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J. Org. Chem., **Just Accepted Manuscript** • Publication Date (Web): 04 Apr 2019

Just Accepted

ACS Publications

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Tandem α-Arylation/Cyclization of 4-Haloacetoacetates with Arynes: A Metal-Free Approach towards 4-Aryl-3-(2*H*)-Furanones

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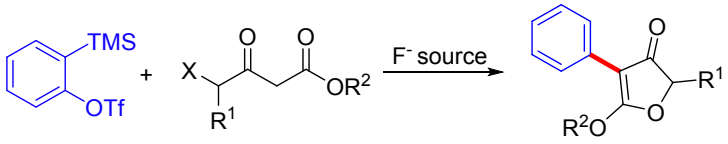
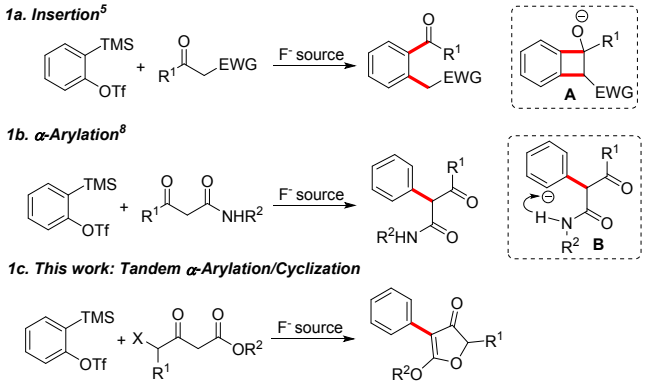
Supporting Information Placeholder



ABSTRACT: An efficacious, metal-free strategy has been developed for the synthesis of 4-aryl-3-(2*H*)-furanones. The reaction proceeds *via* the nucleophilic addition of an active methylene compound to the aryne followed by ring closing of the adduct. The reaction proceeds under mild conditions, is applicable for gram scale synthesis of 4-aryl-3-(2*H*)-furanones and is general for a range of substituted arynes and haloacetates.

The chemistry of arynes,[1] and the associated primarily metal-free methodologies[2] have been in the limelight since the introduction of their fluoride induced generation from *ortho*-silyl aryltriflates.[3] These highly reactive intermediates have been skilfully utilized in a variety of cycloadditions,[4] insertions,[5] multicomponent reactions[6] and also in the total synthesis of natural products.[7] The extreme reactivity of arynes can be attributed to factors such as high electrophilicity (associated with the low-lying LUMO) and the strained carbon-carbon triple bond. These features have also triggered research on the reactivity of neutral nucleophiles towards arynes which has resulted in excellent methodologies for arylation.[1] In contrast, the addition of 1,3-diactivated methylene species across the aryne carbon-carbon triple bond have lead to the generation of 1,2-disubstituted arenes *via* an insertion pathway.[5] Tambar and Stoltz first reported the insertion of β-ketoesters into arynes which proceeded through a formal [2+2] cycloaddition/fragmentation cascade *via* the benzocyclobutene intermediate **A** (Scheme 1a).[5b] Later, several groups reported the insertion of different 1,3-diactivated methylene species such as cyanomethyldiphenylphosphine oxide,[5c] p-toleuenesulfonylacetonirile,[5d] β-keto sulfones[5e] or β-ketophosphonates[5f] into arynes (Scheme 1a). C-Arylation of 1,3-dicarbonyl compounds with arynes was effected by the groups of Mhaske and Rodriguez (Scheme 1b).[8] They used malonamides[8a] and β-ketoamides[8b] which participated in an α-arylation by exploiting the presence of a secondary amide NH proton which transfers quickly to the intermediate aryl anion **B** (Scheme 1b) thereby preventing the insertion of arynes with 1,3-dicarbonyls. Recently, Mohanan and co-workers reported a decarbethoxylative arylation strategy employing arynes and fluoromalonamates towards α-aryl-α-fluoroacetamides.[9]

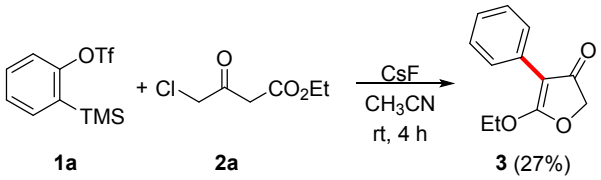
Scheme 1. Reactions of 1,3-dicarbonyl compounds with arynes: Insertion *vs* arylation



The 3-(2*H*)-furanone moiety is found as a core structure inmany natural products; e g. in bullatenone, jatrophone, geiparvarin.[10] Furthermore, a wide range of biological properties such as antiulcer, antiallergic, anti-inflammatory and antitumor activities have been reported for substituted 3-(2*H*)-furanones which makes them interesting targets for organic and medicinal chemists.[11] The known synthetic routes towards this heterocyclic motif include transformations of substituted furans, cyclizations of α-hydroxy-1,3-diketones and allenic hydroxy ketones, transition-metal and organo-catalyzed protocols.[10c, 12] Recently, we have also reported on the synthesis of 4-substituted-3-(2*H*)-furanones by the Pd-catalyzed reaction of 4-haloacetoacetates with activated alkenes, imines and diazocompounds.[13] Inspired by the reports on the reactions of 1,3-diactivated methylene species and arynes and reflecting our continued interest in the development of synthetic protocols towards 4-substituted 3-(2*H*)-furanones, we speculated that a reaction of 4-haloacetoacetate with an aryne would result in a new methodology for accessing 4-aryl-3-(2*H*)-furanones *via* a tandem *α*-arylation/cyclization pathway (Scheme 1c).

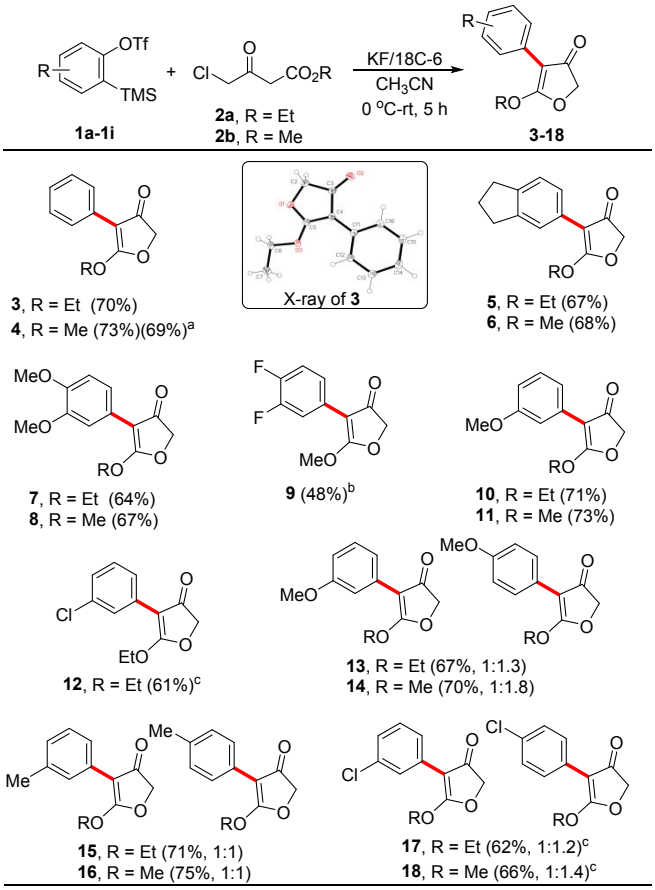
We initiated the investigations with 2-(trimethylsilyl)phenyl trifluoromethanesulfonate **1a** and ethyl 4-chloroacetoacetate **2a** as substrates. The first reaction of **1a** with **2a** was perfomred in the presence of 5 equivalents of CsF (which is the F^- source for the generation of benzyne and also a base) in CH_3CN at room temperature. As expected, 4-phenyl-3-(2*H*)-furanone **3** was isolated from the reaction in 27% yield after 4 h (Scheme 2).

Scheme 2. Synthesis of 4-aryl-3-(2*H*)-furanone from benzyne and 4-chloroacetoacate



The optimization of the reaction conditions were continued with **1a** and **2a** and was found to be a combination of 1.25 equivalents of benzyne precursor, 1.0 equivalent of 4-haloacetoacetate, 5.0 equivalents of KF/18C-6 in CH_3CN at 0 °C, and subsequent stirring at room temperature for 5 h.[14] These optimized conditions for the tandem *α*-arylation/cyclization methodology were utilized for studying the generality of differently substituted arynes (Table 1). Both ethyl **2a** and methyl acetoacetates **2b** participated in the cascade reaction with simple benzyne affording the corresponding 4-phenyl-furanones **3** and **4** in 70% and 73% yields respectively. The compound **4** was also made on the gram scale and that too in good yields (69%). The reactions of **2a** and **2b** with 6-(trimethylsilyl)-2,3-dihydro-1*H*-inden-5-yl triflate afforded the expected products **5** and **6** in good yields. Disubstituted aryne precursors such as 4,5-dimethoxy-*ortho*-silylphenyl triflate and 4,5-difluoro-*ortho*-silylphenyl triflate also participated in the tandem reaction with 4-haloacetoacetates furnishing the 4-arylated furanones **7-9** in moderate to good yields. Importantly, the reaction of 4,5-difluoro-*ortho*-silylphenyl triflate was found to be complete in 2 h at 0 °C. Interestingly, the fluoride-induced tandem reaction of 3-methoxy-1,2-benzyne with **2a** and **2b** afforded furanones **10** and **11** as single regioisomers and in good yields. High regiospecificity was also observed in the reaction between 3-chloro-1,2-benzyne and ethyl-4-chloroacetoacetate **2a** wherein the product **12** was isolated in 61% yield. Nevertheless, the reactions of some other 4-substituted-1,2-benzynes with 4-chloroacetoacetates afforded an inseparable mixture of regioisomers. In the case of 4-methoxybenzyne the products **13** and **14** were obtained as a mixture of regioisomers in the ratios 1:1.3 and 1:1.8 respectively. Whereas, the reactions of **2a** and **2b** with 4-methyl benzyne afforded the products **15** and **16** in good yields but as 1:1 regioisomeric mixtures. The reactions of 4-chloro benzyne with **2a** and **2b** also afforded the corresponding substituted furanones **17-18** as mixtures of regioisomers and in slightly lower yields than the former.

Table 1. Generality of 4-aryl-3-(2*H*)-furanone synthesis with various arynes



Reaction conditions: **1** (1.25 equiv.), **2** (1.0 equiv.), KF (5.0 equiv.), 18C-6 (5.0 equiv.), CH_3CN (4.0 mL), 0 °C-rt, 5 h. [a] started with 1.0 gm of **2b**, [b] 0 °C, 2 h. [c] 0 °C, 4 h.

We then turned our attention in bringing variations to the 4-haloacetoacetate part and thereby chose ethyl 4-bromo-3-oxopentanoate **2c** with the idea of introducing a methyl group at the second position of the 3(2*H*)-furanone moiety (Table 2). The reaction was found to work well with simple benzyne which afforded the 2-methyl-4-phenyl-3(2*H*)-furanone **19** in 69% yield. A 1.2:1 regioisomeric mixture of substituted furanones **20** was obtained in good yield by the reaction of **2c** with 4-methyl benzyne. However, our attempt to introduce two methyl groups at the second position of 3(2*H*)-furanone with

ethyl 4-bromo-4-methyl-3-oxopentanoate **2d** was unsuccessful (intractable reaction mixture) even on heating.

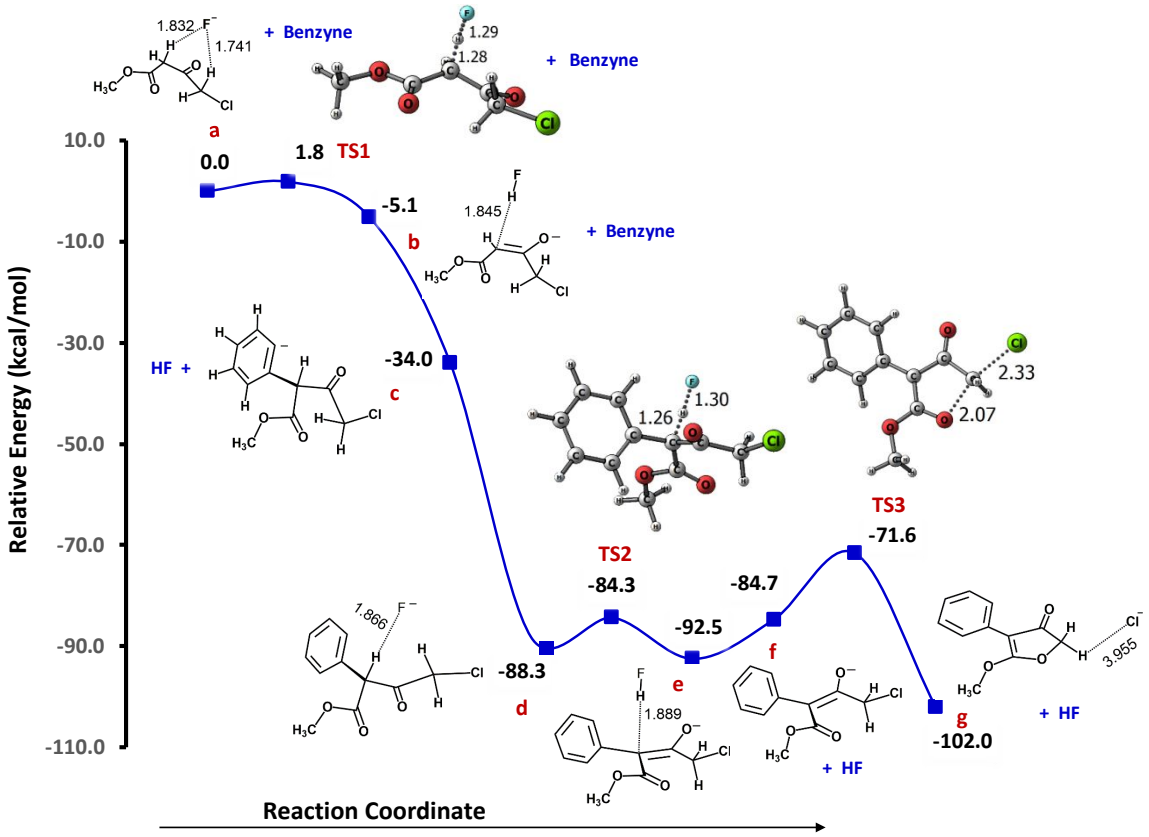
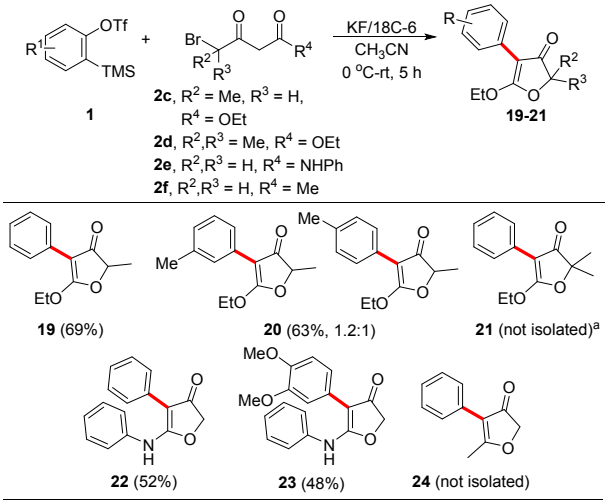


Figure 1. Energy profile for the mechanism of the formation of 4-aryl-3-(2H)-furanone.

Our next effort was to check the reactivity of 4-bromo-3-oxo-*N*-phenylbutanamide **2e** toward the present tandem reaction. The reactions with unsubstituted benzyne (**1a**) and dimethoxy benzyne (**1c**) afforded substituted furanones **22** & **23** in moderate yields. To our dismay, the reaction of 1-bromopentane-2,4-dione **2f** failed to furnish the expected product **24** under the optimized conditions.

Table 2. Generality of 4-aryl-3-(2*H*)-furanone synthesis with various 4-haloacetoacates

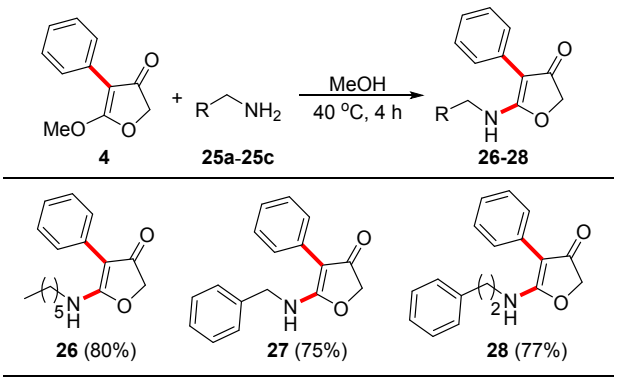


Reaction conditions: **1** (1.25 equiv.), **2** (1.0 equiv.), KF (5.0 equiv.), 18C-6 (5.0 equiv.), CH_3CN (4.0 mL), 0 °C-rt, 5 h. [a] 60 °C, 6 h.

A plausible mechanism for the formation of 4-aryl-3-(2*H*)-furanone (Figure 1) is computed using M06L/SMD/6-311G(d,p) level density functional theory (SI). The fluoride-induced formation of enolate (**a** to **b** *via* **TS1**) is nearly barrier-less and the subsequent formation of the anionic benzyne adduct **c** is spontaneous and highly exothermic. Similarly, the proton abstraction from HF by the aryl anion **c** has to take place instantaneously due to the formation of the highly exothermic product **d**, the arylated ester-flouride ion complex. At this stage, F^- anion abstracts the proton from the remaining C-H bond to form the arylated enolate-HF complex (**e**). The transition state **TS2** for this reaction suggests the barrier height 4.0 kcal/mol. The enolate **f** undergoes an intramolecular cyclisation through the formation of an S_N2 type transition state **TS3** to yield the final product in association with the leaving group Cl^- (**g**). The activation barrier for the cyclisation is 13.1 kcal/mol and the exothermic character of the overall reaction is 102.0 kcal/mol.

Finally, we tried to synthetically modify the 3(2*H*)-furanone skeleton by introducing amine functions at the fifth position. These heterocyclic analogs of prostaglandins[15] were synthesized by treating furanones with various amines in MeOH at 40 °C for 4 hours. From all the reactions, the corresponding azaprostaglandin analogues were isolated in good to excellent yields (Scheme 3).

Scheme 3. Synthesis of heterocyclic analogs of prostaglandins from 4-aryl-3-(2*H*)-furanone **4**



Reaction conditions: **4** (1.0 equiv.), **22** (1.05 equiv.), MeOH (2.0 mL), 40 °C, 4 h.

In conclusion, we have developed a tandem process for the synthesis of 4-aryl-3-(2*H*)-furanone from benzyne and 4-haloacetoacetates. The reaction was found to be general towards a variety of substituted arynes, and in some cases regiospecificity was observed. The reaction proceeds *via* a tandem *α*-arylation-intramolecular cyclization pathway. We have shown that additional substituents can be introduced to the second or fifth position of the 3(2*H*)-furanone moiety by using appropriately substituted 4-halo-1,3-diketo compounds. Finally, different heterocyclic analogs of prostaglandins were synthesized from 4-phenyl-3(2*H*)-furanone. We are currently investigating the effect of substituents on the activated carbon of 4-haloacetoacetates and the results will be reported in due course.

Experimental Section

General experimental methods: All chemicals were of the best grade commercially available and were used without further purification. Benzyne precursors 2-(trimethylsilyl)phenyl triflate **1a**, 4,5-dimethoxy-2-(trimethylsilyl)phenyl triflate **1c**, 3-methoxy-2-(trimethylsilyl)phenyl triflate **1e**, 4-methyl-2-(trimethylsilyl)phenyl trifluoromethanesulfonate **1h** and 4-methoxy-2-(trimethylsilyl)phenyl triflate **1g** were purchased from TCI Chemicals. Benzyne precursor 2-chloro-6-(trimethylsilyl)phenyl triflate **1f**, ethyl 4-chloroacetoacetate **2a**, methyl 4-chloroacetoacetate **2b**, CsF, KF, 18-C-6 and TBAF were purchased from Sigma Aldrich. Benzyne precursors 6-(trimethylsilyl)indan-5-yl triflate **1b**, 4,5-difluoro-2-(trimethylsilyl)phenyl trifluoromethanesulfonate **1d** and 4-chloro-2-(trimethylsilyl)phenyl trifluoromethanesulfonate **1i** were purchased from ABCR chemicals. 4-bromoacetoacetates were prepared by following reported procedures.[16] All solvents were purified according to standard procedures; dry solvents were obtained according to the literature methods and stored over molecular sieves. Analytical thin layer chromatography was performed on polyester sheets pre-coated with silica gel containing fluorescent indicator (POLYGRAM®SIL G/UV254). Gravity column chromatography was performed using silica gel, and mixtures of hexanes/ethyl acetate were used for elution. Melting points were measured with a Büchi 530 melting point apparatus and are uncorrected. NMR spectra were recorded with Bruker Avance-300 (300 MHz for ^{1}H NMR, 75 MHz for ^{13}C{^{1}H} NMR), Bruker DRX-400 (400.1 MHz for ^{1}H NMR, 100.6 MHz for ^{13}C{^{1}H} NMR) and Bruker AMX-500 (500 MHz for ^{1}H NMR, 125 MHz for ^{13}C{^{1}H} NMR) spectrophotometer instruments. All spectra were measured at 300 K, unless otherwise specified. The chemical shifts δ are given in ppm and referenced to the external standard TMS or internal solvent standard. ^{1}H NMR coupling constants (*J*) are reported in Hertz (Hz), and multiplicities are indicated as follows s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (doublet of doublets). Mass spectra were with a ThermoFinnigan MAT95XL, a ThermoFisher Scientific LTQ Orbitrap Velos, and an Agilent 6890 gas chromatograph with JMS-T100GC spectrometer or with a ESI/HRMS at 60,000 resolution using Thermo Scientific Exactive mass spectrometer with orbitrap analyzer.

Synthesis and characterization of 4-aryl-3(2*H*)-furanones

*5-Ethoxy-4-phenylfuran-3(2H)-one (**3**)*. Following the general experimental procedure, 2-(trimethylsilyl) phenyl trifluoromethanesulfonate **1a** (227 mg, 1.25 equiv.), ethyl-4-chloroacetoacetate **2a** (100 mg, 0.61 mmol), KF (177 mg, 5.0 equiv.), 18C-6 (806 mg, 5.0 equiv.) in CH_3CN (4.0 mL) at 0 °C and subsequent stirring at room temperature for 5 h. The crude product was purified over silica gel (100-200 mesh) column chromatography (30% ethyl acetate in hexanes) to afford the desired product **3** as a pale brown solid (87 mg, 70%). Analytical data of **3**: Mp: 104-106 °C. ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ 7.80-7.77 (m, 2H), 7.31-7.26 (m, 2H), 7.15-7.10 (m, 1H), 4.61 (s, 2H), 4.52 (q, 2H, *J* = 9.0 Hz), 1.45 (t, 3H, *J* = 9.0 Hz) ppm. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 194.1, 180.6, 129.5, 128.2, 126.0, 125.9, 93.9, 74.6, 66.6, 14.8 ppm. HRMS (EI) m/z: $(M)^+$ calcd for $C_{12}H_{12}O_3$ 204.0786; Found: 204.0797.

*5-Methoxy-4-phenylfuran-3(2H)-one (**4**)*. Following the general experimental procedure, 2-(trimethylsilyl) phenyl trifluoromethanesulfonate **1a** (248 mg, 1.25 equiv.), methyl-4-chloroacetoacetate **2b** (100 mg, 0.66 mmol), KF (192 mg, 5.0 equiv.), 18C-6 (872 mg, 5.0 equiv.) in CH_3CN (4.0 mL) at 0 °C and subsequent stirring at room temperature for 5 h. The crude product was purified over silica gel (100-200 mesh) column chromatography (30% ethyl acetate in hexanes) to afford the desired product **4** as an off-white solid (92 mg, 73%). For the gram scale preparation of **4**, yield was 69% (1.29 g). Analytical data of **4**. Mp: 59-61 °C. ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ 7.78-7.75 (m, 2H), 7.31-7.26 (m, 2H), 7.15-7.10 (m, 1H), 4.62 (s, 2H), 4.12 (s, 3H) ppm. ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 194.1, 180.8, 129.2, 128.2, 126.1, 126.0, 94.1, 74.7, 56.7 ppm. HRMS (EI) m/z: $(M)^+$ calcd for $C_{11}H_{10}O_3$ 190.0624; Found: 190.0628.

*4-(2,3-Dihydro-1H-inden-5-yl)-5-ethoxyfuran-3(2H)-one (**5**)*. Following the general experimental procedure, 6-(trimethylsilyl)indan-5-yl triflate **1b** (258 mg, 1.25 equiv.), ethyl-4-chloroacetoacetate **2a** (100 mg, 0.61 mmol), KF (177 mg, 5.0 equiv.), 18C-6 (806 mg, 5.0 equiv.) in CH_3CN (4.0 mL) at 0 °C and subsequent stirring at room temperature for 5 h. The crude product was purified over silica gel (100-200 mesh) column chromatography (30% ethyl acetate in hexanes)

to afford the desired product **5** as a pale yellow solid (99 mg, 67%). Analytical data of **5**. Mp: 70-72 °C. ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ 7.63 (s, 1H), 7.51-7.47 (m, 1H), 7.16-7.13 (d, 1H, J = 6.0 Hz), 4.59 (s, 2H), 4.49 (q, 2H, J = 6.0 Hz), 2.87-2.79 (m, 4H), 2.03-1.93 (m, 2H), 1.43 (t, 3H, J = 6.0 Hz) ppm. ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): 194.3, 180.5, 144.1, 142.1, 127.0, 124.1, 124.1, 122.2, 94.4, 74.5, 66.5, 33.0, 32.7, 25.5, 14.9. ppm. HRMS (EI) m/z: $(M)^+$ calcd for $C_{15}H_{16}O_3$ 244.1094; Found: 244.1086.

4-(2,3-Dihydro-1H-inden-5-yl)-5-methoxyfuran-3(2H)-one ***(6)***. Following the general experimental procedure, 6-(trimethylsilyl)indan-5-yl triflate **1b** (279 mg, 1.25 equiv.), methyl-4-chloroacetoacetate **2b** (100 mg, 0.66 mmol), KF (192 mg, 5.0 equiv.), 18C-6 (872 mg, 5.0 equiv.) in CH_3CN (4.0 mL) at 0 °C and subsequent stirring at room temperature for 5 h. The crude product was purified over silica gel (100-200 mesh) column chromatography (30% ethyl acetate in hexanes) to afford the desired product **6** as a pale yellow solid (103 mg, 68%). Analytical data of **6**. Mp: 123-125 °C. ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ 7.60 (s, 1H), 7.50-7.47 (m, 1H), 7.15-7.13 (d, 1H, J = 6.0 Hz), 4.61 (s, 2H), 4.10 (s, 3H), 2.87-2.79 (m, 4H), 2.03-1.94 (m, 2H) ppm. ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 194.3, 180.7, 144.2, 142.2, 126.7, 124.2, 124.1, 122.3, 94.6, 74.6, 56.5, 33.0, 32.7, 25.5 ppm. HRMS (EI) m/z: $(M)^+$ calcd for $C_{14}H_{14}O_3$ 230.0937; Found: 230.0933.

4-(3,4-Dimethoxyphenyl)-5-ethoxyfuran-3(2H)-one ***(7)***. Following the general experimental procedure, 4,5-dimethoxy-2-(trimethylsilyl)phenyl triflate **1c** (273 mg, 1.25 equiv.), ethyl-4-chloroacetoacetate **2a** (100 mg, 0.61 mmol), KF (177 mg, 5.0 equiv.), 18C-6 (806 mg, 5.0 equiv.) in CH_3CN (4.0 mL) at 0 °C and subsequent stirring at room temperature for 5 h. The crude product was purified over silica gel (100-200 mesh) column chromatography (30% ethyl acetate in hexanes) to afford the desired product **7** as a pale brown solid (103 mg, 64%). Analytical data of **7**. Mp: 136-138 °C. ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ 7.51 (d, 1H, J = 1.8 Hz), 7.32 (dd, 1H, J_1 = 8.4 Hz, J_2 = 2.1 Hz), 6.80 (d, 1H, J = 8.4 Hz), 4.59 (s, 2H), 4.51 (q, 2H, J =7.2 Hz), 3.84 (s, 3H), 3.81 (s, 3H), 1.45 (t, 3H, J = 7.2 Hz) ppm. ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): 194.2, 180.2, 148.6, 147.1, 122.3, 118.4, 111.0, 109.5, 74.5, 66.5, 55.8, 55.7, 14.8 ppm. HRMS (EI) m/z: $(M)^+$ calcd for $C_{14}H_{16}O_5$ 264.0992; Found: 264.0984.

4-(3,4-Dimethoxyphenyl)-5-methoxyfuran-3(2H)-one ***(8)***. Following the general experimental procedure, 4,5-dimethoxy-2-(trimethylsilyl)phenyl triflate **1c** (296 mg, 1.25 equiv.), methyl-4-chloroacetoacetate **2b** (100 mg, 0.66 mmol), KF (192 mg, 5.0 equiv.), 18C-6 (872 mg, 5.0 equiv.) in CH_3CN (4.0 mL) at 0 °C and subsequent stirring at room temperature for 5 h. The crude product was purified over silica gel (100-200 mesh) column chromatography (30% ethyl acetate in hexanes) to afford the desired product **8** as a brown solid (110 mg, 67%). Analytical data of **8**. Mp: 122-124 °C. ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ 7.47 (d, 1H, J = 2.1 Hz), 7.27 (dd, 1H, J_1 = 8.4 Hz, J_2 = 2.1 Hz), 6.78 (d, 1H, J = 8.4 Hz), 4.61 (s, 2H), 4.12 (s, 3H), 3.84 (s, 3H), 3.81 (s, 3H) ppm. ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 194.2, 180.5, 148.6, 147.3, 122.1, 118.5, 111.1, 109.7, 74.6, 56.7, 55.9 ppm. HRMS (EI) m/z: $(M)^+$ calcd for $C_{13}H_{14}O_5$ 250.0836; Found: 250.0828.

4-(3,4-Difluorophenyl)-5-methoxyfuran-3(2H)-one ***(9)***. Following the general experimental procedure, 4,5-difluoro-2-(trimethylsilyl)phenyl trifluoromethanesulfonate **1d** (276 mg, 1.25 equiv.), methyl-4-chloroacetoacetate **2b** (100 mg, 0.66 mmol), KF (192 mg, 5.0 equiv.), 18C-6 (872 mg, 5.0 equiv.) in CH_3CN (4.0 mL) at 0 °C for 2 h. The crude product was purified over silica gel (100-200 mesh) column chromatography (30% ethyl acetate in hexanes) to afford the desired product **9** as a light yellow oil (72 mg, 48%). Analytical data of **9**. TLC (SiO_2): R_f 0.26 (50% ethyl acetate in hexane). ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ 7.72-7.65 (m, 1H), 7.60-7.55 (m, 1H), 7.09-7.00 (m, 1H), 4.63 (s, 2H), 4.15 (s, 3H) ppm. ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 193.6, 180.6, 121.8, 121.8, 121.8, 121.7, 117.0, 116.7, 114.7, 114.5, 92.5, 74.8, 57.0 ppm. HRMS (EI) m/z: $(M)^+$ calcd for $C_{11}H_8F_2O_3$ 226.0436; Found: 226.0441.

5-Ethoxy-4-(3-methoxyphenyl)furan-3(2H)-one ***(10)***. Following the general experimental procedure, 3-methoxy-2-(trimethylsilyl)phenyl triflate **1e** (250 mg, 1.25 equiv.), ethyl-4-chloroacetoacetate **2a** (100 mg, 0.61 mmol), KF (177 mg, 5.0 equiv.), 18C-6 (806 mg, 5.0 equiv.) in CH_3CN (4.0 mL) at 0 °C and subsequent stirring at room temperature for 5 h. The crude product was purified over silica gel (100-200 mesh) column chromatography (30% ethyl acetate in hexanes) to afford the desired product **10** as a pale yellow solid (101 mg, 71%). Analytical data of **10**. Mp: 67-69 °C. ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ 7.45-7.44 (m, 1H), 7.42-7.38 (m, 1H), 7.22-7.17 (m, 1H), 6.71-6.66 (m, 1H), 4.60 (s, 2H), 4.52 (q, 2H, J = 6.0 Hz), 3.75 (s, 3H), 1.45 (t, 3H, J = 6.0 Hz) ppm. ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): 194.1, 180.6, 159.4, 130.8, 129.1, 118.4, 111.8, 111.3, 93.7, 74.6, 66.7, 55.2, 14.8. ppm. HRMS (EI) m/z: $(M)^+$ calcd for $C_{13}H_{14}O_4$ 234.0892; Found: 234.0882.

5-Methoxy-4-(3-methoxyphenyl)furan-3(2H)-one ***(11)***. Following the general experimental procedure, 3-methoxy-2-(trimethylsilyl)phenyl triflate **1e** (271 mg, 1.25 equiv.), methyl-4-chloroacetoacetate **2b** (100 mg, 0.66 mmol), KF (192 mg, 5.0 equiv.), 18C-6 (872 mg, 5.0 equiv.) in CH_3CN (4.0 mL) at 0 °C and subsequent stirring at room temperature for 5 h. The crude product was purified over silica gel (100-200 mesh) column chromatography (30% ethyl acetate in hexanes) to afford the desired product **11** as a pale yellow solid (106 mg, 73%). Analytical data of **11**. Mp: 95-97 °C. ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ 7.42-7.41 (m, 1H), 7.39-7.35 (m, 1H), 7.22-7.17 (m, 1H), 6.71-6.67 (m, 1H), 4.61 (s, 2H), 4.12 (s, 3H), 3.75 (s, 3H) ppm. ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 194.0, 180.8, 159.4, 130.6, 129.1, 118.5, 111.7, 111.5, 93.9, 74.7, 56.7, 55.2 ppm. HRMS (EI) m/z: $(M)^+$ calcd for $C_{12}H_{12}O_4$ 220.0730; Found: 220.0725.

4-(3-Chlorophenyl)-5-ethoxyfuran-3(2H)-one ***(12)***. Following the general experimental procedure, 2-chloro-6-(trimethylsilyl)phenyl triflate **1f** (253 mg, 1.25 equiv.), ethyl-4-chloroacetoacetate **2a** (100 mg, 0.61 mmol), KF (177 mg, 5.0 equiv.), 18C-6 (806 mg, 5.0 equiv.) in CH_3CN (4.0 mL) at 0 °C for 4 h. The crude product was purified over silica gel (100-200 mesh) column chromatography (30% ethyl acetate in hexanes) to afford the desired product **12** as a pale yellow viscous liquid (89 mg, 61%). Analytical data of **12**. TLC (SiO_2): R_f 0.37 (50% ethyl acetate in hexane). ^{1}H NMR (500 MHz, $CDCl_3$, TMS): δ 7.89 (t, 1H, J = 1.5 Hz), 7.81 (d, 1H, J = 8Hz), 7.28 (d, 1H, J = 8 Hz,), 7.16 (dd, 1H, J_1 = 7.5 Hz, J_2 = 1.0 Hz) 4.69 (s, 2H) 4.62 (q, 2H, J = 6.0 Hz) 1.54 (t, 3H, J = 6.0 Hz) ppm. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): 193.7, 180.6, 134.1, 129.4, 125.9, 125.6, 123.8, 74.7, 67.0, 14.9 ppm. HRMS (ESI): calcd for $C_{12}H_{11}ClNaO_3$, $(M+Na)^+$: 261.0289, Found: 261.0298.

*5-Ethoxy-4-(4-methoxyphenyl)furan-3(2H)-one & 5-ethoxy-4-(3-methoxyphenyl)furan-3(2H)-one **(13)***. Following the general experimental procedure, 4-methoxy-2-(trimethylsilyl)phenyl triflate **1g** (250 mg, 1.25 equiv.), ethyl-4-chloroacetoacetate **2a** (100 mg, 0.61 mmol), KF (177 mg, 5.0 equiv.), 18C-6 (806 mg, 5.0 equiv.) in CH_3CN (4.0 mL) at 0 °C and subsequent stirring at room temperature for 5 h. The crude product was purified over silica gel (100-200 mesh) column chromatography (30% ethyl acetate in hexanes) to afford the desired product **13** as a pale yellow solid and as regioisomers in a ratio of 1.3:1 (96 mg, 67%). Analytical data of **13**. Mp: 132-134 °C. ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ 7.74-7.69 (m, 2.6H), 7.45-7.44 (m, 1H), 7.41-7.38 (m, 1H), 7.22-7.17 (m, 1H), 6.86-6.81 (m, 2.6H), 6.70-6.66 (m, 1H), 4.59 (s, 2H), 4.58 (s, 2.6H), 4.55-4.46 (m, 4.6H), 3.75 (s, 3H), 3.73 (s, 3.9H) 1.47-1.41 (m, 7H) ppm. ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): 194.2, 194.0, 180.6, 180.2, 159.4, 157.7, 130.8, 129.1, 127.2, 121.9, 118.4, 113.7, 111.7, 111.3, 93.7, 93.6, 74.5, 74.5, 66.7, 66.5, 55.2, 55.1, 14.9, 14.8 ppm. HRMS (EI) m/z: $(M)^+$ calcd for $C_{13}H_{14}O_4$ 234.0892; Found: 234.0888.

*5-Methoxy-4-(4-methoxyphenyl)furan-3(2H)-one & 5-methoxy-4-(3-methoxyphenyl)furan-3(2H)-one **(14)***. Following the general experimental procedure, 4-methoxy-2-(trimethylsilyl)phenyl triflate **1g** (271 mg, 1.25 equiv.), methyl-4-chloroacetoacetate **2b** (100 mg, 0.66 mmol), KF (192 mg, 5.0 equiv.), 18C-6 (872 mg, 5.0 equiv.) in CH_3CN (4.0 mL) at 0 °C and subsequent stirring at room temperature for 5 h. The crude product was purified over silica gel (100-200 mesh) column chromatography (30% ethyl acetate in hexanes) to afford the desired product **14** as a pale yellow and as regioisomers in a ratio of 1.8:1 (102 mg, 70%). Analytical data of **14**. Mp: 86-88 °C. ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ 7.71-7.66 (m, 3.7H), 7.42-7.41 (m, 1H), 7.39-7.35 (m, 1H), 7.22-7.17 (m, 1H), 6.86-6.81 (m, 3.8H), 6.71-6.67 (m, 1H), 4.61 (s, 2H), 4.60 (s, 3.6H), 4.12 (s, 3H), 4.10 (s, 5.7H), 3.75 (s, 3H), 3.73 (s, 5.6H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): 194.2, 180.5, 159.5, 157.8, 130.6, 129.1, 127.3, 121.7, 118.5, 113.7, 111.7, 111.5, 93.9, 74.7, 56.6, 55.2 ppm. HRMS (ESI) m/z: $(M+H)^+$ calcd for $C_{12}H_{13}O_4$ 221.0808; Found: 221.0808.

*5-Ethoxy-4-(p-tolyl)furan-3(2H)-one & 5-ethoxy-4-(m-tolyl)furan-3(2H)-one **(15)***. Following the general experimental procedure, 4-methyl-2-(trimethylsilyl)phenyl trifluoromethanesulfonate **1h** (238 mg, 1.25 equiv.), ethyl-4-chloroacetoacetate **2a** (100 mg, 0.61 mmol), KF (177 mg, 5.0 equiv.), 18C-6 (806 mg, 5.0 equiv.) in CH_3CN (4.0 mL) at 0 °C and subsequent stirring at room temperature for 5 h. The crude product was purified over silica gel (100-200 mesh) column chromatography (30% ethyl acetate in hexanes) to afford the desired product **15** as a pale brown solid and as regioisomers in a ratio of 1:1 (95 mg, 71%). Analytical data of **15**. Mp: 75-77 °C. ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ 7.69-7.64 (m, 2H), 7.63-7.62 (m, 1H), 7.55-7.52 (m, 1H), 7.20-7.15 (m, 1H), 7.11-7.07 (m, 2H), 6.96-6.93 (m, 1H), 4.59 (s, 2H), 4.59 (s, 2H), 4.54-4.46 (m, 4H), 2.29 (s, 3H), 2.26 (s, 3H) 1.46-1.41 (m, 6H) ppm. ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): 194.2, 194.2, 180.6, 180.5, 137.7, 135.5 129.2, 128.9, 128.1, 126.8, 126.7, 126.4, 125.9, 123.1, 94.0, 93.9, 74.5, 66.6, 66.5, 21.6, 21.2, 14.8 ppm. HRMS (EI) m/z: $(M)^+$ calcd for $C_{13}H_{14}O_3$ 218.0937; Found: 218.0926.

*5-Methoxy-4-(p-tolyl)furan-3(2H)-one & 5-methoxy-4-(m-tolyl)furan-3(2H)-one **(16)***. Following the general experimental procedure, 4-methyl-2-(trimethylsilyl)phenyl trifluoromethanesulfonate **1h** (258 mg, 1.25 equiv.), methyl-4-chloroacetoacetate **2b** (100 mg, 0.66 mmol), KF (192 mg, 5.0 equiv.), 18C-6 (872 mg, 5.0 equiv.) in CH_3CN (4.0 mL) at 0 °C and subsequent stirring at room temperature for 5 h. The crude product was purified over silica gel (100-200 mesh) column chromatography (30% ethyl acetate in hexanes) to afford the desired product **16** as a pale brown solid and as regioisomers in a ratio of 1:1 (101 mg, 75%). Analytical data of **16**. Mp: 57-59 °C. ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ 7.66-7.62 (m, 2H), 7.59-7.58 (m, 1H), 7.54-7.51 (m, 1H), 7.20-7.14 (m, 1H), 7.11-7.08 (m, 2H), 6.96-6.93 (m, 1H), 4.61 (s, 2H), 4.60 (s, 2H), 4.10 (s, 3H), 4.10 (s, 3H), 2.29 (s, 3H), 2.26 (s, 3H) ppm. ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): 194.2, 194.2, 180.8, 180.7, 137.7, 135.7, 129.0, 128.9, 128.1, 126.9, 126.7, 126.2, 125.9, 123.2, 94.2, 94.0, 74.7, 56.6, 56.6, 21.6, 21.2 ppm. HRMS (EI) m/z: $(M)^+$ calcd for $C_{12}H_{12}O_3$ 204.0786; Found: 204.0796.

*4-(4-Chlorophenyl)-5-ethoxyfuran-3(2H)-one & 4-(3-chlorophenyl)-5-ethoxyfuran-3(2H)-one **(17)***. Following the general experimental procedure, 4-chloro-2-(trimethylsilyl)phenyl trifluoromethanesulfonate **1i** (254 mg, 1.25 equiv.), ethyl-4-chloroacetoacetate **2a** (100 mg, 0.61 mmol), KF (177 mg, 5.0 equiv.), 18C-6 (806 mg, 5.0 equiv.) in CH_3CN (4.0 mL) at 0 °C for 4 h. The crude product was purified over silica gel (100-200 mesh) column chromatography (30% ethyl acetate in hexanes) to afford the desired product **17** as a pale yellow oil and as regioisomers in a ratio of 1:1.2 (90 mg, 62%). Analytical data of **17**. TLC (SiO_2): R_f 0.38 (50% ethyl acetate in hexane). ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ 7.82-7.81 (m, 1H), 7.79-7.72 (m, 3.6H), 7.26-7.19 (m, 3.4H), 7.10-7.06 (m, 1H), 4.61 (s, 2H), 4.61 (s, 2.4H), 4.58-4.40 (m, 4.4H), 1.49-1.43 (m, 6.6H) ppm. ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): 194.0, 193.8, 180.6, 180.5, 134.0, 131.3, 131.3, 129.4, 128.3, 128.0, 127.0, 125.9, 125.6, 123.7, 93.0, 92.8, 74.7, 67.1, 67.0, 14.8 ppm. HRMS (ESI) m/z: $(M)^+$ calcd for $C_{12}H_{12}ClO_3$ 239.0469; Found: 239.0469.

*4-(4-Chlorophenyl)-5-methoxyfuran-3(2H)-one & 4-(3-chlorophenyl)-5-methoxyfuran-3(2H)-one **(18)***. Following the general experimental procedure, 4-chloro-2-(trimethylsilyl)phenyl trifluoromethanesulfonate **1i** (275 mg, 1.25 equiv.), methyl-4-chloroacetoacetate **2b** (100 mg, 0.66 mmol), KF (192 mg, 5.0 equiv.), 18C-6 (872 mg, 5.0 equiv.) in CH_3CN (4.0 mL) at 0 °C for 4 h. The crude product was purified over silica gel (100-200 mesh) column chromatography (30% ethyl acetate in hexanes) to afford the desired product **18** as a pale yellow oil and as regioisomers in a ratio of 1:1.4 (101 mg, 66%). Analytical data of **18**. TLC (SiO_2): R_f 0.32 (50% ethyl acetate in hexane). ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ 7.79-7.77 (m, 1H), 7.76-7.71 (m, 3.8H), 7.25-7.17 (m, 3.8H), 7.10-7.07 (m, 1H), 4.62 (s, 2H), 4.62 (s, 2.8H), 4.14 (s, 3H), 4.13 (s, 4.2H) ppm. ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): 193.9, 193.7, 180.9, 180.8, 134.1, 131.4, 131.1, 129.4, 128.3, 127.8, 127.1, 126.0, 125.6, 123.8, 93.2, 93.0, 74.8, 56.9, 56.9 ppm. HRMS (EI) m/z: $(M)^+$ calcd for $C_{11}H_9ClO_3$ 224.0240; Found: 224.0252.

*5-ethoxy-2-methyl-4-phenylfuran-3(2H)-one **(19)***. Following the general experimental procedure, 2-(trimethylsilyl) phenyl trifluoromethanesulfonate **1a** (167 mg, 1.25 equiv.), ethyl 4-bromo-3-oxopentanoate **2c** (100 mg, 0.45 mmol), KF (130 mg, 5.0 equiv.), 18C-6 (592 mg, 5.0 equiv.) in CH_3CN (3.0 mL) at 0 °C and subsequent stirring at room temperature for 5 h. The crude product was purified over silica gel (100-200 mesh) column chromatography (30% ethyl acetate in hexanes) to afford the desired product **19** as a pale

yellow solid (69 mg, 69%). Analytical data of **19**. Mp: 77-79 °C. ^{1}H NMR (500 MHz, $CDCl_3$, TMS): δ 7.88 (d, 2H, *J* = 7.5 Hz), 7.35 (t, 2H, *J* = 7.5 Hz), 7.18 (t, 1H, *J* = 7.0 Hz), 4.74 (q, 1H, *J* = 7.0 Hz,), 4.58 (q, 2H, *J* = 7.0 Hz,), 1.57 (d, 3H, 7.0 Hz), 1.52 (t, 3H, *J* = 7.0 Hz,) ppm. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 196.9, 179.2, 129.8, 128.2, 125.9, 125.8, 92.4, 82.8, 66.4, 16.7, 14.8 ppm. HRMS (ESI) m/z: calcd for $C_{13}H_{14}NaO_3$, $(M+Na)^+$: 241.0835, Found: 241.0826.

*5-Ethoxy-2-methyl-4-(p-tolyl)furan-3(2H)-one & 5-ethoxy-2-methyl-4-(m-tolyl)furan-3(2H)-one **(20)***. Following the general experimental procedure, 4-methyl-2-(trimethylsilyl)phenyl trifluoromethanesulfonate **1h** (176 mg, 1.25 equiv.), ethyl 4-bromo-3-oxopentanoate **2c** (100 mg, 0.45 mmol), KF (130 mg, 5.0 equiv.), 18C-6 (592 mg, 5.0 equiv.) in CH_3CN (3.0 mL) at 0 °C and subsequent stirring at room temperature for 5 h. The crude product was purified over silica gel (100-200 mesh) column chromatography (30% ethyl acetate in hexanes) to afford the desired product **20** as a pale yellow solid and as regioisomers in a ratio of 1.2:1 (66 mg, 63%). Analytical data of **20**. Mp: 140-142 °C. ^{1}H NMR (500 MHz, $CDCl_3$, TMS): δ 7.76-7.73 (m, 3.2H), 7.62 (d, 1.2H, *J* = 8.0 Hz) 7.24 (t, 1.2H, *J* = 8.0 Hz), 7.16 (d, 2H, *J* = 8.5 Hz), 7.00 (d, 1.2H, *J* = 7.5 Hz,) 4.75-4.70 (m, 2.2H), 4.60-4.55 (m, 4.4H), 2.36 (s, 3.6H), 2.33 (s, 3H), 1.57 (d, 3.6H, *J* = 1.5 Hz), 1.56 (d, 3H, *J* = 1.5 Hz), 1.53-1.49 (m, 6.6H) ppm. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): 197.0, 179.3, 179.1, 137.7, 135.4, 129.6, 128.9, 128.1, 126.8, 126.7, 126.7, 125.9, 123.1, 92.5, 92.4, 82.8, 66.4, 66.3, 21.6, 21.2, 16.7, 14.9. ppm. HRMS (ESI) m/z: calcd for $C_{14}H_{16}NaO_3$, $(M+Na)^+$: 255.0992, Found: 255.0984.

*4-phenyl-5-(phenylamino)furan-3(2H)-one **(22)***. Following the general experimental procedure, 2-(trimethylsilyl) phenyl trifluoromethanesulfonate **1a** (148 mg, 1.25 equiv.), 4-bromo-3-oxo-*N*-phenylbutanamide **2e** (100 mg, 0.39 mmol), KF (114 mg, 5.0 equiv.), 18C-6 (516 mg, 5.0 equiv.) in CH_3CN (3.0 mL) at 0 °C and subsequent stirring at room temperature for 5 h. The crude product was purified over silica gel (100-200 mesh) column chromatography (40% ethyl acetate in hexanes) to afford the desired product **22** as a pale brown solid (51 mg, 52%). Analytical data of **22**. Mp: 158-160 °C. ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ 7.43-7.38 (m, 3H), 7.37-7.36 (m, 1H), 7.35-7.32 (m, 1H), 7.30-7.29 (m, 1H), 7.28-7.26 (m, 1H), 7.24-7.20 (m, 3H), 7.15-7.09 (m, 1H), 4.65 (s, 2H) ppm. ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): 192.2, 174.9, 136.2, 130.2, 129.8, 129.8, 128.3, 127.3, 125.8, 121.8, 96.4, 75.2 ppm. HRMS (EI) m/z: calcd for $C_{16}H_{13}NO_2$, $(M)^+$: 251.0946, Found: 251.0941.

*4-(3,4-dimethoxyphenyl)-5-(phenylamino)furan-3(2H)-one **(23)***. Following the general experimental procedure, 4,5-dimethoxy-2-(trimethylsilyl)phenyl triflate **1c** (175 mg, 1.25 equiv.), 4-bromo-3-oxo-*N*-phenylbutanamide **2e** (100 mg, 0.39 mmol), KF (114 mg, 5.0 equiv.), 18C-6 (516 mg, 5.0 equiv.) in CH_3CN (3.0 mL) at 0 °C and subsequent stirring at room temperature for 5 h. The crude product was purified over silica gel (100-200 mesh) column chromatography (80% ethyl acetate in hexanes) to afford the desired product **23** as an amorphous solid (58 mg, 48%). Analytical data of **23**. TLC (SiO_2): R_f 0.29 (80% ethyl acetate in hexane). ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ 7.33-7.28 (m, 3H), 7.24-7.21 (m, 2H), 7.15-7.09 (m, 1H), 6.99 (s, 1H), 6.86 (s, 2H), 4.69 (s, 2H), 3.82 (s, 6H) ppm. ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): 191.7. 174.5, 149.7, 148.1, 135.9, 129.4, 125.3, 122.2, 121.1, 119.9, 111.9, 111.9, 96.0, 74.9, 56.0 ppm. HRMS (EI) m/z: calcd for $C_{18}H_{17}NO_4$, $(M)^+$: 311.1158, Found: 311.1152.

*5-(hexylamino)-4-phenylfuran-3(2H)-one **(26)***. 5-methoxy-4-phenylfuran-3(2H)-one **4** (100 mg, 1.0 equiv., 0.53 mmol) and n-hexylamine **25a** (1.1 equiv.) were weighed into a dry Schlenk tube. Dry methanol (2.0 mL) was added and the reaction mixture was stirred at 40 °C for 4 h. Upon completion of the reaction, the solvent was removed and the residue was subjected to column chromatography on neutral alumina using hexanes/ethyl acetate mixture as eluent to afford the product **26** as a pale yellow viscous liquid (110 mg, 80%). Analytical data of **26**. TLC (SiO_2): R_f 0.23 (50% ethyl acetate in hexane). ^{1}H NMR (500 MHz, $CDCl_3$, TMS): δ 7.42-7.38 (m, 4H), 7.22-7.20 (m, 1H), 5.63 (brs, 1H), 4.62 (s, 2H), 3.41 (m, 2H), 1.67-1.66 (m, 2H), 1.62-1.59 (m, 2H), 1.32-1.25 (m, 4H), 0.90 (t, 3H, *J* = 7.0 Hz) ppm. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 191.1, 176.8, 130.7, 129.2, 127.4, 126.1, 93.7, 74.5, 41.6, 31.3, 30.1, 29.7, 26.3, 22.5, 13.9 ppm. HRMS (ESI) m/z: $(M+Na)^+$ calcd for $C_{16}H_{21}NNaO_2$ 282.1465; Found: 282.1455.

*5-(benzylamino)-4-phenylfuran-3(2H)-one **(27)***: 5-methoxy-4-phenylfuran-3(2H)-one **4** (100 mg, 1.0 equiv., 0.53 mmol) and benzylamine **25b** (1.1 equiv.) were weighed into a dry Schlenk tube. Dry methanol (2.0 mL) was added and the reaction mixture was stirred at 40 °C for 4 h. Upon completion of the reaction, the solvent was removed and the residue was subjected to column chromatography on neutral alumina using hexanes/ethyl acetate mixture as eluent to afford the product **27** as a pale yellow viscous liquid (105 mg, 75%). Analytical data of **27**. TLC (SiO_2): R_f 0.19 (50% ethyl acetate in hexane). ^{1}H NMR (500 MHz, $CDCl_3$, TMS): δ 7.42- 7.29 (m, 9H), 7.21-7.19 (m, 1H), 5.9 (brs, 1H), 4.65 (s, 2H), 4.60 (d, 2H, *J* = 6.0 Hz,) ppm. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 191.5, 176.5, 136.8, 130.4, 129.1, 129.1, 128.2, 127.5, 127.4, 126.3, 94.1, 74.6, 45.4 ppm. HRMS (ESI) m/z: $(M+Na)^+$ calcd for $C_{17}H_{15}NNaO_2$ 288.0995; Found: 288.0988.

*5-(phenethylamino)-4-phenylfuran-3(2H)-one **(28)***. 5-methoxy-4-phenylfuran-3(2H)-one **4** (100 mg, 1.0 equiv., 0.53 mmol) and 2-phenylethylamine **25c** (1.1 equiv.) were weighed into a dry Schlenk tube. Dry methanol (2.0 mL) was added and the reaction mixture was stirred at 40 °C for 4 h. Upon completion of the reaction, the solvent was removed and the residue was subjected to column chromatography on neutral alumina using hexanes/ethyl acetate mixture as eluent to afford the product **28** as a pale yellow viscous liquid (114 mg, 77%). Analytical data of **28**. TLC (SiO_2): R_f 0.18 (50% ethyl acetate in hexane). ^{1}H NMR (500 MHz, $CDCl_3$, TMS): δ 7.36-7.19 (m, 10H), 5.58 (brs, 1H), 4.62 (s, 2H), 3.68 (q, 2H, *J* = 6.3 Hz,), 2.92 (t, 2H, *J* = 6.6 Hz,) ppm. ^{13}C{^{1}H} NMR (125 MHz, CDCl3): δ 190.4, 176.7, 137.5, 132.2, 132.1, 132.0, 130.0, 129.1, 129.0, 128.8, 128.6, 128.5, 127.4, 127.2, 126.4, 94.5, 74.8, 42.8, 36.2 ppm. HRMS (ESI) m/z: $(M+Na)^+$ calcd for $C_{18}H_{17}NNaO_2$ 302.1152; Found: 302.1157.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

Optimisation studies, theoretical calculations and copies of NMR spectra for all the compounds. X-ray crystallography data and CIF file for **3**.

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The authors declare no competing financial interest.

ACKNOWLEDGMENT

JJ thanks Alexander von Humboldt Foundation for an experienced research grant. VKO thank UGC for research fellowship.

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