 2948, 1718, 1630, 1391, 1275, 1208, 1010, 772.

*4.3.12. 2,2,6-Trimethyl-5-(thiophen-3-yl)-4H-1,3-dioxin-4-one (**4l**).* Yellow oil. ^1H NMR (300 MHz, $CDCl_3$) δ 1.71 (s, 6H), 2.01 (s, 3H), 7.05 (dd, J=4.9, 1.2 Hz, 1H), 7.21 (dd, J=3.0, 1.2 Hz, 1H), 7.28 (dd, J=4.9, 3.0 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.8, 25.1, 103.5, 105.2, 124.8, 124.9, 129.3, 132.0, 160.8, 165.2. GC–MS: m/z (relative intensity): 224 (10) [M^+], 166 (100), 124 (91), 96 (42), 70 (33), 57 (25), 43 (28). HRMS (ESI, positive) m/z calcd for $C_{11}H_{12}SO_3$: 225.0506 $(M+H)^+$; found: 225.0519 $(M+H)^+$. IR ($CHCl_3$ solution, cm^{-1}): 3010, 2941, 1719, 1630, 1270, 1209, 1012, 778.

*4.3.13. 2,2-Dimethyl-5,6-diphenyl-1,3-dioxin-4-one (**4m**).* White solid. Mp 151–152 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 1.78 (s, 6H), 7.29 (d, J=8.2 Hz, 2H), 7.38–7.56 (m, 6H), 7.88 (d, J=8.0 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.1, 102.5, 104.8, 127.1, 127.8, 128.2, 128.5, 128.7, 128.8, 130.1, 132.3, 161.7, 168.2. GC–MS: m/z (relative intensity): 280 (3) [M^+], 225 (56), 175 (35), 120 (27), 105 (100), 91 (45), 77 (20). HRMS (ESI, positive) m/z calcd for $C_{18}H_{16}O_3$: 281.1178 $(M+H)^+$; found: 281.1190 $(M+H)^+$. IR ($CHCl_3$ solution, cm^{-1}): 3011, 2940, 1718, 1632, 1273, 1207, 1010, 779.

*4.3.14. 5-(4-Methoxyphenyl)-2,2-dimethyl-6-phenyl-1,3-dioxin-4-one (**4n**).* White solid. Mp 175–173 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 1.81 (s, 6H), 3.85 (s, 3H), 6.93 (d, J=8.1 Hz, 2H), 7.31 (d, J=8.1 Hz, 2H), 7.38–7.50 (m, 3H), 7.95 (d, J=8.2 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.8, 56.4, 101.6, 103.5, 113.8, 125.9, 126.6, 127.8, 128.3, 128.8, 139.4, 146.3, 160.9, 168.5. GC–MS: m/z (relative intensity): 310 (16) [M^+], 282 (45), 252 (76), 233 (25), 207 (10), 152 (21), 103 (42), 77 (13). HRMS (ESI, positive) m/z calcd for $C_{19}H_{18}O_4$: 311.1284 $(M+H)^+$; found: 311.1290 $(M+H)^+$. IR ($CHCl_3$ solution, cm^{-1}): 3010, 2942, 1718, 1635, 1279, 1207, 779.

4.4. General procedure for reaction of 5-phenyl-2,2,6-trimethyl-1,3-dioxin-4-one with benzylic alcohol

The preparation of benzyl 3-oxo-2-phenylbutanoate (**6a**) is representative. A mixture of 5-phenyl-2,2,6-trimethyl-1,3-dioxin-4-one **4a** (109 mg; 0.50 mmol; 1.0 equiv) and benzylic alcohol (81 mg; 0.75 mmol; 1.5 equiv) under a nitrogen atmosphere was stirred at 100 °C for 2 h. The reaction was monitored by TLC until consumption of **4a** was complete. The crude product **6a** was purified by column chromatography in hexanes–ethyl acetate (98:2), affording **6a** as a colorless oil in 93% yield (124 mg).

*4.4.1. Benzyl 3-oxo-2-phenylbutanoate (**6a**).* Colorless oil. ^1H NMR (300 MHz, $CDCl_3$) δ 1.85 (s, 3H), 2.15 (s, 3H), 4.72 (s, 1H), 5.11 (d, J=15.0 Hz, 1H), 5.40 (d, J=15.0 Hz, 1H), 7.14–7.39 (m, 10H), 12.9 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 27.2, 62.4, 71.2, 127.4, 128.0, 128.2, 128.4, 128.5, 129.1, 130.3, 132.2, 164.8, 206.2. GC–MS: m/z (relative intensity): 268 (4) [M^+], 208 (16), 160 (30), 118 (82), 91 (100), 43 (78). HRMS (ESI, positive) m/z calcd for $C_{13}H_{14}O_3$: 219.1021 $(M+H)^+$; found: 219.1008 $(M+H)^+$. IR ($CHCl_3$ solution, cm^{-1}): 3015, 2937, 1717, 1632, 1397, 1275.

*4.4.2. (R+S)-(1R,2S,5R)-2-Isopropyl-5-methylcyclohexyl 3-oxo-2-phenylbutanoate (**6b**).* Colorless oil. ^1H NMR (300 MHz, $CDCl_3$) (keto+enol) δ 0.73 (d, J=7.2 Hz, 3H), 0.86 (d, J=7.1 Hz, 3H), 0.95 (d, J=7.1 Hz, 3H), 1.52–1.76 (m, 6H), 1.84 (s, 3H), 1.88–2.09 (m, 3H), 2.18 (s, 3H), 4.66 (s, 1H), 4.73–4.89 (m, 1H), 7.11 (d, J=8.5 Hz, 2H), 7.26–7.37 (m, 3H), 13.1 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) (keto-+enol) δ 15.9, 16.1, 20.6, 20.7, 21.9, 23.2, 23.3, 25.9, 26.0, 31.3, 31.4, 34.1, 40.5, 46.6, 46.9, 65.9, 75.8, 104.7, 126.7, 127.8, 128.1, 128.7, 129.3, 131.1, 132.8, 132.9, 135.3, 168.1, 172.2, 173.5, 201.5. GC–MS: m/z (relative intensity): 316 (4) [M^+], 178 (20), 160 (23), 136 (28), 118 (100), 83 (56), 69 (34), 55 (24), 43 (64). HRMS (ESI, positive) m/z calcd for $C_{20}H_{28}O_3$: 317.2117 $(M+H)^+$; found: 317.2108 $(M+H)^+$. IR ($CHCl_3$ solution, cm^{-1}): 3009, 2941, 1757, 1729, 1638, 1510, 1285.

*4.4.3. (R+S)-(R)-(3,7-Dimethyl-oct-6-enyl)-3-oxo-2-phenylbutanoate (**6c**).* Colorless oil. ^1H NMR (300 MHz, $CDCl_3$) (keto-+enol) δ 0.88 (d, J=7.2 Hz, 3H), 1.23–1.50 (m, 4H), 1.61 (s, 3H), 1.70 (s, 3H), 1.82–1.96 (m, 2H), 2.14 (s, 3H), 2.23 (s, 3H), 4.12 (t, J=7.3 Hz, 2H), 4.62 (s, 1H), 5.09 (t, J=6.0 Hz, 1H), 7.23–7.51 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$) (keto+enol) δ 18.9, 19.1, 20.8, 23.1, 24.4, 27.8, 35.5, 37.6, 62.4, 70.3, 124.5, 127.5, 128.4, 129.1, 131.8, 138.5, 169.8, 174.3, 105.7, 203.7. GC–MS: m/z (relative intensity): 316 (2) [M^+], 274 (33), 179 (48), 160 (100), 138 (44), 118 (77), 95 (52), 81 (62), 69 (70), 55 (47), 43 (66), 41 (89). HRMS (ESI, positive) m/z calcd for $C_{20}H_{28}O_3$: 317.2117 $(M+H)^+$; found: 317.2123 $(M+H)^+$. IR ($CHCl_3$ solution, cm^{-1}): 3010, 2945, 1753, 1728, 1630, 1513, 1275.

*4.4.4. (S+R)-(R)-(Octan-2-yl)-3-oxo-2-phenylbutanoate (**6d**).* Colorless oil. ^1H NMR (300 MHz, $CDCl_3$) (keto+enol) δ 0.88 (t, J=7.3 Hz, 3H), 1.25–1.31 (m, 8H), 1.37 (d, J=7.2 Hz, 3H), 1.53 (q, J=7.3H, 2H), 2.13 (s, 3H), 2.24 (s, 3H), 4.07 (sext, J=7.3 Hz, 1H), 4.40 (s, 1H), 7.20–7.35 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$) (keto-+enol) δ 14.1, 20.2, 22.7, 23.1, 27.8, 29.0, 29.3, 31.8, 36.7, 62.7, 72.3, 103.4, 128.1, 128.3, 129.7, 134.5, 168.0, 169.8, 174.3, 203.6. GC–MS: m/z (relative intensity): 290 (2) [M^+], 247 (23), 177 (32), 133 (25), 113 (35), 77 (12), 57 (13), 43 (100). HRMS (ESI, positive) m/z calcd for $C_{18}H_{26}O_3$: 291.1960 $(M+H)^+$; found: 291.1978 $(M+H)^+$. IR ($CHCl_3$ solution, cm^{-1}): 3012, 2947, 1754, 1729, 1631, 1510, 1279.

*4.4.5. Allyl 3-oxo-2-phenylbutanoate (**6e**).* Colorless oil. ^1H NMR (300 MHz, $CDCl_3$) (keto+enol) δ 2.13 (s, 3H), 2.25 (s, 3H), 4.49 (s, 1H), 4.75 (d, J=6.1 Hz, 2H), 5.28 (dd, J=16.3, 3.2 Hz, 1H), 5.42 (dd, J=10.1, 3.2 Hz, 1H), 6.06 (dd, J=16.3, 10.1 Hz, 1H), 12.7 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) (keto+enol) δ 23.5, 27.8, 62.6, 78.6, 101.2, 118.1, 128.3, 128.7, 129.0, 132.5, 133.9, 168.3, 169.1, 172.8, 202.8. GC–MS: m/z (relative intensity): 218 (2) [M^+], 177 (23), 175 (32), 43

(100), 41 (79). HRMS (ESI, positive) m/z calcd for $C_{13}H_{14}O_3$: 219.1021 $(M+H)^+$; found: 219.1030 $(M+H)^+$.

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References and notes

1. Sheldon, R. A.; Arends, I.; Henefeld, U. *Green Chemistry and Catalysis*; Wiley-VCH: Weinheim, Germany, 2007.
2. (a) Li, C.-J.; Chan, T.-H. *Comprehensive Organic Reactions in Aqueous Media*, 2nd ed.; Wiley-VCH: Hoboken, NJ, 2007; (b) Lindström, U. M. *Organic Reactions in Water: Principles, Strategies, and Applications*; Blackwell: Oxford, UK, 2007; (c) Blackmand, D. G.; Armstrong, A.; Coombe, V.; Wells, A. *Angew. Chem., Int. Ed.* **2007**, *46*, 3798.
3. de Meijere, A.; Diederich, F. *Metal-Catalyzed Cross-Coupling Reactions*, 2nd ed.; Wiley-VCH: Weinheim, 2004.
4. Negishi, E. *Handbook of Organopalladium Chemistry for Organic Synthesis*; Wiley: New York, NY, 2002.
5. For reviews concerning Suzuki–Miyaura cross-coupling reactions, see: (a) Kotha, S.; Lahiri, K.; Kashinath, D. *Tetrahedron* **2002**, *58*, 9633–9695; (b) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457–2483.
6. (a) Suzuki, A. In *Boronic Acids. Preparation and Applications in Organic Synthesis and Medicine*; Hall, D. G., Ed.; Wiley-VCH: Weinheim, 2005; (b) Miyaura, N. *Top. Curr. Chem.* **2002**, *119*, 11–59; (c) Molander, G. A.; Ellis, N. *Acc. Chem. Res.* **2007**, *40*, 275–286; (d) Anderson, K. W.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2005**, *44*, 6173–6177.
7. (a) Yang, X.; Dou, X.; Müllen, K. *Chem. Asian J.* **2008**, *3*, 759–762; (b) Grimsdale, A. C.; Müllen, K. *Macromol. Rapid Commun.* **2007**, *28*, 1676–1702; (c) Kim, J.; Swager, T. M. *Nature* **2001**, *411*, 1030–1034.
8. Nicolaou, K. C.; Bulger, P. G.; Sarlah, D. *Angew. Chem., Int. Ed.* **2005**, *44*, 4442–4489.
9. King, A. O.; Yasuda, N. In *Organometallics in Process Chemistry*; Larsen, R. D., Ed.; Springer: Berlin, 2004; pp 205–246.
10. (a) Darses, S.; Genêt, J.-P. *Chem. Rev.* **2008**, *108*, 288–325; (b) Stefani, H. A.; Cella, R.; Vieira, A. S. *Tetrahedron* **2007**, *63*, 3623–3658; (c) Molander, G. A.; Figueroa, R. *Aldrichimica Acta* **2005**, *38*, 49–56; (d) Molander, G. A.; Rivero, M. R. *Org. Lett.* **2002**, *4*, 107–109; (e) Molander, G. A.; Ham, J. *Org. Lett.* **2006**, *8*, 2031–2034.
11. Frohn, H.-J.; Franke, H.; Fritzen, P.; Bardin, V. V. *J. Organomet. Chem.* **2000**, *598*, 127–135.
12. (a) Leadbeater, N. E.; Marco, M. *J. Org. Chem.* **2003**, *68*, 5660–5667; (b) Leadbeater, N. E.; Marco, M. *Angew. Chem., Int. Ed.* **2003**, *42*, 1407–1409; (c) Leadbeater, N. E.; Marco, M. *J. Org. Chem.* **2003**, *68*, 888–892; (d) Leadbeater, N. E.; Marco, M. *Org. Lett.* **2002**, *4*, 2973–2976; (e) Arvela, R. K.; Leadbeater, N. E.; Sangi, M. S.; Williams, V.; Granados, P.; Singer, R. D. *J. Org. Chem.* **2005**, *70*, 161–168; (f) Chanthavong, F.; Leadbeater, N. E. *Tetrahedron Lett.* **2006**, *47*, 1909–1912.
13. (a) Cella, R.; Cunha, R. L. O. R.; Reis, A. E. S.; Pimenta, D. C.; Klitzke, C. F.; Stefani, H. A. *J. Org. Chem.* **2006**, *71*, 244–250; (b) Vieira, A. S.; Ferreira, F. P.; Fiorante, P. F.; Guadagnin, R. C.; Stefani, H. A. *Tetrahedron* **2008**, *64*, 3306–3314; (c) Vieira, A. S.; Fiorante, P. F.; Hough, T. L. S.; Ferreira, F. P.; Lüdtke, D. S.; Stefani, H. A. *Org. Lett.* **2008**, *10*, 5215–5218; (d) Vieira, A. S.; Fiorante, P. F.; Zukerman-Schpector, J.; Alves, D.; Botteselle, G. V.; Stefani, H. A. *Tetrahedron* **2008**, *64*, 7234–7241; (e) Guadagnin, R. C.; Suganuma, C. A.; Singh, F. V.; Vieira, A. S.; Cella, R.; Stefani, H. A. *Tetrahedron Lett.* **2008**, *49*, 4713–4716; (f) Botteselle, G. V.; Hough, T. L. S.; Venturoso, R. C.; Cella, R.; Vieira, A. S.; Stefani, H. A. *Aust. J. Chem.* **2008**, *61*, 870–873.
14. (a) D'Annibale, A.; Pesce, A.; Resta, S.; Trogolo, C. *Tetrahedron Lett.* **1996**, *37*, 7429–7432; (b) Chiang, Y.; Guo, H.-X.; Kresge, A. J.; Tee, O. S. *J. Am. Chem. Soc.* **1996**, *118*, 3386–3391; (c) Clemens, R. J.; Hyatt, J. A. *J. Org. Chem.* **1985**, *50*, 2431–2435; (d) Clemens, R. J.; Witzeman, J. S. *J. Am. Chem. Soc.* **1989**, *111*, 2186–2193; (e) Sato, M.; Ogasawara, H.; Yoshizumi, E.; Kato, T. *Chem. Pharm. Bull.* **1983**, *31*, 1902–1909; (f) Sato, M.; Ogasawara, H.; Oi, K.; Kato, T. *Chem. Pharm. Bull.* **1983**, *31*, 1896.
15. (a) Vu, V. A.; Bérillon, L.; Knochel, P. *Tetrahedron Lett.* **2001**, *42*, 6847–6850; (b) Iwaoka, T.; Murohashi, T.; Katagiri, N.; Sato, M.; Kaneko, C. *J. Chem. Soc., Perkin Trans. 1* **1992**, 1393–1397; (c) Hayashizaki, K.; Usui, Y.; Tsutsumi, Y.; Go, A. *Jpn. Kokai Tokkyo Koho* **1995**, 11 pp; CAN, 123:256690.
16. Batey, R. A.; Quach, T. D. *Tetrahedron Lett.* **2001**, *42*, 9099–9103.
17. (a) Carey, F. A.; Sundberg R. J. *Advanced Organic Chemistry, Part B: Reactions and Synthesis*, 4th ed.; Springer: New York, NY, 2001; (b) Roy, O.; Riahi, A.; Hénin, F.; Muzart, J. *Eur. J. Org. Chem.* **2002**, 3986–3994.
18. Zukerman-Schpector, J.; Vieira, A. S.; Stefani, H. A.; Tiekink, E. R. T. *Acta Crystallogr., Sect. E* **2009**, *E65*, o1694. Complete structural details have been published elsewhere, where it is shown that the compound crystallizes as a discrete molecule in a monoclinic system.