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A New Powerful Approach to Multi-Substituted 3(2*H*)-Furanones via Brønsted Acid-Catalyzed Reactions of 4-Diazodihydrofuran-3-ones

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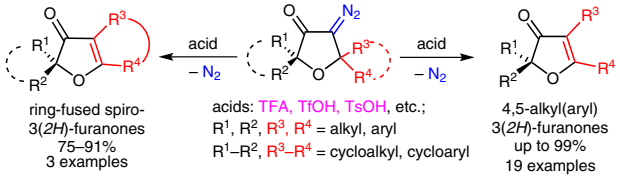

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Abstract The interaction of 5,5-dialkyl(diaryl)-substituted 4-diazo-3(2*H*)furanones with Brønsted acids (TFA, TsOH, etc.) causes elimination of nitrogen accompanied by 1,2-nucleophilic rearrangement, giving rise to exclusive formation of 4,5-dialkyl(diaryl)-substituted 3(2*H*)-furanones, ring-fused 3(2*H*)-furanones, and phenanthro[9,10-*b*]furan-3(2*H*)-ones in yields of up to 99%. The reaction is a new highly efficient way for the synthesis of multisubstituted 3(2*H*)furanones.

Key words diazo compounds, Brønsted acids, catalysis, rearrangement, carbocation

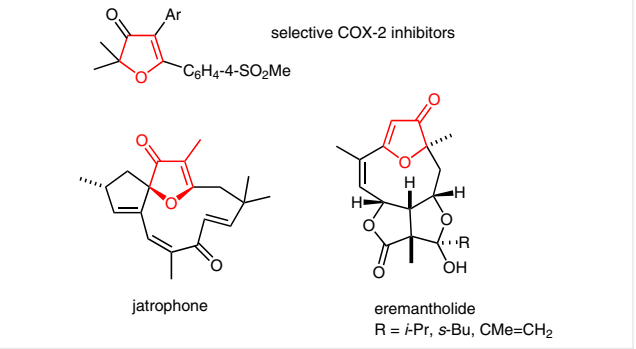


Figure 1 Examples of naturally occurring and biologically active 3(2*H*)-furanones

Highly functionalized 3(2*H*)-furanones exhibit a wide range of biological activities[1] and in recent years have attracted much attention of different specialists. Thus, 4,5-diaryl-substituted 3(2*H*)-furanones were found to be selective inhibitors of COX-2,[1a,b] and a series of furanones display cytotoxic activity.[1c–e] It is also known that a wealth of 3(2*H*)-furanones possess antiallergic, antibacterial, and antifungal activities.[1c,f] Many natural compounds contain structural elements of 3(2*H*)-furanones,[1c,f] as for instance *Jatrophone*, isolated from *Jatropha gossypiifolia L* and *Ermantholides*, which are shown in Figure 1.[1h]

In spite of a considerable body of known approaches for the structure of substituted 3(2*H*)-furanones,[1h,2] the synthesis of their multi-substituted derivatives continue to be a challenging task in synthetic organic chemistry.[1a–c,2a,3,4] One of the recent examples in this field represents a powerful one-pot synthesis of multi-substituted 3(2*H*)-furanones from cyanopropargylic alcohols and carboxylic acids, which furnishes a variety of 4-CN-substituted 3(2*H*)-furanones attractive for subsequent functionalizations.[4] Another instance for the efficient preparation of furanones is a one-pot synthesis of 4,5-diaryl-substituted 3(2*H*)-furanones from 1,2-diarylethanones and 2-bromoisobutyryl cyanide.[3b]

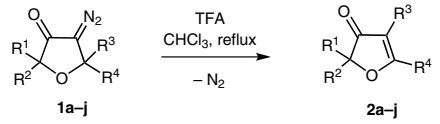
It was shown previously that a great body of O-containing heterocycles, such as 3(2*H*)-furanones, dihydrofuran-3(2*H*)-ones, phenanthro[9,10-*b*]furan-3(2*H*)-ones, oxetanecarboxylic acids, and so on,[5,6] are basically available using thermal[5] or photochemical[6] reactions of diazoketones of the tetrahydrofuran series. However 3(2*H*)-furanones are usually formed in these processes as a mixture with other reaction products.[5,6] In this connection, we tried to employ for this purpose Brønsted acids catalyzed reactions of 4-diazodihydrofuran-3(2*H*)-ones **1**, instead of photochemically or thermally activated processes. Herein we present the principal results of this study.

During preliminary experiments it was established that 4-diazodihydrofuran-3(2*H*)-ones **1**[7] were completely stable in the presence of acetic and formic acids and did not decompose even on heating their solutions in chloroform up to 60–62 °C. At the same time, employment of more strong Brønsted acids, such as trifluoroacetic acid (TFA), trifluoro-

methanesulfonic acid (TfOH), etc. produced a notable decomposition of these diazoketones at room temperature. Furthermore, unlike photochemical[6] and thermal[5] processes, reactions with acids occurred very selectively yielding essentially only the corresponding 3(2*H*)-furanones **2**.

Initially, reactions of diazoketones **1a–j**, bearing two identical substituents at the carbon atom C5 of heterocycle, with Brønsted acids were studied. It was shown that decomposition of these diazoketones using trifluoroacetic acid afforded the appropriate 3(2*H*)-furanones **2a–j** in yields of 73–98% (Table 1).

Table 1 Scope of 3(2*H*)-Furanones Prepared from Diazo Ketones **1a–j**



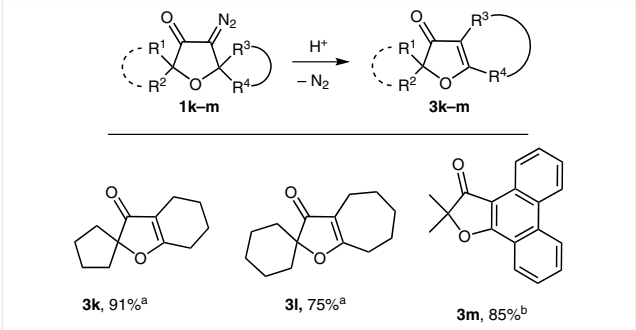
Entry	Diazoketone	R^1	R^2	R^3, R^4	Time (min)	Yield (%) of **2**
1[a]	**1a**	Me	Me	Me	60	82
2[a]	**1b**	Ph	Ph	Me	60	87
3[a]	**1c**	4-FC_6H_4	4-FC_6H_4	Me	360	82
4[a]	**1d**	PMP	PMP	Me	50	98
5[b]	**1e**	Ph	Me	Me	60	83
6[b]	**1f**	*p*-Tol	Me	Me	60	73
7[b]	**1g**	Me	Me	Ph	50	98
8[a]	**1h**	Me	Me	4-FC_6H_4	360	93
9[b]	**1i**	Me	Me	4-ClC_6H_4	300	98
10[b]	**1j**	Me	Me	PMP	30	97

[a] Two equivalents of TFA were used.
[b] Six equivalents of TFA were used.

The decomposition rate of diazoketones **1a**,**b**,**d–f** with two methyl groups at the C5 atom, regardless of the nature of substituents at atom C2, looked much the same and these reactions (using 2 equiv of TFA) were completed in one hour producing 4,5-dimethyl-substituted 3(2*H*)-furanones **2a**,**b**,**d–f**. The only exception in this case was found to be diazoketone **1c** with a 4-FC_6H_4 group on atom C2, decomposition of which took around six hours.

Reactions of diazoketones **1g–j** with both aryl groups on atom C5 of the heterocycle occurred at more rigorous conditions. It took approximately 6 equivalents of TFA to carry out the reaction at a notable rate. More than that, the duration of these reactions, unlike the decomposition of diazoketones **1a–f**, was strongly dependent on the electronic effects of substituents on the aryl rings. Thus, incorporation of electron-donating MeO group in the aryl ring (R^3, R^4 = PMP) markedly accelerated decomposition of diazoketone **1j** and its full conversion was observed already in half an hour, while an electron-withdrawing group (R^3, R^4 = 4-FC_6H_4) significantly slowed down the process and it took up to six hours for complete decomposition of diazo compound **1h** in the same reaction conditions.

One would expect that in the case of diazoketones **1k–m**, bearing spirocyclic substituents at the C5 atom of heterocycle, a similar reaction (1,2-alkyl shift) will lead to the formation of ring-fused systems, which would be a useful method for the synthesis of these structures (Scheme 1). It was actually found that decomposition of diazoketones **1k**,**l** with spirocyclopentyl and -cyclohexyl substituents [$(CH_2)_4$ and $(CH_2)_5$, respectively] easily occurred even at room temperature producing in high yields (75–91%) annulated 3(2*H*)-furanones **3k**,**l**. Related Brønsted acid catalyzed transformation of diazoketone **1m** with fluorenyl substituent gave phenanthro[9,10-*b*]furan-3(2*H*)-one **3m** in a yield of 85%. However, this reaction proceeded only at more drastic conditions (+60 °C), than with spiro analogues **1k**,**l** (r.t.), and required application of TfOH as a catalyst for the process.



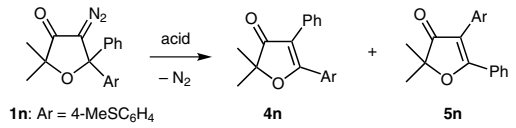
Scheme 1 Scope of ring-fused 3(2*H*)-furanones. [a] *Reagents and conditions*: diazoketone **1** (1 equiv), TFA (1–1.4 equiv), CH_2Cl_2, r.t., 1 h. [b] *Reagents and conditions*: diazoketone **1** (1 equiv), TfOH (1 equiv), $CHCl_3$, reflux, 2 h.

When employing diazoketones **1** with nonequivalent substituents R^3, R^4 at atom C5 in similar reactions, one would expect the appearance of two regioisomeric 3(2*H*)-furanones owing to a different migratory aptitude of nonequivalent R^3, R^4 groups. To elucidate the most workable conditions for these reactions, a series of different acid catalysts and solvents of variable polarity were tested on the example of diazoketone **1n** having in the structure Ph and 4-$MeSC_6H_4$ groups at C5 atom of the heterocycle (Tables 2 and 3).

On catalytic decomposition of diazoketone **1n** with two nonequivalent substituents R^3, R^4, two regioisomeric 3(2*H*)-furanones **4n** and **5n** were obtained. It was established in this case that yields of reaction products were to some extent controlled by the nature of employed acid. The best results were obtained with trifluoroacetic acid as the catalyst (Table 2, entry 1; yield 99%, ratio **4n**:**5n** = 1:3.2). Rather moderate yields of regioisomers **4n**, **5n** (65–74%) were gained by using stronger acids as, for example, TfOH or

H_2SO_4 (entries 5, 6). This was most likely caused by side reactions of furan heterocycle cleavage in the initial **1n** and/or final reaction products **4n**, **5n**, induced by these acids.

Table 2 Search for the Best Acid Catalysts for Decomposition of Diazoketone **1n** ($CHCl_3$, Reflux)



Entry	Acid	Time (min)	Yield (%) **4n** + **5n**	Ratio **4n**:**5n**
1	TFA (6 equiv)	80	99	1:3.2
2	TsOH (1 equiv)	80	98	1:2.7
3	$HClO_4$[a]	360	99	1:1.3
4	HCl (gas)[b]	360	98	1:3
5	H_2SO_4[c]	360	74	1:2.1
6	TfOH (1 equiv)	< 10	65	1:3

[a] Decomposition of diazoketone **1n** in a mixture of 70% aq solution of $HClO_4$ with CH_2Cl_2 (1:1).
[b] HCl (gas) was bubbled through a boiling $CHCl_3$ solution of **1n** during 3 h.
[c] Mixture of 1 equiv of 98% H_2SO_4 with 3 mL of $CHCl_3$.

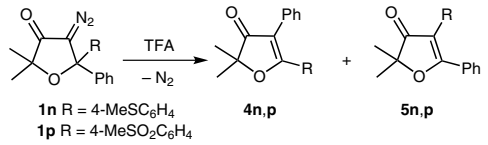
As to the regioselectivity of the process, it did not depend on the nature of the acid in most of the cases and ranged around a ratio of 1:3 (**4n**/**5n**; Table 2, entries 1, 2, 4, 6). Thus, as one would expect[8] the predominant migration of the aryl group with the electron-donating substituent (4-$MeSC_6H_4$) was established. A notable decrease in regioselectivity was observed only when using $HClO_4$ and H_2SO_4 (entries 3,5; ratio **4n**/**5n** = up to 1:2.1), which was probably associated with a high polarity of the medium during decomposition of diazoketone **1n**.

To clarify the effect of the nature of the solvent on the efficiency and regioselectivity of the process, decomposition of diazoketones **1n** and **1p** was studied in nonpolar or weakly polar solvents (benzene, chloroform, hexane; Table 3, entries 1–3) and polar solvents (entry 5, acetone) as well for in the pure trifluoroacetic acid (entry 4).

During these experiments it was ascertained that the sole reaction products in all cases were 3(2*H*)-furanones, which were formed in 98–99% yields (^{1}H NMR analysis). However, the ratio of regioisomers **4**:**5** was substantially dependent on the solvent polarity.

The most regioselective reactions proceeded in nonpolar or weakly polar solvents (Table 3, entries 1–3), whereas carrying out the process in acetone or acid solutions notably diminished the regioselectivity of the process (entries 4, 5). A limiting case appears to be the reaction in a two phase system with 70% $HClO_4$/CH_2Cl_2 where essentially full loss of selectivity occurred with the ratio of reaction products being 1:1.3 (Table 2, entry 3 for **1n**). This effect is most likely

Table 3 Effect of Solvent Polarity on the Ratio of Regioisomers **4**:**5**[a]



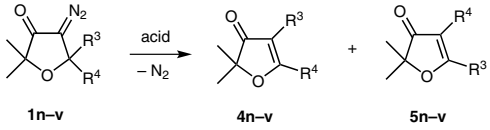
Entry	Solvent	Ratio[b] **4n**/**5n**	Ratio[b] **4p**/**5p**
1	benzene	1:3.8	6.1:1
2	$CHCl_3$	1:3.2	5.9:1
3	hexane	1:3	4.5:1
4	TFA	1:2.6	2.7:1
5	acetone	1:2.3	2.4:1

[a] Reaction conditions: refluxing with 6 equiv of TFA for up to 24 h.
[b] Ratio determined by ^{1}H NMR spectroscopy.

due to a very high dielectric permeability of $HClO_4$ (ε = 115).

Hence it was established by these studies that the most useful conditions for the preparation of 3(2*H*)-furanones from diazoketones **1** with two different substituents R^3, R^4 at the C5 atom of heterocycle were the use of TFA as a decomposition catalyst and a reaction temperature of 60 °C in chloroform solution. These conditions were used in the subsequent reactions with diazoketones **1n–v**, which resulted in the formation of 3(2*H*)-furanones **4n–v** and **5n–v** in total yields of 84–99% for two regioisomers (Table 4).

Table 4 Scope of 3(2*H*)-Furanones **4** and **5**[a]



Entry	**1n–v**; R^3, R^4	Yield (%) of **4** + **5**	Ratio of **4**/**5**
1	**1n**; Ph, 4-$MeSC_6H_4$	99	1:3.3
2	**1o**; Ph, 4-$MeSOC_6H_4$	98	4.4:1
3	**1p**; Ph, 4-$MeSO_2C_6H_4$	98	6.1:1
4	**1q**; 4-$MeSC_6H_4$, 4-FC_6H_4	99	3.3:1
5	**1r**; 4-$MeSC_6H_4$, 4-ClC_6H_4	86	3.1:1
6	**1s**; 4-$MeSC_6H_4$, 3-ClC_6H_4	94	5.3:1
7	**1t**; Me, Ph	94	1:2
8	**1u**; Me, 4-MeC_6H_4	84	1:3.4
9	**1v**; Me, 4-$CF_3C_6H_4$	97	1.3:1

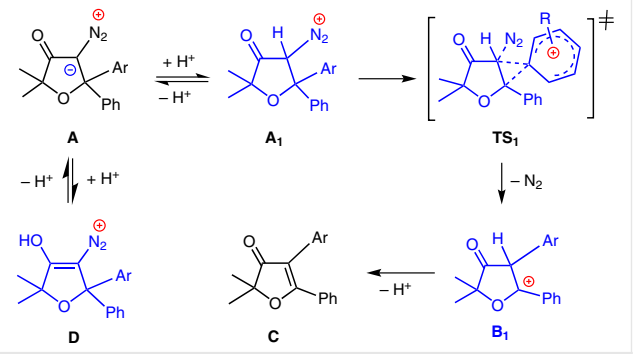
[a] Reaction conditions: 6.5 equiv of TFA, $CHCl_3$, reflux, 2–6 h.

The regioselectivity of the process in this case was again found to be dependent on the nature of substituents on the aryl rings.[9] A preferable migration was observed for aryl groups with electron-donating substituents (4-$MeSC_6H_4$,

Ph), whereas an EWG (in 4-XC_6H_4, X = MeSO, $MeSO_2$, CF_3) hindered migration and these groups mostly remained at the atom C5 of the heterocycle (Table 4). Accordingly, the greater the difference in migratory aptitudes of aryl groups at C5 atom, the higher the regioselectivity of the process.

These results, together with the effect of solvent polarity, open a good opportunity to manage the process and use it for the preparation of different regioisomers. In nonpolar solvents, predominantly one of the isomers can be obtained, while carrying out the decomposition process in $HClO_4$ solution provides a way for the synthesis of another (minor) regioisomer in a yield of around 50%.

As for the pathway for the formation of 3(2*H*)-furanones **2** from diazoketones **1**, the most plausible scheme for this process, based on the known literature data,[10] is given below for the example of diazoketone **A** with two nonidentical substituents (Ph and Ar) at the carbon atom C5 (Scheme 2).



Scheme 2 The assumed scheme for the formation of 3(2*H*)-furanones **C**

Initially, diazoketone **A** is reversibly protonated by Brønsted acid at the diazocarbon atom C4 with the formation of diazonium intermediate $\mathbf{A_1}$.[11] On the next reaction steps, a concerted elimination[10] of nitrogen molecule (N_2) and simultaneous migration of one of aryl groups from carbon atom C5 to C4 take place via transition state $\mathbf{TS_1}$ affording the protonated form of the final product $\mathbf{B_1}$. Stabilization of this intermediate by way of proton elimination results in the formation of 3(2*H*)furanone **C**.

Another alternative for the first step of this process is the O-protonation of the diazoketone carbonyl group producing diazoniun ion **D** (Scheme 2). However, in this case elimination of nitrogen apparently does not occur.[11] It is very likely that just this step is realized in the case of weak acetic and formic acids, whereas for C-protonation of the diazo group much stronger acid like TFA or TfOH is required.

Following the foregoing scheme, electron-donating groups in aryl rings should stabilize transition state $\mathbf{TS_1}$ increasing the migration aptitude of an aryl (Ar) as compared to the phenyl (Ph) group (Scheme 2), which was actually observed in our experiments. Thus, the 4-$MeSC_6H_4$ group demonstrated considerably higher migratory aptitude than Ph, 4-FC_6H_4, 4-ClC_6H_4, or 3-ClC_6H_4 group (Table 4, entries 1, 4–6), preferably giving rise to a regioisomer with electron-donating group at the atom C4 of heterocycle (selectivity up to 5.3:1). Aryl groups with electron-withdrawing substituents migrated much worse than phenyl group, resulting in predominant formation of regioisomer with Ph group at the atom C4 (entries 2, 3; selectivity up to 6:1). The migratory aptitude of CH_3 group in these reactions proved to be much lower than for aryl counterparts, even relative to the aryl rings with a strong EWG. In these cases, methyl group remained predominantly on the spot at atom C5 of the heterocycle (entries 7, 8; selectivity up to 3.4:1).

Summing up, we have established that on interaction of 5,5-dialkyl(diaryl)-substituted 4-diazodihydrofuran-3(2*H*)-ones with Brønsted acids (TFA, TsOH, TfOH, $HClO_4$, etc.) the elimination of a nitrogen molecule occurred, which is attended by simultaneous 1,2-nucleophilic rearrangement to produce the associated 4,5-dialkyl(diaryl)-substituted 3(2*H*)-furanones in yields of up to 99%. The reaction is likewise a new powerful way for the synthesis of ring-fused 3(2*H*)-furanones and phenanthro[9,10-*b*]furan-3(2*H*)-ones from the appropriate diazoketones of tetrahydrofuran series in yields of 75–91%.

All reactions were carried out under an argon atmosphere in solvents dried and purified before use by common methods. Monitoring of the reaction course was accomplished by TLC on precoated silica gel SIL G/UV254 plates (Macherey-Nagel & Co.). Flash chromatography was performed using Merck silica gel 60, 230–400 mesh (eluent: hexane/CH_2Cl_2). IR spectra of the compounds were measured in CCl_4 solution by means of compact size FTIR spectrometer TENSOR 37 (Bruker). ^1H, ^{13}C, and ^{19}F NMR spectra were recorded on a Bruker 400 Avance NMR spectrometer. Chemical shifts are reported in ppm, and coupling constants are given in Hz. All signals in NMR spectra were normalized relative to signals of $CDCl_3$ (δ = 7.26 for ^1H NMR and δ = 77.0 for ^{13}C NMR spectra). Spectral parameters for all known compounds corresponded to the literature data.

Melting points are uncorrected. All the ESI/HR mass spectra were recorded on a «MaXis» (Bruker Daltonik GmbH). All diazo compounds **1a–u** were prepared using previously described protocols.[7]

3(2*H*)-Furanones; General Procedure

To a solution of diazoketone **1a–v** (0.6 mmol) in anhydrous solvent (mostly $CHCl_3$, 5 mL) was added dropwise up to 0.3 mL (3.8 mmol, 6.5 equiv) of TFA. After refluxing for 2–6 h (until completion of the reaction according to TLC), the mixture was washed with aq $NaHCO_3$, and the aqueous fractions were extracted with CH_2Cl_2 (3 × 15 mL). The combined organic fractions were dried over K_2CO_3. After removal of the solvent, pure 3(2*H*)-furanones **2–5** were obtained as a single compound (**2a–j**, **3a–c**) or as a mixture of isomers (**4n–v** and **5n–v**). Isomers were separated by flash chromatography or preparative TLC.

In some cases (see Table 2), instead of TFA for decomposition of 0.6 mmol of starting diazoketone **1n** other Brønsted acids were used: 0.6 mmol TsOH; 5 mL of 70% $HClO_4$; 0.3 mmol of HCl (gas); 0.6 mmol of 98% H_2SO_4; 0.6 mmol TfOH.

2,2,4,5-Tetramethylfuran-3(2*H*)-one (2a)[5]

Colorless liquid; yield: 69 mg (82%).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.34 (s, 6 H), 1.67 (s, 3 H), 2.18 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 6.0, 15.8, 23.1, 88.7, 109.2, 188.5, 210.8.

4,5-Dimethyl-2,2-diphenylfuran-3(2*H*)-one (2b)[5]

Colorless solid; yield: 138 mg (87%); mp 110–111 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.71 (s, 3 H), 2.31 (s, 3 H), 7.21–7.59 (m, 10 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 6.3, 15.5, 91.3, 110.2, 126.9, 128.6, 128.8, 139.1, 183.9, 203.1.

2,2-Bis(4-fluorophenyl)-4,5-dimethylfuran-3(2*H*)-one (2c)[5]

Colorless solid; yield: 148 mg (82%); mp 70–71 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.72 (s, 3 H), 2.32 (s, 3 H),6.98–7.44 (m, 8 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 5.9, 15.1, 89.8, 109.8, 115.4 (d, $^2J_{C,F}$ = 21.0 Hz), 128.4 (d, $^3J_{C,F}$ = 8 Hz), 134.4 (d, $^4J_{C,F}$ = 3.0 Hz), 162.6 (d, $^1J_{C,F}$ = 246.0 Hz), 183.8, 202.5.

2,2-Bis(4-methoxyphenyl)-4,5-dimethylfuran-3(2*H*)-one (2d)[5]

Colorless oil; yield: 191 mg (98%).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.72 (s, 3 H), 2.31 (s, 3 H), 3.78 (s, 6 H), 6.85 (d, *J* = 9.0 Hz, 4 H), 7.34 (d, *J* = 9.0 Hz, 4 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 5.9, 15.1, 55.3, 91.1, 109.7, 113.7, 128.0, 130.9, 159.5, 184.0, 203.7.

2,4,5-Trimethyl-2-phenylfuran-3(2*H*)-one (2e)

Colorless oil; yield: 101 mg (83%).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.68 (s, 3 H), 1.72 (s, 3 H), 2.30 (s, 3 H), 7.19–7.40 (m, 3 H), 7.49 (d, *J* = 7.0 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 5.8, 15.0, 24.5, 88.6, 108.7, 124.6, 128.0, 128.4, 138.3, 184.3, 205.6.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{13}H_{14}O_2Na$: 225.0891; found: 225.0889.

2,4,5-Trimethyl-2-(*p*-tolyl)furan-3(2*H*)-one (2f)

Colorless oil; yield: 95 mg (73%).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.67 (s, 3 H), 1.69 (s, 3 H), 2.28 (s, 3 H), 2.32 (s, 3 H), 7.15 (d, *J* = 8.0 Hz, 2 H), 7.37 (d, *J* = 8.1 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 5.8, 15.0, 21.0, 24.5, 88.4, 108.6, 124.5, 129.1, 135.6, 137.7, 183.4, 205.3.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{14}H_{16}O_2Na$: 17.1238; found: 217.1229.

2,2-Dimethyl-4,5-diphenylfuran-3(2*H*)-one (2g)[5]

Colorless solid; yield: 155 mg (98%); mp 81–82 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.58 (s, 6 H), 7.28–7.68 (m, 10 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 23.8, 87.4, 114.0, 127.9, 128.8, 129.0, 129.9, 130.4, 132.2, 178.4, 205.8.

4,5-Bis(4-fluorophenyl)-2,2-dimethylfuran-3(2*H*)-one (2h)[5]

Colorless solid; yield: 167 mg (93%); mp 109–110 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.55 (s, 6 H), 7.03–7.30 (m, 6 H), 7.63–7.68 (dd, *J* = 9.0, $J_{H,F}$ = 6.0 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 23.3, 87.2, 112.5, 115.8 (d, $^2J_{C,F}$ = 21.9 Hz), 125.9 (d, $^3J_{C,F}$ = 18.9 Hz), 130.7 (d, $^3J_{C,F}$ = 9.0 Hz), 131.2 (d, $^3J_{C,F}$ = 8.3 Hz), 162.3 (d, $^1J_{C,F}$ = 247.5 Hz), 164.7 (d, $^1J_{C,F}$ = 256.6 Hz), 177.0, 205.1.

4,5-Bis(4-chlorophenyl)-2,2-dimethylfuran-3(2*H*)-one (2i)

Colorless oil; yield: 196 mg (98%).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.58 (s, 6 H), 7.26 (d, *J* = 8.4 Hz, 2 H), 7.33–7.44 (m, 4 H), 7.60 (d, *J* = 8.5 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 23.3, 87.4, 112.7, 128.1, 128.9, 129.0, 129.7, 130.7, 133.6, 138.2, 177.0, 204.9.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{18}H_{14}Cl_2O_2Na$: 355.0269; found: 355.0265.

4,5-Bis(4-methoxyphenyl)-2,2-dimethylfuran-3(2*H*)-one (2j)[5]

Colorless solid; yield: 189 mg (97%); mp 127–128 °C.

^{1}H NMR (300 MHz,$CDCl_3$): δ = 1.55 (s, 6 H), 3.84 (s, 6 H), 6.85 (d, *J* = 9.0 Hz, 2 H), 6.92 (d, *J* = 9.0 Hz, 2 H), 7.25 (d, *J* = 9.0 Hz, 2 H), 7.64 (d, *J* = 9.0 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.2, 55.4, 86.5, 112.0, 113.7, 114.1, 122.4, 122.6, 130.1, 130.8, 158.9, 162.3, 177.4, 205.4.

4,5,6,7-Tetrahydro-3*H*-spiro[benzofuran-2,1′-cyclopentan]-3-one (3k)

Colorless oil; yield: 105 mg (91%).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.55-2.06 (m, 12 H), 2.19 (t, *J* = 6.0 Hz, 2 H), 2.41 (t, *J* = 6.2 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.3, 21.8, 25.5, 26.1, 36.9, 98.2, 111.9, 187.5, 205.1.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{12}H_{16}O_2Na$: 215.1048; found: 215.1045.

5,6,7,8-Tetrahydrospiro[cyclohepta[*b*]furan-2,1′-cyclohexan]-3(4*H*)-one (3l)

Colorless solid; yield: 99 mg (75%); mp 83–85 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.25–1.40 (m, 1 H), 1.42–1.85 (m, 15 H), 2.09–2.33 (m, 2 H), 2.55–2.65 (m, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 20.4, 21.8, 24.4, 25.0, 27.5, 30.1, 31.7, 32.2, 89.1, 114.6, 190.0, 206.8.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{14}H_{20}O_2Na$: 243.1361; found: 243.1366.

2,2-Dimethylphenanthro[9,10-*b*]furan-3(2*H*)-one (3m)

Bright-yellow oil; yield: 134 mg (85%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.63 (s, 6 H), 7.54–7.63 (m, 1 H), 7.69 (td, *J* = 7.8, 0.9 Hz, 2 H), 7.85–7.90 (m, 1 H), 8.36 (dd, *J* = 8.0, 0.9 Hz, 1 H), 8.57 (d, *J* = 8.2 Hz, 1 H), 8.67 (d, *J* = 8.4 Hz, 1 H), 8.86 (dd, *J* = 8.0, 1 Hz, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 23.3 , 89.6, 108.2, 122.0, 122.8, 123.4, 123.5, 123.8, 125.6, 126.7, 127.1, 127.6, 128.7, 131.5, 135.8, 172.8, 203.5.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{18}H_{14}O_2Na$: 285.0891; found: 285.0882.

2,2-Dimethyl-5-[4-(methylthio)phenyl]-4-phenylfuran-3(2*H*)-one (4n)[12]

Colorless oil; yield: 44 mg (24%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.55 (s, 6 H), 2.48 (s, 3 H), 7.15–7.17 (m, 1 H), 7.25 (d, *J* = 7.6 Hz, 2 H), 7.30–7.40 (m, 4 H), 7.56 (d, *J* = 7.4 Hz, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 15.7, 23.4, 86.9, 113.1, 125.0, 128.6, 128.6, 129.6, 131.8, 144.3, 177.6, 205.2.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{18}O_2SH$: 311.1106; found: 311.1113.

2,2-Dimethyl-4-[4-(methylthio)phenyl]-5-phenylfuran-3(2*H*)-one (5n)

Bright yellow crystals; yield: 140 mg (75%); mp 120–121 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.55 (s, 6 H), 2.49 (s, 3 H), 7.24–7.25 (m, 4 H), 7.36 (d, *J* = 7.6 Hz, 2 H), 7.45–7.49 (m, 1 H), 7.66 (d, *J* = 7.4 Hz, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 15.7, 23.4, 87.0, 113.0, 126.6, 128.4, 128.4, 129.8, 131.8, 137.8, 178.1, 205.4.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{18}O_2SH$: 311.1106; found: 311.1107.

2,2-Dimethyl-5-[4-(methylsulfinyl)phenyl]-4-phenylfuran-3(2*H*)-one (4o)

Colorless crystals; yield: 157 mg (80%); mp 178–179 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.57 (s, 6 H), 2.74 (s, 3 H), 7.28–7.39 (m, 5 H), 7.64 (d, *J* = 8.3 Hz, 2 H), 7.78 (d, *J* = 8.2 Hz, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 23.4, 43.8, 87.3, 114.7, 123.6, 127.9, 128.8, 129.2, 129.4, 132.6, 149.5, 176.2, 205.3.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{18}O_3SNa$: 349.0874; found: 349.0874.

2,2-Dimethyl-4-[4-(methylsulfinyl)phenyl]-5-phenylfuran-3(2*H*)-one (5o)

Colorless oil; yield: 35 mg (18%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.58 (s, 6 H), 2.74 (s, 3 H), 7.27–7.42 (m, 2 H), 7.49–7.51 (m, 3 H), 7.55–7.68 (m, 4 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 23.3, 23.4, 43.9, 87.6, 112.4, 123.9, 127.8, 128.5, 128.7, 129.6, 130.4, 132.3, 144.6, 179.2, 204.9.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{18}O_3SNa$: 349.0874; found: 349.0876.

2,2-Dimethyl-5-[4-(methylsulfonyl)phenyl]-4-phenylfuran-3(2*H*)-one (4p)

Colorless crystals; yield: 172 mg (84%); mp 201–202 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.58 (s, 6 H), 3.06 (s, 3 H), 7.26–7.40 (m, 5 H), 7.73 (d, *J* = 8.5 Hz, 2 H), 8.03 (d, *J* = 8.4 Hz, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 23.3, 43.3, 87.5, 115.6, 127.4, 128.2, 128.9, 129.2, 129.4, 135.1, 142.8, 175.2, 205.2.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{18}O_4SH$: 343.1004; found: 343.0996.

2,2-Dimethyl-4-[4-(methylsulfonyl)phenyl]-5-phenylfuran-3(2*H*)-one (5p)

Colorless crystals; yield: 29 mg (14%); mp 181–182 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.58 (s, 6 H), 3.05 (s, 3 H), 7.39 (t, *J* = 7.7 Hz, 2 H), 7.50–7.55 (m, 3 H), 7.60 (d, *J* = 8.5 Hz, 2 H), 7.90 (d, *J* = 8.4 Hz, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 23.3, 43.5, 87.9, 111.7, 127.6, 128.4, 128.7, 129.2, 130.1, 132.4, 136.2, 139.0, 179.8, 204.4.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{18}O_4SNa$: 365.0823; found: 365.0823.

2,2-Dimethyl-4-(4′-fluorophenyl)-5-[4′-(methylthio)phenyl]furan-3(2*H*)-one (5q)

Bright yellow oil; yield: 150 mg (76%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.54 (s, 6 H), 2.48 (s, 3 H), 7.00–7.15 (m, 2 H), 7.20–7.25 (m, 2 H), 7.40 (d, *J* = 8.1 Hz, 1 H), 7.54 (d, *J* = 8.5 Hz, 2 H), 7.84 (d, *J* = 8.3 Hz, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 14.7, 21.7, 86.9, 112.0, 115.6 (d, *J* = 21.4 Hz), 126.09, 126.12, 127.5, 130.2, 131.2 (d, *J* = 8.0 Hz), 146.1, 164.6 (d, *J* = 254.0 Hz), 177.6, 205.0.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –114.2.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{17}FO_2SNa$: 351.0831; found: 351.0836.

2,2-Dimethyl-4-[4′-(methylthio)phenyl]-5-(4′-fluorophenyl)furan-3(2*H*)-one (4q)

Bright yellow oil; yield: 45 mg (23%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.54 (s, 6 H), 2.49 (s, 3 H), 7.00–7.19 (m, 2 H), 7.20–7.25 (m, 4 H), 7.68 (dd, *J* = 8.9, 5.4 Hz, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 15.6, 23.4, 87.1, 112.8, 115.7 (d, *J* = 21.9 Hz), 126.4, 126.6, 128.5, 129.8, 130.7 (d, *J* = 8.9 Hz), 138.0, 164.7 (d, *J* = 254.0 Hz), 176.8, 205.2.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –106.3.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{17}FO_2SH$: 329.1012; found: 329.1007.

2,2-Dimethyl-4-(4′-chlorophenyl)-5-[4′-(methylthio)phenyl]furan-3(2*H*)-one (5r)

Bright yellow oil; yield: 43 mg (21%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.54 (s, 6 H), 2.49 (s, 3 H), 7.18 (d, *J* = 8.6 Hz, 2 H), 7.33 (d, *J* = 8.6 Hz, 2 H), 7.26 (d, *J* = 8.1 Hz, 2 H), 7.33 (d, *J* = 8.6 Hz, 2 H), 7.54 (d, *J* = 8.6 Hz, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 14.8, 23.3, 87.1, 111.8, 125.1, 125.7, 126.2, 128.4, 128.6, 128.7, 133.3, 144.7, 177.9, 204.8.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{17}ClO_2SNa$: 367.0535; found: 367.0536.

2,2-Dimethyl-4-[4′-(methylthio)phenyl]-5-(4′-chlorophenyl)furan-3(2*H*)-one (4r)

Bright yellow oil; yield: 135 mg (65%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.54 (s, 6 H), 2.49 (s, 3 H), 7.20–7.24 (m, 4 H), 7.33 (d, *J* = 8.6 Hz, 2 H), 7.60 (d, *J* = 8.6 Hz, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 15.6, 23.3, 87.1, 113.3, 126.6, 128.8, 128.9, 129.7, 129.8, 130.8, 138.0, 138.2, 176.6, 205.2.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{17}ClO_2SH$: 345.0716; found: 345.0720.

2,2-Dimethyl-4-(3′-chlorophenyl)-5-[4′-(methylthio)phenyl]furan-3(2*H*)-one (5s)

Bright yellow oil; yield: 31 mg (15%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.55 (s, 6 H), 2.47 (s, 3 H), 7.17–7.28 (m, 4 H), 7.55 (d, *J* = 8.6 Hz, 2 H), 7.84 (d, *J* = 8.3 Hz, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 14.7, 23.3, 87.2, 111.8, 125.0, 125.5, 125.9, 127.6, 127.7, 128.6, 129.5, 129.9, 132.1, 134.4, 178.0, 204.6.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{17}ClO_2SNa$: 367.0535; found: 367.0536.

2,2-Dimethyl-4-[4′-(methylthio)phenyl]-5-(3′-chlorophenyl)furan-3(2*H*)-one (4s)

Bright yellow oil; yield: 164 mg (79%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.55 (s, 6 H), 2.49 (s, 3 H), 7.21–7.26 (m, 4 H), 7.36 (s, 1 H), 7.43 (d, *J* = 9.1 Hz, 1 H), 7.48 (d, *J* = 7.8 Hz, 1 H), 7.72 (s, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 15.6 , 23.3, 87.2, 113.7, 126.6, 126.7, 128.0, 128.3, 129.7, 129.8, 131.7, 131.8, 134.7, 138.2, 176.1, 205.3.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{17}ClO_2SNa$: 345.0716, found: 345.0718.

2,2,4-Trimethyl-5-phenylfuran-3(2*H*)-one (4t)[13]

Colorless oil; yield: 38 mg (31%).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.43 (s, 6 H), 1.97 (s, 3 H), 7.35–7.50 (m, 3 H), 7.68–7.88 (m, 2 H).

2,2,5-Trimethyl-4-phenylfuran-3(2*H*)-one (5t)

Colorless oil; yield: 76 mg (63%).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.48 (s, 6 H), 2.40 (s, 3 H), 7.21–7.3 (m, 1 H), 7.38–7.45 (m, 4 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 16.3, 23.1, 87.2, 114.1, 127.0, 128.4, 128.5, 129.8, 183.3, 204.7.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{13}H_{14}O_2Na$: 225.0891; found: 225.0885.

2,2,4-Trimethyl-5-(*p*-tolyl)furan-3(2*H*)-one (4u)[13]

Colorless oil; yield: 25 mg (19%).

^{1}H NMR (300 MHz, $CDCl_3$): δ = (s, 6 H), 1.92 (s, 3 H), 2.41 (s, 3 H), 7.10–7.25 (m, 2 H), 7.55–7.72 (m, 2 H).

2,2,5-Trimethyl-4-(*p*-tolyl)furan-3(2*H*)-one (5u)

Colorless oil; yield: 84 mg (65%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.44 (s, 6 H), 2.35 (s, 3 H), 2.36 (s, 3 H), 7.21 (d, *J* = 8.0 Hz, 2 H), 7.28 (d, *J* = 8.2 Hz, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 16.2, 21.2, 23.1, 87.1, 114.0, 126.8, 128.3, 129.1, 136.8, 182.9, 204.8.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{14}H_{16}O_2Na$: 217.1238; found: 217.1231.

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

Colorless oil; yield: 68 mg (42%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.47 (s, 6 H), 2.40 (s, 3 H), 7.53 (d, *J* = 8.1 Hz, 2 H), 7.65 (d, *J* = 8.2 Hz, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 16.5, 23.1, 87.8, 113.1, 125.4 (q, *J* = 3.8 Hz), 128.5, 133.7, 184.1, 204.2.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{13}F_3O_2H$: 271.0946; found: 271.0951.

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

Colorless oil; yield: 89 mg (55%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.46 (s, 6 H), 2.01 (s, 3 H), 7.76 (d, *J* = 8.3 Hz, 2 H), 7.94 (d, *J* = 8.2 Hz, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 7.4, 23.2, 86.3, 109.5, 125.6 (q, *J* = 3.8 Hz), 128.2, 134.0, 175.7, 208.1.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{13}F_3O_2H$: 271.0946; found: 271.0948.

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Supporting Information

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