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Rh(III)-Catalyzed Cascade Nucleophilic Addition/Annulation of 2-Diazo-1,3-diketones with 1,3-Dicarbonyl Compounds To Access 6,7-Dihydrobenzofuran-4(5*H*)-ones

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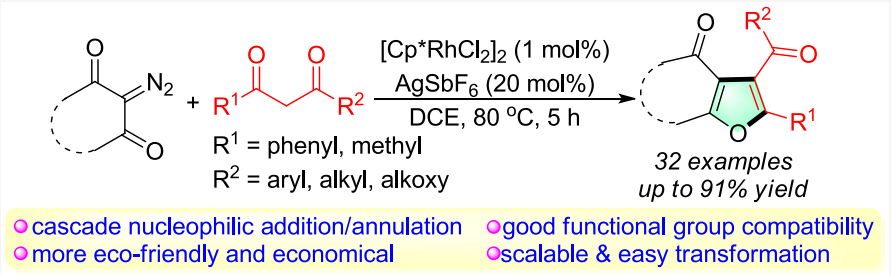

ABSTRACT: A Rh(III)-catalyzed cascade nucleophilic addition/intramolecular annulation of 2-diazo-1,3-diketones with 1,3-dicarbonyl compounds (e.g., 1,3-diketones and β-keto esters) is achieved to afford 6,7-dihydrobenzofuran-4(5*H*)-ones in up to 91% yields. Notably, a wide range of substrates and functional groups were well-tolerated under the optimized reaction conditions to give desired products in moderate to excellent yields with release of N_2 and H_2O as byproducts. Moreover, the method described is scalable and adaptable to late-stage functionalization.

INTRODUCTION

Fused and substituted furan derivatives are important heterocycles which widely exist in natural products, drugs, and other bioactive molecules and exhibit extraordinary biological activities.[1] Among them, the 6,7-dihydrobenzofuran-4(5*H*)-one skeleton and derivatives thereof not only are present in natural products (Figure 1)[2] but also play a role as an important intermediate in the preparation of a wide range of synthetic compounds with diverse biological applications.[3] To date, considerable efforts have been devoted to construct 6,7-dihydrobenzofuran-4(5*H*)-one derivatives.[4] Recently, the unique structures are typically constructed by the simple and efficient domino and three-component reactions starting from dimendone (Scheme 1a).[5−8] In addition, Hashmi and co-workers demonstrated that 6,7-dihydrobenzofuran-4(5*H*)-ones and benzofurans can be formed from chemoselective gold(I)-catalyzed transformation of 1-(arylethynyl)-7-oxabicyclo-[4.1.0]heptan-2-ones (Scheme 1b).[9] Despite considerable efforts toward their synthesis, there still is a strong demand for more efficient synthetic approaches.

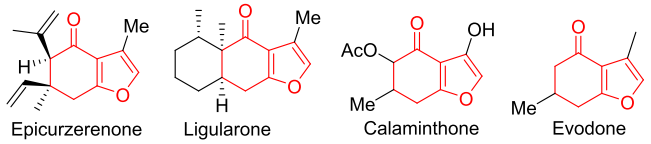

Figure 1. Selected examples of natural 6,7-dihydrobenzofuran-4(5*H*)-one derivatives.

Diazo compounds have been widely used as a powerful substrate for the construction of natural and unnatural compounds via transition-metal-catalyzed addition, insertion, cyclization, C−H activation, rearrangement, and others.[10,11] Recently, Bi and co-workers described a catalyst-dependent chemoselective formal insertion of α-diazo esters into C−C or C−H bonds of 1,3-dicarbonyl compounds leading to a 1,4-dicarbonyl product containing an all-carbon α-quaternary center and 2-alkylated 1,3-dicarbonyl products (Scheme 2a).[12] On the other hand, Lee and co-workers developed a novel and selective Ru-catalyzed cyclization of cyclic diazodicarbonyls with β-ketoamides for the synthesis of cyclohexanone-fused γ-butenolides via C−C coupling and amide cleavage process by aniline extrusion (Scheme 2b).[13]

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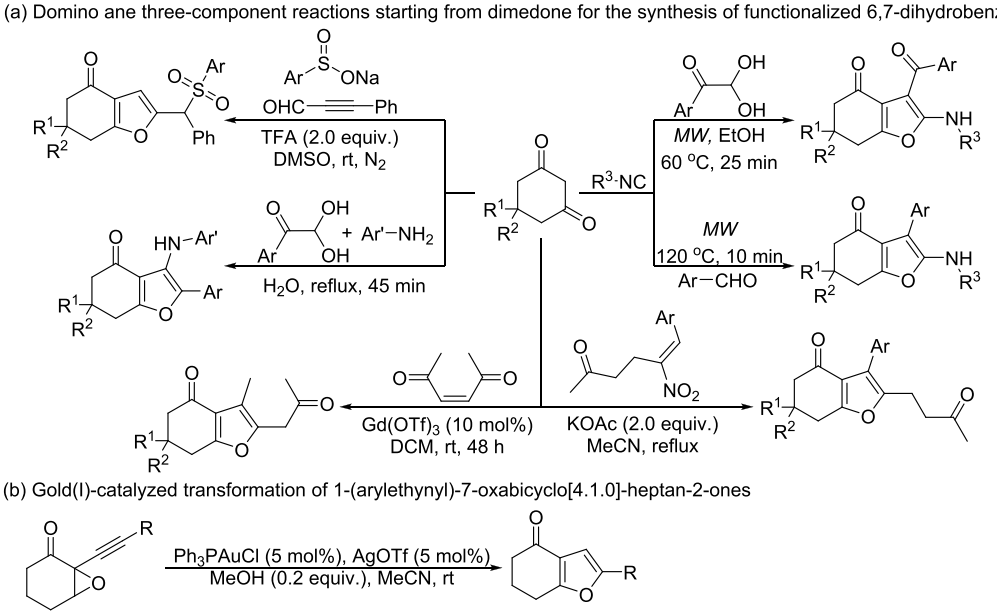
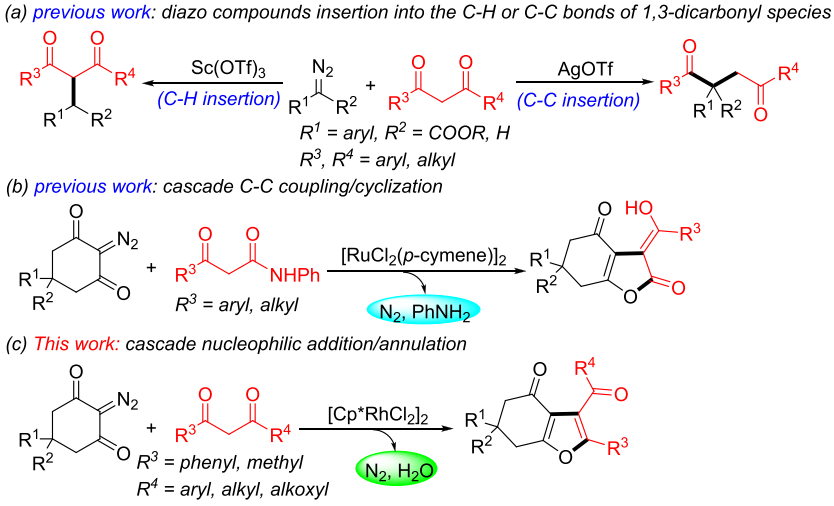
Scheme 1. Previous Synthetic Strategies for 6,7-Dihydrobenzofuran-4(5*H*)-ones



Scheme 2. Transition-Metal-Catalyzed C−C Bond Formation of Diazo Compounds with 1,3-Dicarbonyl Compounds



We previously reported the Rh-catalyzed diazo compounds with various substrates for the construction of heterocycles.[14] As a result of our continued exploration in this area, we herein report a novel and efficient Rh(III)-catalyzed cascade nucleophilic addition/intramolecular annulation of 2-diazo-1,3-diketones with 1,3-dicarbonyl compounds affording 6,7-dihydrobenzofuran-4(5*H*)-ones in moderate to excellent yields (Scheme 2c).

RESULTS AND DISCUSSION

We began our investigation utilizing 2-diazo-5,5-dimethylcyclohexane-1,3-dione (**1a**) and 1-phenylbutane-1,3-dione (**2a**) as the model substrates in the presence of $Rh_2(OAc)_4$ and $AgSbF_6$ as the catalyst system in 1,2-dichloroethane (DCE) at 80 °C for 5 h, and only a trace amount of product **3a** was monitored (Table 1, entry 1). To our delight, the desired product **3a** was isolated in 83% yield when $[Cp^*RhCl_2]_2$ was used as the catalyst (Table 1, entry 2). The transformation did not take place by using other transition-metal catalysts (Table 1, entries 3−6). Further investigation indicated that $[Cp^*RhCl_2]_2$ (1 mol %) together with $AgSbF_6$ (20 mol %) as a cocatalyst was the optimal catalyst system (Table 1, entries 7−16). The subsequent solvent screening revealed that DMF (*N*,*N*-dimethyl formamide), MeCN, toluene, THF (tetrahydrofuran), and ethanol did not improve the yield of product **3a** (Table 1, entries 17−22). Finally, examining the effect of temperature and reaction time ultimately provided the optimal conditions listed in entry 2 in Table 1.

Having obtained the optimized conditions, we next explored the substrate scope using various cyclic 2-diazo-1,3-diketones and 1,3-diketones (Table 2). Benzoylacetones bearing an electron-donating and electron-withdrawing substituent (e.g., Me, OMe, Cl, Br) smoothly reacted with diazo compound **1a** to give the corresponding products **3a**−**3e** in 76−87% yields. Chloro and bromo substituents at the *para*- and *ortho*-position of benzene ring were well tolerated, which makes this transformation particularly attractive in terms of increasing the molecular complexity via transition-metal-catalyzed coupling reactions. Aside from benzoylacetones, 1,3-diphenylpro-

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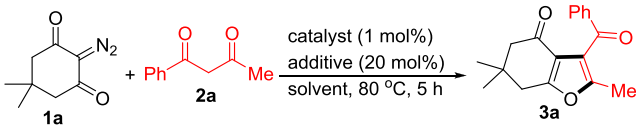
Table 1. Optimization of the Reaction Conditions[a]



entry	catalyst	additive	solvent	yield/%[b]
1	$Rh_2(OAc)_4$	$AgSbF_6$	DCE	trace
2	$[Cp^*RhCl_2]_2$	$AgSbF_6$	DCE	83
3	$Rh(PPh_3)Cl$	$AgSbF_6$	DCE	trace
4	$Pd(OAc)_2$	$AgSbF_6$	DCE	nr
5	$[Ru(p\text{-cymene})Cl_2]_2$	$AgSbF_6$	DCE	trace
6	CuI	$AgSbF_6$	DCE	nr
7[c]	$[Cp^*RhCl_2]_2$	$AgSbF_6$	DCE	68
8[d]	$[Cp^*RhCl_2]_2$	$AgSbF_6$	DCE	82
9	$[Cp^*RhCl_2]_2$	CsOAc	DCE	trace
10	$[Cp^*RhCl_2]_2$	Ag_2CO_3	DCE	trace
11	$[Cp^*RhCl_2]_2$	AgOTf	DCE	46
12	$[Cp^*RhCl_2]_2$	$AgNTf_2$	DCE	trace
13	$[Cp^*RhCl_2]_2$	$AgBF_4$	DCE	32
14	$[Cp^*RhCl_2]_2$	Cs_2CO_3	DCE	trace
15[e]	$[Cp^*RhCl_2]_2$	$AgSbF_6$	DCE	73
16[f]	$[Cp^*RhCl_2]_2$	$AgSbF_6$	DCE	80
17	$[Cp^*RhCl_2]_2$	$AgSbF_6$	DMF	trace
18	$[Cp^*RhCl_2]_2$	$AgSbF_6$	DCM	trace
19	$[Cp^*RhCl_2]_2$	$AgSbF_6$	MeCN	trace
20	$[Cp^*RhCl_2]_2$	$AgSbF_6$	toluene	trace
21	$[Cp^*RhCl_2]_2$	$AgSbF_6$	THF	56
22	$[Cp^*RhCl_2]_2$	$AgSbF_6$	C_2H_5OH	trace
23[g]	$[Cp^*RhCl_2]_2$	$AgSbF_6$	DCE	74
24[h]	$[Cp^*RhCl_2]_2$	$AgSbF_6$	DCE	75
25[i]	$[Cp^*RhCl_2]_2$	$AgSbF_6$	DCE	61
26[j]	$[Cp^*RhCl_2]_2$	$AgSbF_6$	DCE	82

[a]Reaction conditions: **1a** (1 mmol), **2a** (1 mmol), catalyst (1 mol %), and additive (20 mol %) in solvent (3 mL) at 80 °C for 5 h. [b]Isolated yields. [c]The catalyst loading was 0.5 mol %. [d]The catalyst loading was 2 mol %. [e]The additive loading was 10 mol %. [f]The additive loading was 30%. [g]50 °C. [h]100 °C. [i]For 3 h. [j]For 6 h. nr = no reaction.

pane-1,3-dione (**2f**), and acetylacetone (**2g**) were also suitable substrates, affording the corresponding products **3f** and **3g** in 91% and 67% yields, respectively. Subsequently, 2-diazocyclohexane-1,3-dione bearing substituents such as hydrogen (**1b**), monomethyl (**1c**), phenyl (**1d**), and 4-chlorophenyl (**1f**) were detected, giving the corresponding products **3h**−**3j** and **3t** in 47−69% yields. In addition, a series of desired products **3k**−**3s** were obtained in satisfactory yields (41−75%) through the cross reaction of different cyclic diazo compounds with 1,3-diketones. Notably, the reaction also proceeded well by using 1-phenylpentane-1,3-dione and 4-methyl-1-phenylpentane-1,3-dione as substrates, and the corresponding products **3u** and **3v** were obtained in 86% and 89% yield, respectively.

Next, we tried to extend the scope of the reaction with respect to the *β*-keto esters (Table 3). Various 4,5,6,7-tetrahydrobenzofuran-3-carboxylates were obtained in moderate to good yields with wide functional group compatibility: aryl (bearing with halogen, nitro group), alkyl, and trifluoromethyl groups were all tolerated. *β*-Keto esters bearing a strong electron-withdrawing group had higher reactivity, producing the corresponding products in higher yields (**5c**, **5h**). Unfortunately, *β*-keto esters bearing either a cyclopropyl (**4f**) or 2-furyl (**4g**) group failed to provide the corresponding products **5i** and **5j**.

In order to investigate the efficiency and utility of this method, an acyclic 2-diazo-1,3-diketone, such as 3-diazopentane-2,4-dione (**6**), was also compatible with the reaction conditions, delivering the corresponding products **7a** and **7b** in 87% and 79% yields, respectively (Scheme 2a). Furthermore, a gram-scale reaction was carried out, giving the corresponding product **3f** with almost comparable yield (0.89 g, 86%). Then, further synthetic transformations of the products were performed to showcase the applicability of this methodology. Derivatizations of compound **3f** were performed by reacting with hydrazine hydrate, generating a fused-tricyclic product 7,7-dimethyl-3,4-diphenyl-7,8-dihydro-6*H*-furo[4,3,2-*de*]-cinnoline **8** in 67% yield (Scheme 3c). In addition, treating compounds **3f**, **3r**, and **3v** with sodium borohydride and hydroxylamine hydrochloride successfully realized the formation of the products **9**, **10**, and **11** in 65%, 85%, and 68% yields, respectively (Scheme 3c). The structures of **9**, **10**, and **11** were confirmed by X-ray diffraction (see the Supporting Information).

In order to have more insight toward the reaction mechanism, we initially performed the H/D exchange experiment in deuterium oxide under the standard conditions, affording the deurerated product **2f-*d*$_1$** in 71% yield (Scheme 4a). Spectroscopic data showed that one H atom on the methylene group of **2f** was exchanged with a deuterium atom (>99%). Furthermore, we determined the kinetic isotope effect (KIE) of this cascade reaction. A KIE value of 1.4 was determined from two parallel independent kinetic reactions, giving the corresponding product **3f** in 51% and 36% yields, respectively (Scheme 4b). On the basis of these results and literature precedents,[11,12] a plausible reaction mechanism was proposed in Scheme 4c. The catalyst $[Cp^*RhCl_2]_2$ initially reacted with cocatalyst $AgSbF_6$ to form the active catalyst species $[Cp^*RhL_2]_2$ (L = SbF_6), followed by the formation of metalcarbene species **A** with release of the N_2 molecule. Subsequent, the metalcarbene species **A** reacted with intermediate **B** resulting from the enolization of 1,3-diketones **2** to form intermediate **C** through an intermolecular nucleophilic addition. Then the protonolysis of the Rh−C bond of intermediate **C** produced the intermediate **D** and regenerated the active catalyst for a new catalytic cycle. Finally, intermediate **D** was proposed to undergo enol−ketone tauisomerization and intramolecular nucleophilic cyclization followed by dehydration to eventually furnish the desired products **3**.

■ CONCLUSIONS

In summary, we have developed a mild and efficient strategy for construction 6,7-dihydrobenzofuran-4(5*H*)-ones through Rh(III)-catalyzed cascade C−H insertion/annulation of 2-diazo-1,3-diketones with 1,3-dicarbonyl compounds and *β*-keto esters. This intermolecular annulation procedure undergoes a cascade nucleophilic addition and intramolecular nucleophilic annulation process. Particularly noteworthy is that the byproducts of N_2 and H_2O in the reaction make the process environmentally benign. In addition, this operationally simple method offers direct access to an important furan skeleton starting from simple and readily available 1,3-dicarbonyl compounds and may find applications in medicinal chemistry.

■ EXPERIMENTAL SECTION

General Information. Reactions were monitored by using thin-layer chromatography (TLC) on commercial silica gel plates (GF

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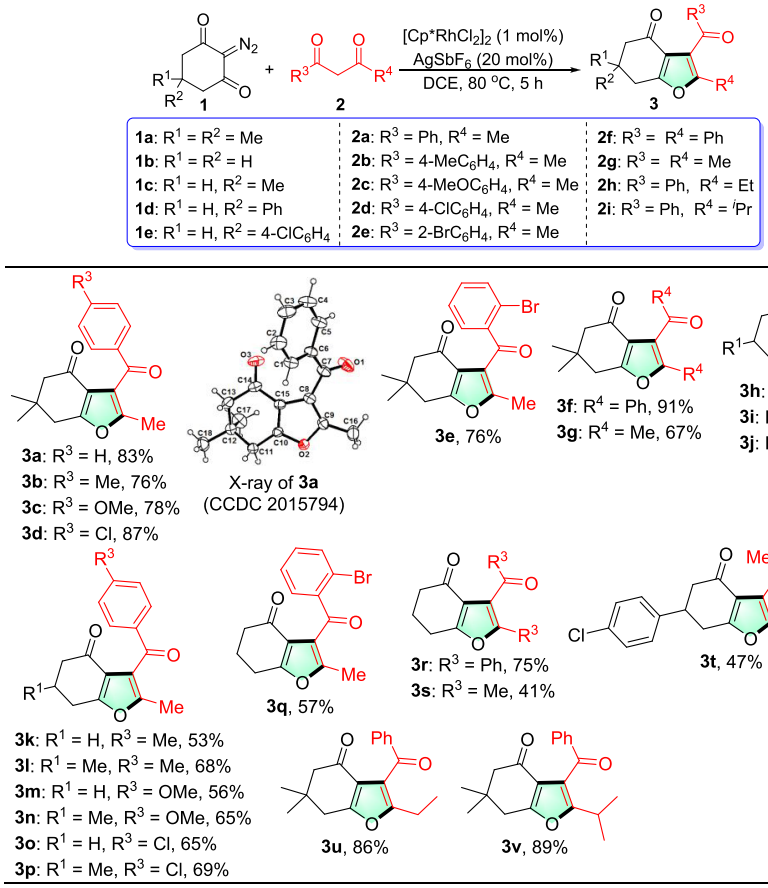
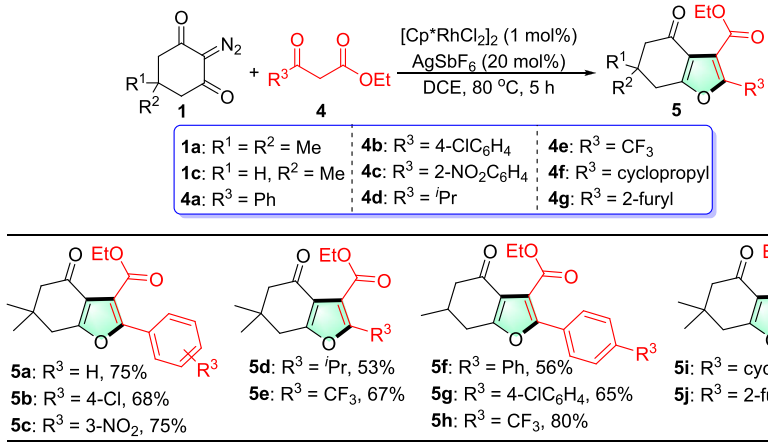
Table 2. Substrate Scope[a,b]



[a]Reaction conditions: cyclic 2-diazo-1,3-diketones **1** (1 mmol), 1,3-diketones **2** (1 mmol), $[Cp^*RhCl_2]_2$ (1 mol %), and $AgSbF_6$ (20 mol %) in DCE (3 mL) at 80 °C for 5 h. [b]Isolated yields.

Table 3. Synthesis of 6,7-Dihydrobenzofuran-4(5*H*)-ones from Cyclic 2-Diazo-1,3-diketones with *β*-Keto Esters[a,b]



[a]Reaction conditions: cyclic 2-diazo-1,3-diketones **1** (1 mmol), *β*-keto esters **4** (1 mmol), $[Cp^*RhCl_2]_2$ (1 mol %), and $AgSbF_6$ (20 mol %) in DCE (3 mL) at 80 °C for 5 h. [b]Isolated yields.

254). Visualization of the developed plates was performed under UV lights (GF 254 nm). Flash column chromatography was performed on silica gel (200−300 mesh). ^1H and ^{13}C NMR spectra were recorded on a 300 and 400 MHz spectrometer. Chemical shifts were expressed in parts per million (δ); the signals were reported as s (singlet), br s (broad singlet), d (doublet), dd (doublet of doublet), t (triplet), q (quartet), and m (multiplet); and coupling constants (J) were given in Hz. $^{13}C\{^1H\}$ NMR spectra were recorded at 75 and 100 MHz in $CDCl_3$ solution. Chemical shifts as internal standard were referenced to $CDCl_3$ (δ = 7.26 for ^1H and δ = 77.16 for $^{13}C\{^1H\}$ NMR) as an internal standard. HRMS analysis with a quadrupole time-of-flight mass spectrometer yielded ion mass/charge (m/z) ratios in atomic mass units. IR spectra were measured as dry films (KBr), and the peaks are reported in terms of wavenumber (cm^{-1}). The melting points were measured using an SGWX-4 melting point apparatus.

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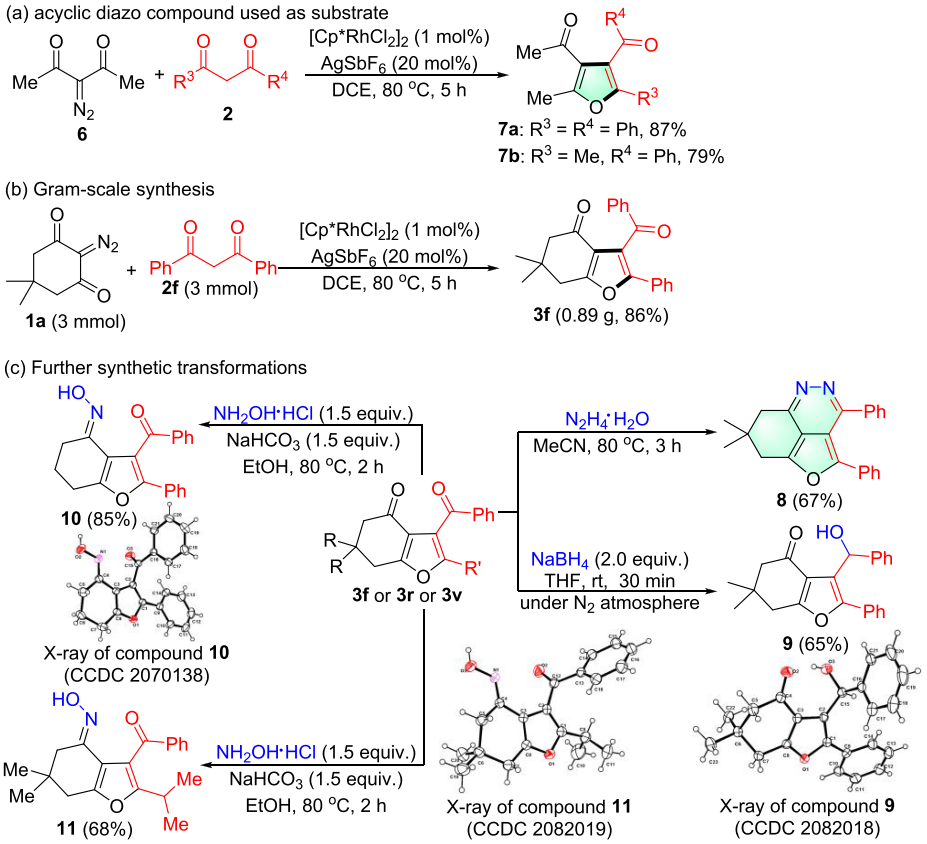
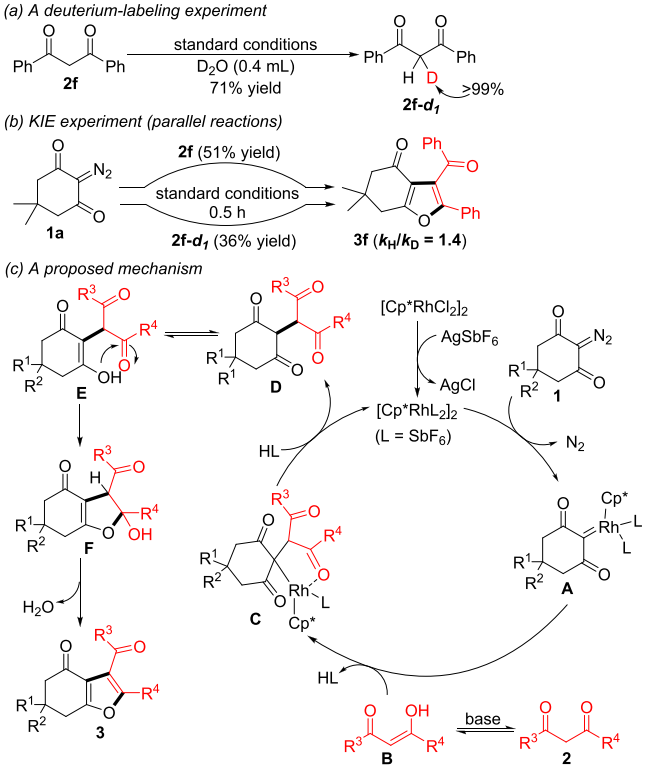
Scheme 3. Further Studies



Scheme 4. Control Experiments and Proposed Mechanism



General Procedure for the Synthesis of Dihydrobenzofuran-4(5*H*)-ones 3. A mixture of cyclic 2-diazo-1,3-diketones **1** (1 mmol), 1,3-diketones **2** (1 mmol), $[Cp^*RhCl_2]_2$ (1 mol %), and $AgSbF_6$ (20 mol %) in 1,2-dihaloethane (3 mL) was heated to 80 °C in an oil bath for 5 h. After the reaction completed (as determined using TLC), the reaction mixture was cooled to room temperature, extracted with dichloromethane (3 × 10 mL), and washed with brine. The organic layers were combined, dried over Na_2SO_4, filtered, and then evaporated under vacuum. The residue was purified using flash column chromatography with a silica gel (200−300 mesh), using ethyl acetate and petroleum ether (1:6, v/v) as the elution solvent to give desired product **3**.

Gram-Scale Synthesis of Compound 3f. A mixture of 2-diazo-5,5-dimethylcyclohexane-1,3-dione **1a** (498 mg, 3 mmol), 1,3-diphenylpropane-1,3-dione **2f** (672 mg, 3 mmol), $[Cp^*RhCl_2]_2$ (1 mol %), and $AgSbF_6$ (20 mol %) in 1,2-dihaloethane (3 mL) was heated to 80 °C in an oil bath for 5 h. After the reaction completed (as determined using TLC), the reaction mixture was cooled to room temperature, extracted with dichloromethane (3 × 20 mL), and washed with brine. The organic layers were combined, dried over Na_2SO_4, filtered, and then evaporated under vacuum. The residue was purified using flash column chromatography with silica gel (200−300 mesh), using ethyl acetate and petroleum ether (1:6, v/v) as the elution solvent to give desired product **3f** in 86% yield (0.89 g).

*3-Benzoyl-2,6,6-trimethyl-6,7-dihydrobenzofuran-4(5H)-one (**3a**).* The title compound was prepared from 2-diazo-5,5-dimethylcyclohexane-1,3-dione and 1-phenylbutane-1,3-dione according to the general procedures and purified by column chromatography (petroleum ether/ethyl acetate 6:1, R_f = 0.5) to afford a white solid in 83% yield (234 mg); mp 152−154 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80 (d, J = 8.1 Hz, 2H), 7.54 (t, J = 8.1 Hz, 1H) 7.54−7.40 (m, 2H), 2.77 (s, 2H), 2.35 (s, 3H), 2.32 (s, 2H), 1.15 (s, 6H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 192.0, 191.5, 164.5, 155.8, 138.4, 133.2, 129.4, 128.4, 119.7, 1118.3, 52.4, 37.4, 35.4, 28.7, 13.0; IR (KBr) ν 2957, 2356, 1673, 1656, 1594, 1581, 1447, 1426, 1380, 1323, 1302, 1227, 1056, 1009, 899, 716, 699 cm^{-1}; HRMS (APCI-TOF) m/z: $[M + H]^+$ calcd for $C_{18}H_{19}O_3$ 283.1329; found 283.1333.

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*2,6,6-Trimethyl-3-(4-methylbenzoyl)-6,7-dihydrobenzofuran-4(5H)-one (**3b**).* The title compound was prepared from 2-diazo-5,5-dimethylcyclohexane-1,3-dione and 1-(*p*-tolyl)butane-1,3-dione according to the general procedures and purified by column chromatography (petroleum ether/ethyl acetate 6:1, R_f = 0.5) to afford a white solid in 76% yield (225 mg); mp 151−152 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.70 (d, J = 8.7 Hz, 2H), 7.19 (d, J = 8.7 Hz, 2H), 2.76 (s, 2H), 2.39 (s, 3H), 2.33(s, 3H), 2.32 (s, 2H), 1.15 (s, 6H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 192.3, 191.2, 164.5, 155.6, 144.1, 135.9, 129.7, 129.2, 119.8, 118.4, 52.5, 37.5, 35.5, 28.7, 22.0, 13.0; IR (KBr) ν 2961, 2369, 1673, 1645, 1596, 1577, 1509, 1426, 1320, 1227, 1169, 1148, 1023, 905, 844, 773 cm^{-1}; HRMS (APCI-TOF) m/z: [M + H]$^+$ calcd for $C_{19}H_{21}O_3$ 297.1481; found 297.1482.

*3-(4-Methoxybenzoyl)-2,6,6-trimethyl-6,7-dihydrobenzofuran-4(5H)-one (**3c**).* The title compound was prepared from 2-diazo-5,5-dimethylcyclohexane-1,3-dione and 1-(4-methoxyphenyl)butane-1,3-dione according to the general procedures and purified by column chromatography (petroleum ether/ethyl acetate 6:1, R_f = 0.5) to afford a white solid in 78% yield (244 mg); mp 135−136 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.79 (d, J = 9.6 Hz, 2H), 6.87 (d, J = 9.6 Hz, 2H), 3.86 (s, 3H), 2.76 (s, 2H), 2.33 (s, 2H), 2.32(s, 3H), 1.16 (s, 6H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 192.0, 191.1, 164.5, 155.4, 144.0, 135.8, 129.6, 129.1, 119.8, 118.3, 52.4, 37.4, 35.4, 28.7, 21.9, 12.9; IR (KBr) ν 2960, 2368, 1672, 1643, 1595, 1575, 1508, 1425, 1319, 1225, 1168, 1147, 1020, 904, 842, 771 cm^{-1}; HRMS (APCI-TOF) m/z: [M + H]$^+$ calcd for $C_{19}H_{21}O_4$ 313.1434; found 313.1437.

*3-(4-Chlorobenzoyl)-2,6,6-trimethyl-6,7-dihydrobenzofuran-4(5H)-one (**3d**).* The title compound was prepared from 2-diazo-5,5-dimethylcyclohexane-1,3-dione and 1-(4-chlorophenyl)butane-1,3-dione according to the general procedures and purified by column chromatography (petroleum ether/ethyl acetate 6:1, R_f = 0.5) to afford a yellow solid in 87% yield (276 mg); mp 91−92 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, J = 5.5 Hz, 2H), 7.34 (d, J = 5.5 Hz, 2H), 2.75 (s, 2H), 2.34 (s, 3H), 2.30 (s, 2H), 1.13 (s, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 192.0, 190.1, 164.8, 156.2, 139.3, 136.8, 130.6, 126.6, 119.4, 117.8, 52.3, 37.3, 35.3, 28.5, 12.8; IR (KBr) ν 2960, 2362, 2339, 1674, 1654, 1583, 1419, 1317, 1220, 1147, 1087, 1045, 893, 837, 759 cm^{-1}; HRMS (APCI-TOF) calcd for $C_{18}H_{18}ClO_3$ [M + H]$^+$ 317.0939; found 317.0940.

*3-(3-Bromobenzoyl)-2,6,6-trimethyl-6,7-dihydrobenzofuran-4(5H)-one (**3e**).* The title compound was prepared from 2-diazo-5,5-dimethylcyclohexane-1,3-dione and 1-(2-bromophenyl)butane-1,3-dione according to the general procedures and purified by column chromatography (petroleum ether/ethyl acetate 6:1, R_f = 0.5) to afford a white solid in 76% yield (275 mg); mp 121−122 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (t, J = 1.3 Hz, 1H), 7.71−7.68 (m, 1H), 7.67−7.64 (m, 1H), 7.29 (t, J = 4.8 Hz, 1H), 2.78 (s, 2H), 2.37 (s, 3H), 2.32 (s, 2H), 1.16 (s, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 192.0, 190.0, 164.8, 156.6, 140.4, 135.9, 132.3, 130.0, 127.9, 122.7, 119.6, 117.8, 52.4, 37.4, 35.5, 28.7, 13.1; IR (KBr) ν 2964, 2368, 2343, 1664, 1639, 1581, 1562, 1427, 1379, 1305, 1217, 1147, 1049, 927, 904, 750, 729 cm^{-1}; HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{18}H_{18}BrO_3$ 361.0434; found 361.0433.

*3-Benzoyl-6,6-dimethyl-2-phenyl-6,7-dihydrobenzofuran-4(5H)-one (**3f**).* The title compound was prepared from 2-diazo-5,5-dimethylcyclohexane-1,3-dione and 1,3-diphenylpropane-1,3-dione according to the general procedures and purified by column chromatography (petroleum ether/ethyl acetate 6:1, R_f = 0.5) to afford a white solid in 91% yield (313 mg); mp 181−182 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (dd, J = 8.0, 1.2 Hz, 2H), 7.57−7.50 (m, 3H), 7.39 (t, J = 8.0 Hz, 2H), 7.31−7.25 (m, 3H), 2.87 (s, 2H), 2.34 (s, 2H), 1.18 (s, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 192.5, 192.1, 165.0, 152.2, 137.5, 133.8, 129.6, 129.1, 129.0, 128.9, 128.8, 126.1, 121.6, 117.5, 52.2, 37.6, 35.5, 28.8; IR (KBr) ν 2968, 2368, 2351, 1718, 1683, 1527, 1444, 1350, 1336, 1236, 1058, 1035, 734, 680 cm^{-1}; HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{23}H_{21}O_3$ 345.1485; found 345.1493.

*3-Acetyl-2,6,6-trimethyl-6,7-dihydrobenzofuran-4(5H)-one (**3g**).* The title compound was prepared from 2-diazo-5,5-dimethylcyclohexane-1,3-dione and pentane-2,4-dione according to the general procedures and purified by column chromatography (petroleum ether/ethyl acetate 6:1, R_f = 0.5) to afford a yellow solid in 67% yield (148 mg); mp 46−48 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.72 (s, 2H), 2.64 (s, 3H), 2.41(s, 3H), 2.39(s, 2H), 1.14(s, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 197.2, 193.3, 165.0, 158.4, 119.8, 118.1, 53.3, 37.6, 35.1, 32.1, 28.6, 13.8; IR (KBr) ν 2960, 2364, 1678, 1662, 1556, 1492, 1413, 1371, 1301, 1213, 1089, 835, 516 cm^{-1}; HRMS (APCI-TOF) m/z: [M + H]$^+$ calcd for $C_{13}H_{17}O_3$ 221.1172; found 221.1168.

*3-Benzoyl-2-methyl-6,7-dihydrobenzofuran-4(5H)-one (**3h**).* The title compound was prepared from 2-diazocyclohexane-1,3-dione and 1-phenylbutane-1,3-dione according to the general procedures and purified by column chromatography (petroleum ether/ethyl acetate 6:1, R_f = 0.5) to afford a white solid in 60% yield (153 mg); mp 109−110 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, J = 3.0 Hz, 2H), 7.54 (t, J = 3.0 Hz, 1H), 7.42 (t, J = 3.0 Hz, 2H), 2.90 (t, J = 2.4 Hz, 2H), 2.44 (t, J = 2.4 Hz, 2H), 2.33 (s, 3H), 2.21−2.16 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 192.5, 191.6, 165.5, 155.2, 138.5, 133.3, 129.5, 128.5, 121.0, 118.5, 38.1, 23.5, 22.6, 12.9; IR (KBr) ν 2956, 2355, 1670, 1654, 1595, 1579, 1446, 1425, 1379, 1321, 1300, 1226, 1055, 1008, 898, 715, 698 cm^{-1}; HRMS (APCI-TOF) m/z: [M + H]$^+$ calcd for $C_{16}H_{15}O_3$ 255.1016; found 255.1012.

*3-Benzoyl-2,6-dimethyl-6,7-dihydrobenzofuran-4(5H)-one (**3i**).* The title compound was prepared from 2-diazo-5-methylcyclohexane-1,3-dione and 1,3-diphenylpropane-1,3-dione according to the general procedures and purified by column chromatography (petroleum ether/ethyl acetate 6:1, R_f = 0.5) to afford a white solid in 65% yield (215 mg); mp 181−182 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (dt, J_1 = 1.0 Hz, J_2 = 4.3 Hz, 2H), 7.53 (dd, J_1 = 1.0 Hz, J_2 = 4.5 Hz, 1H), 7.41 (t, J = 4.7 Hz, 2H), 2.97 (m, 1H), 2.54 (m, 1H), 2.46 (m, 2H), 2.32 (s, 3H), 2.19 (m, 1H), 1.16 (d, J = 4.0 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 192.1, 191.4, 165.1, 155.4, 138.3, 133.2, 129.4, 128.3, 48.4, 31.4, 30.7, 21.1, 12.9; IR (KBr) ν 2960, 2360, 2338, 1676, 1657, 1586, 1421, 1319, 1223, 1151, 1090, 1044, 895, 841, 760 cm^{-1}; HRMS (APCI-TOF) m/z: [M + H]$^+$ calcd for $C_{17}H_{17}O_3$ 269.1172; found 269.1170.

*3-Benzoyl-2-methyl-6-phenyl-6,7-dihydrobenzofuran-4(5H)-one (**3j**).* The title compound was prepared from 2-diazo-5-phenylcyclohexane-1,3-dione and 1-phenylbutane-1,3-dione according to the general procedures and purified by column chromatography (petroleum ether/ethyl acetate 6:1, R_f = 0.5) to afford a white solid in 69% yield (227 mg); mp 121−123 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 (d, J = 3.0 Hz, 2H), 7.56 (t, J = 3.0 Hz 1H), 7.44 (t, J = 3.2 Hz, 2H), 7.37 (t, J = 3.0 Hz, 2H), 7.30 (t, J = 2.0 Hz, 3H), 3.60 (m, 1H), 3.16 (m, 2H), 2.72 (m, 2H), 2.36 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 191.4, 164.9, 156.1, 142.6, 138.6, 133.5, 129.7, 129.3, 128.7, 127.7, 127.2, 121.1, 118.7, 45.5, 41.4, 31.5, 12.3; IR (KBr) 2926, 2364, 1677, 1647, 1580, 1497, 1456, 1436, 1409, 1380, 1325,1306, 1237, 1209, 1045, 908, 765, 733, 694, 669 cm^{-1}; HRMS (APCI-TOF) m/z: [M + H]$^+$ calcd for $C_{22}H_{19}O_3$ 331.1329; found 331.1323.

*2-Methyl-3-(4-methylbenzoyl)-6,7-dihydrobenzofuran-4(5H)-one (**3k**).* The title compound was prepared from 2-diazocyclohexane-1,3-dione and 1-(*p*-tolyl)butane-1,3-dione according to the general procedures and purified by column chromatography (petroleum ether/ethyl acetate 6:1, R_f = 0.5) to afford a white solid in 53% yield (142 mg); mp 129−130 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 (d, J = 8.0 Hz, 2H), 7.21 (d, J = 8.0 Hz, 2H), 2.90 (t, J = 6.0 Hz, 2H), 2.44 (t, J = 6.0 Hz, 2H), 2.40 (s, 3H), 2.31 (s, 3H), 2.21−2.16 (m, 2H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 192.7, 191.2, 165.5, 154.8, 144.1, 135.8, 129.7, 129.2, 121.0, 118.6, 38.1, 23.5, 22.6, 22.0, 12.9; IR (KBr) ν 2956, 2355, 1670, 1654, 1595, 1579, 1446, 1425, 1379, 1321, 1300, 1226, 1055, 1008, 898, 715, 698 cm^{-1}; HRMS (APCI-TOF) m/z: [M + H]$^+$ calcd for $C_{17}H_{17}O_3$ 2695.1172; found 269.1170.

*2,6-Dimethyl-3-(4-methylbenzoyl)-6,7-dihydrobenzofuran-4(5H)-one (**3l**).* The title compound was prepared from 2-diazo-5-methylcyclohexane-1,3-dione and 1-(*p*-tolyl)butane-1,3-dione accord-

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ing to the general procedures and purified by column chromatography (petroleum ether/ethyl acetate 6:1, R_f = 0.5) to afford a yellow solid in 68% yield (193 mg); mp 108−109 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, J = 8.0 Hz, 2H), 7.18 (d, J = 8.0 Hz, 2H), 2.98−2.91 (m, 1H), 2.58−2.50 (m, 1H), 2.47−2.40 (m, 2H), 2.37 (s, 3H), 2.29 (s, 3H), 2.22−2.13 (m, 1H), 1.15 (m, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 192.3, 191.1, 165.1, 155.0, 144.1, 135.8, 129.7, 129.2, 120.7, 118.5, 46.6, 31.6, 30.8, 21.9, 21.2, 12.9; IR (KBr) ν 2963, 2366, 1673, 1645, 1596, 1577, 1509, 1426, 1320, 1226, 1169, 1148, 1021, 905, 843, 772 cm^{-1}; HRMS (APCI-TOF) m/z: [M + H]$^+$ calcd for $C_{18}H_{19}O_3$ 283.1329; found 283.1331.

*3-(4-Methoxybenzoyl)-2-methyl-6,7-dihydrobenzofuran-4(5H)-one (**3m**).* The title compound was prepared from 2-diazocyclohexane-1,3-dione and 1-(4-methoxyphenyl)butane-1,3-dione according to the general procedures and purified by column chromatography (petroleum ether/ethyl acetate 6:1, R_f = 0.5) to afford a white solid in 56% yield (158 mg); mp 129−130 °C; ^{1}H NMR (400 MHz, CDCl3) δ 7.70 (d, J = 8.0 Hz, 2H), 7.20 (d, J = 8.0 Hz, 2H), 2.87 (t, J = 6.0 Hz, 2H), 2.42 (t, J = 6.0 Hz, 2H), 2.37 (s, 3H), 2.29 (s, 3H), 2.19−2.13 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 192.7, 191.2, 165.5, 154.8, 144.1, 135.8, 129.7, 129.2, 121.0, 118.6, 38.1, 23.5, 22.6, 22.0, 12.9; IR (KBr) ν 2956, 2355, 1670, 1654, 1595, 1579, 1446, 1425, 1379, 1321, 1300, 1226, 1055, 1008, 898, 715, 698. cm^{-1}; HRMS (APCI-TOF) m/z: [M + H]$^+$ calcd for $C_{17}H_{17}O_4$ 285.1121; found 285.1124.

*3-(4-Methoxybenzoyl)-2,6-dimethyl-6,7-dihydrobenzofuran-4(5H)-one (**3n**).* The title compound was prepared from 2-diazo-5-methylcyclohexane-1,3-dione and 1-(4-methoxyphenyl)butane-1,3-dione according to the general procedures and purified by column chromatography (petroleum ether/ethyl acetate 6:1, R_f = 0.5) to afford a white solid in 65% yield (194 mg); mp 91−92 °C; ^{1}H NMR (400 MHz, $CDCl_{3)}$ δ 7.98−7.64 (m, 2H), 7.01−6.75 (m, 2H), 3.85 (s, 3H), 3.01−2.94 (m, 1H), 2.61−2.52 (m, 1H), 2.52−2.44 (m, 2H), 2.30 (s, 3H), 2.25−2.17 (m, 1H), 1.17 (d, J = 6.4 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 192.3, 189.9, 165.1, 163.7, 154.5, 131.9, 131.2, 120.6, 118.4, 113.7, 55.5, 46.5, 46.4, 31.5, 30.8, 21.1, 12.8; ppm; IR (KBr) ν cm^{-1}; HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{18}H_{19}O_4$ 299.1278; found 299.1281.

*3-(4-Chlorobenzoyl)-2-methyl-6,7-dihydrobenzofuran-4(5H)-one (**3o**).* The title compound was prepared from 2-diazocyclohexane-1,3-dione and 1-(4-chlorophenyl)butane-1,3-dione according to the general procedures and purified by column chromatography (petroleum ether/ethyl acetate 6:1, R_f = 0.5) to afford a yellow solid in 65% yield (188 mg); mp 113−115 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 (d, J = 8.5 Hz, 2H), 7.37 (d, J = 8.5 Hz, 2H), 2.90 (t, J = 6.0 Hz, 2H), 2.44 (t, J = 6.0 Hz, 2H), 2.34 (s, 3H), 2.25−2.12 (m, 2H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 192.6, 190.3, 165.7, 155.6, 139.6, 136.9, 130.8, 128.8, 120.9, 118.2, 38.1, 23.5, 22.6, 12.9, 12.8; IR (KBr) ν 2961, 2363, 2340, 1676, 1653, 1586, 1420, 1319, 1221, 1148, 1086, 1046, 893, 837, 758 cm^{-1}; HRMS (APCI-TOF) m/z: [M + H]$^+$ calcd for $C_{16}H_{14}ClO_3$ 289.0626; found 289.0630.

*3-(4-Chlorobenzoyl)-2,6-dimethyl-6,7-dihydrobenzofuran-4(5H)-one (**3p**).* The title compound was prepared from 2-diazo-5-methylcyclohexane-1,3-dione and 1-(4-chlorophenyl)butane-1,3-dione according to the general procedures and purified by column chromatography (petroleum ether/ethyl acetate 6:1, R_f = 0.5) to afford a yellow solid in 69% yield (209 mg); mp 131−132 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74−7.71 (m, 2H), 7.39−7.36 (m, 2H), 3.00−2.95 (m, 1H), 2.60−2.53 (m, 1H), 2.49−2.44 (m, 2H), 2.34 (s, 3H), 2.23−2.15 (m, 1H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$) δ 192.4, 190.3, 165.4, 158.0, 139.5 136.7, 130.7, 128.7, 120.3, 117.9, 46.5, 31.4, 30.8, 21.1 12.9; IR (KBr) ν 2961, 2363, 2340, 1675, 1655, 1585, 1420, 1318, 1221, 1149, 1089, 1046, 894, 839, 761 cm^{-1}; HRMS (APCI-TOF) m/z: [M + H]$^+$ calcd for $C_{17}H_{16}ClO_3$ 303.0782; found 303.0781.

*3-(2-Bromobenzoyl)-2-methyl-6,7-dihydrobenzofuran-4(5H)-one (**3q**).* The title compound was prepared from 2-diazocyclohexane-1,3-dione and 1-(2-bromophenyl)butane-1,3-dione according to the general procedures and purified by column chromatography (petroleum ether/ethyl acetate 6:1, R_f = 0.5) to afford a white solid in 57% yield (180 mg); mp 101−102 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (t, J = 1.7 Hz, 1H), 7.69 (m, 2H), 7.30 (dd, J = 12.7, 4.8 Hz, 1H), 2.93 (t, J = 6.3 Hz, 2H), 2.45 (t, 6.3 Hz, 2H), 2.36 (s, 3H), 2.21 (dd, J = 12.9, 6.5 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 192.5, 190.0, 186.7, 156.8, 140.1, 135.9, 132.1, 129.9, 127.9, 122.6, 120.6, 117.8, 37.9, 23.3, 22.4, 12.9; IR (KBr) ν 2965, 2369, 2345, 1665, 1641, 1583, 1564, 1429, 1381, 1307, 1219, 1149, 1051, 929, 905, 752, 731 cm^{-1}; HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{16}H_{14}O_3Br$ 333.0125; found 333.0121.

*3-Benzoyl-2-phenyl-6,7-dihydrobenzofuran-4(5H)-one (**3r**).* The title compound was prepared from 2-diazocyclohexane-1,3-dione and 1,3-diphenylpropane-1,3-dione according to the general procedures and purified by column chromatography (petroleum ether/ethyl acetate 6:1, R_f = 0.5) to afford a white solid in 75% yield (237 mg); mp 101−102 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (m, 2H), 7.55 (m, 3H), 7.41 (t, 5.0 Hz, 2H), 7.30 (m, 3H), 3.02 (t, J = 4.0 Hz, 2H), 2.48 (t, J = 3.0 Hz, 2H), 2.25 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 207.3, 192.8, 192.7, 165.9, 151.5, 137.3, 133.8, 129.6, 129.0, 128.9, 128.7, 125.9, 122.6, 117.5, 37.8, 31.1, 23.6, 22.5; IR (KBr) ν 2922, 2360, 1675, 1649, 1579, 1495, 1450, 1434, 1407, 1378, 1320,1304, 1232, 1211, 1043, 906, 762, 731, 691, 668 cm^{-1}; HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{21}H_{17}O_3$ 317.1172; found 317.1170.

*3-Acetyl-2-methyl-6,7-dihydrobenzofuran-4(5H)-one (**3s**).* The title compound was prepared from 2-diazocyclohexane-1,3-dione and pentane-2,4-dione according to the general procedures and purified by column chromatography (petroleum ether/ethyl acetate 6:1, R_f = 0.5) to afford a yellow liquid in 41% yield (79 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.85 (t, J = 6.3 Hz, 2H), 2.64 (s, 3H), 2.53 (t, J = 6.3 Hz, 2H), 2.45 (s, 3H), 2.20−2.12 (m, 2H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 197.3, 193.7, 165.8, 157.7, 119.8, 119.2, 38.7, 32.1, 32.0, 23.5, 13.6; IR (KBr) ν 2372, 2339, 1381 cm^{-1}; HRMS (APCI-TOF) m/z: [M + H]$^+$ calcd for $C_{11}H_{13}O_3$ 193.0859; found 193.0858.

*3-Acetyl-6-(4-chlorophenyl)-2-methyl-6,7-dihydrobenzofuran-4(5H)-one (**3t**).* The title compound was prepared from 5-(4-chlorophenyl)-2-diazocyclohexane-1,3-dione and pentane-2,4-dione according to the general procedures and purified by column chromatography (petroleum ether/ethyl acetate 6:1, R_f = 0.5) to afford a white solid in 47% yield (142 mg); mp 148−150 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32 (d, J = 8.4 Hz, 2H), 7.20 (d, J = 8.4 Hz, 2H), 3.58−3.46 (m, 1H), 3.19−2.96 (m, 2H), 2.83−2.78 (m, 2H), 2.67 (s, 3H), 2.48 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 197.0, 191.8, 164.7, 158.8, 140.6, 133.3, 129.2, 128.2, 119.8, 119.1, 45.8, 40.2, 32.1, 31.2, 13.7; IR (KBr) ν 2960, 2364, 1678, 1662, 1556, 1492, 1413, 1371, 1301, 1213, 1089, 835, 516 cm^{-1}; HRMS (APCI-TOF) m/z: [M + H]$^+$ calcd for $C_{17}H_{16}ClO_3$ 303.0782; found 303.0778.

*3-Benzoyl-2-ethyl-6,6-dimethyl-6,7-dihydrobenzofuran-4(5H)-one (**3u**).* The title compound was prepared from 2-diazo-5,5-dimethylcyclohexane-1,3-dione and 1-phenylpentane-1,3-dione according to the general procedures and purified by column chromatography (petroleum ether/ethyl acetate 6:1, R_f = 0.5) to afford a yellow liquid in 86% yield (254 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, J = 4.4 Hz, 2H), 7.52 (t, J = 4.8 Hz, 1H), 7.40 (t, J = 5.0 Hz, 2H), 2.77(s, 2H), 2.67 (q, J = 4.8 Hz, 2H), 2.30 s, 2H), 1.21 (t, J = 4.8 Hz, 3H), 1.14 (s, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 192.2, 191.9, 164.2, 162.7, 138.5, 133.2, 129.3, 128.4, 119.7, 116.2, 52.3, 37.5, 35.4, 28.7, 27.3, 21.3; IR (KBr) ν 2958, 2355, 1674, 1652, 1590, 1583, 1449, 1427, 1389, 1320, 1300, 1225, 1057, 1010, 900, 715, 702 cm^{-1}; HRMS (APCI-TOF) m/z: [M + H]$^+$ calcd for $C_{19}H_{21}O_3$ 297.1485; found 297.1486.

*3-Benzoyl-2-isopropyl-6,6-dimethyl-6,7-dihydrobenzofuran-4(5H)-one (**3v**).* The title compound was prepared from 2-diazo-5,5-dimethylcyclohexane-1,3-dione and 4-methyl-1-phenylpentane-1,3-dione according to the general procedures and purified by column chromatography (petroleum ether/ethyl acetate 6:1, R_f = 0.5) to afford a white solid in 89% yield (275 mg); mp 118−119 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J = 4.4 Hz, 2H), 7.54 (t, J = 4.4 Hz, 1H), 7.41 (t, J = 5.0 Hz, 2H), 3.08 (m, 1H), 2.78 (s, 2H), 2.30 (s, 2H), 1.24 (d, J = 4.4 Hz, 6H), 1.16 (s, 6H); ^{13}C{^{1}H} NMR (100

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MHz, $CDCl_3$) δ 192.0, 191.5, 154.5, 160.2, 138.4, 133.1, 129.3, 128.3, 119.6, 117.2, 52.3, 37.4, 35.3, 28.6, 20.6, 12.7; IR (KBr) ν 2957, 2350, 1672, 1654, 1585, 1589, 1450, 1431, 1391, 1322, 1298, 1227, 1059, 1013, 901, 715, 702 cm^{-1}; HRMS (APC) m/z: $[M + H]^+$ calcd for 311.1642; found 311.1648.

*Ethyl 6,6-Dimethyl-4-oxo-2-phenyl-4,5,6,7-tetrahydrobenzofuran-3-carboxylate (**5a**).* The title compound was prepared from 2-diazo-5,5-dimethylcyclohexane-1,3-dione and ethyl 3-oxo-3-phenylpropanoate according to the general procedures and purified by column chromatography (petroleum ether/ethyl acetate 6:1, R_f = 0.5) to afford a yellow solid in 75% yield (234 mg); mp 58−59 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 7.73−7.71 (m, 2H), 7.6−7.49 (m, 3H), 4.40 (q, J = 3.0 Hz, 2H), 2.81 (s, 2H), 2.43 (s, 2H), 1.35 (t, J = 3.0 Hz, 3H), 1.18 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 192.0, 165.0, 164.5, 153.8, 129.4, 128.9, 128.7, 126.7, 119.9, 111.5, 61.8, 52.6, 37.4, 35.3, 28.7, 14.1; IR (KBr) ν 2964, 2362, 2339, 1726, 1680, 1560, 1492, 1438, 1365, 1325, 1222, 1195, 1028, 769, 684 cm^{-1}; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{19}H_{21}O_4$ 313.1434; found 313.1438.

*Ethyl 2-(4-Chlorophenyl)-6,6-dimethyl-4-oxo-4,5,6,7-tetrahydrobenzofuran-3-carboxylate (**5b**).* The title compound was prepared from 2-diazo-5,5-dimethylcyclohexane-1,3-dione and ethyl 3-(4-chlorophenyl)-3-oxopropanoate according to the general procedures and purified by column chromatography (petroleum ether/ethyl acetate 6:1, R_f = 0.5) to afford a yellow solid in 68% yield (236 mg); mp 110−111 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, J = 4.4 Hz, 2H), 7.38 (d, J = 4.4 Hz, 2H), 4.37(q, J = 7.2 Hz, 2H), 2.80 (s, 2H), 2.43 (s, 2H), 1.35 (t, J = 4.4 Hz, 3H), 1.17(s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 191.9, 165.1, 164.3, 162.8, 135.4, 129.0, 128.0, 127.4, 120.0, 111.9, 61.9, 52.6, 50.3, 37.4, 35.3, 28.7, 14.1; IR (KBr) ν 2965, 2361, 2337, 1729, 1681, 1563, 1494, 1440, 1366, 1324, 1221, 1197, 1025, 771, 681 cm^{-1}; HRMS (APCI-TOF) m/z: $[M + H]^+$ calcd for $C_{19}H_{20}ClO_4$ 347.1045; found 347.1051.

*Ethyl 6,6-Dimethyl-2-(3-nitrophenyl)-4-oxo-4,5,6,7-tetrahydrobenzofuran-3-carboxylate (**5c**).* The title compound was prepared from 2-diazo-5,5-dimethylcyclohexane-1,3-dione and ethyl 3-(3-nitrophenyl)-3-oxopropanoate according to the general procedures and purified by column chromatography (petroleum ether/ethyl acetate 6:1, R_f = 0.5) to afford a white solid in 88% yield (315 mg); mp 127−129 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 8.62 (t, J = 1.7 Hz, 1H), δ 8.22 (m, 1H), δ 8.11(m, 1H), δ 7.61 (t, J = 1.8 Hz, 1H), δ 4.44 (q, J = 6.0 Hz, 2H), 2.85 (s, 2H), 2.46 (s, 2H), 1.38 (t, J = 6.0 Hz 2H), 1.19 (s, 6H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 207.3, 191.8, 165.8, 163.9, 151.1, 148.5, 132.3, 130.5, 129.9, 123.8, 121.6, 120.1, 113.5, 62.3, 52.6, 37.4, 35.4, 28.7, 14.1; IR (KBr) ν 2978, 2365, 2341, 1729, 1683, 1564, 1497, 1441, 1367, 1329, 1220, 1193, 1027, 770, 685 cm^{-1}; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{19}H_{20}O_6$ 358.1285; found 358.1288.

*Ethyl 2-Isopropyl-6,6-dimethyl-4-oxo-4,5,6,7-tetrahydrobenzofuran-3-carboxylate (**5d**).* The title compound was prepared from 2-diazo-5,5-dimethylcyclohexane-1,3-dione and ethyl 4-methyl-3-oxopentanoate according to the general procedures and purified by column chromatography (petroleum ether/ethyl acetate 6:1, R_f = 0.5) to afford a yellow solid in 53% yield (148 mg); mp 47−49 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 4.34 (q, J = 7.2 Hz, 2H), 3.54 (m, 1H), 2.71 (s, 2H), 2.39 (s, 2H), 1.37 (t, J = 7.2 Hz, 3H), 1.26 (d, J = 6.8 Hz, 6H), 1.13 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 192.0, 166.2, 164.6, 163.4, 118.3, 109.8, 53.2, 37.5, 35.1, 28.7, 27.2, 21.0, 14.3; IR (KBr) ν 2961, 2360, 1679, 1663, 1557, 1494, 1415, 1375, 1398, 1210, 1089, 833, 517, 496 cm^{-1}; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{16}H_{23}O_4$ 279.1591; found 279.1583.

*Ethyl 6,6-Dimethyl-4-oxo-2-(trifluoromethyl)-4,5,6,7-tetrahydrobenzofuran-3-carboxylate (**5e**).* The title compound was prepared from 2-diazo-5,5-dimethylcyclohexane-1,3-dione and ethyl 4,4,4-trifluoro-3-oxobutanoate according to the general procedures and purified by column chromatography (petroleum ether/ethyl acetate 6:1, R_f = 0.5) to afford a yellow solid in 67% yield (205 mg); mp 45−47 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 4.40 (q, J = 7.2 Hz, 2H), 2.80 (s, 2H), 2.43 (s, 2H), 1.36 (t, J = 6.4 Hz, 3H), 1.16 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 191.2, 166.8, 160.9, 140.5 (q, J_{C-F} = 43 Hz), 119 (q, J_{C-F} = 257 Hz), 118.9, 118.0, 62.5, 52.3, 37.2, 35.3, 28.5, 13.9; ^{19}F NMR (377 MHz, $CDCl_3$) δ −62.8; IR (KBr) ν 2365, 1673, 1597, 1584, 1561, 1498, 1461, 1410, 1354, 1317, 1237, 1206, 1177, 1119, 1077, 1015, 953, 900, 773, 761, 731, 710, 692, 671, 657, 616, 578, 544, 480 cm^{-1}; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{14}H_{16}F_3O_4$ 305.0995; found 305.0988.

*Ethyl 6-Methyl-4-oxo-2-phenyl-4,5,6,7-tetrahydrobenzofuran-3-carboxylate (**5f**).* The title compound was prepared from 2-diazo-5-methylcyclohexane-1,3-dione and ethyl 3-oxo-3-phenylpropanoate according to the general procedures and purified by column chromatography (petroleum ether/ethyl acetate 6:1, R_f = 0.5) to afford a yellow solid in 56% yield (168 mg); mp 65−67 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, J = 7.6 Hz, 2H), 7.43−7.37 (m, 3H), 4.40 (q, J = 7.2 Hz, 2H), 3.02 (dd, J = 4.4 Hz, 21.2 Hz, 1H), 2.64−2.53 (m, 2H), 2.52−2.45 (m, 1H), 2.42−2.27 (m, 2H), 1.35 (t, J = 7.2 Hz, 3H), 1.20 (d, J = 6.4 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 191.9, 165.3, 164.3, 163.0, 129.1, 128.4, 126.4, 120.4, 111.3, 61.6, 46.3, 31.2, 30.4, 20.9, 13.8; IR (KBr) ν 2975, 2365, 2342, 1743, 1687, 1626, 1578, 1457, 1363, 1276, 1201, 1124, 1052, 1025, 860, 419 cm^{-1}; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{18}H_{19}O_4$ 299.1278; found 299.1280.

*2-(4-Chlorophenyl)-6-methyl-4-oxo-4,5,6,7-tetrahydrobenzofuran-3-carboxylate (**5g**).* The title compound was prepared from 2-diazo-5-methylcyclohexane-1,3-dione and ethyl 3-(4-chlorophenyl)-3-oxopropanoate according to the general procedures and purified by column chromatography (petroleum ether/ethyl acetate 6:1, R_f = 0.5) to afford a yellow solid in 65% yield (217 mg); mp 116−118 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, J = 8.6 Hz, 2H), 7.38 (d, J = 8.6 Hz, 2H), 4.40 (q, J = 7.2 Hz, 2H), 3.02 (dd, J = 4.4 Hz, 16.0 Hz, 1H), 2.64−2.57 (m, 2H), 2.51−2.48 (m, 1H), 2.35−2.27 (m, 1H), 1.36 (t, J = 7.2 Hz, 3H), 1.20 (d, J = 6.4 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 192.1, 165.7, 164.4, 152.4, 135.4, 129.0, 128.0, 127.4, 120.8, 112.0, 62.0, 46.7, 31.5, 30.7, 21.2, 14.1; IR (KBr) ν 2980, 2364, 2346, 1746, 1691, 1622, 1579, 1458, 1364, 1275, 1219, 1126, 1052, 1026, 860, 743, 419 cm^{-1}; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{18}H_{18}ClO_4$ 333.0888; found 333.0895.

*Ethyl 6-Methyl-4-oxo-2-(trifluoromethyl)-4,5,6,7-tetrahydrobenzofuran-3-carboxylate (**5h**).* The title compound was prepared from 2-diazo-5-methylcyclohexane-1,3-dione and ethyl 4,4,4-trifluoro-3-oxobutanoate according to the general procedures and purified by column chromatography (petroleum ether/ethyl acetate 6:1, R_f = 0.5) to afford a white solid in 80% yield (232 mg); mp 67−69 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 4.41(q, J = 7.2 Hz, 2H), 3.03 (dd, J = 4.4 Hz, 16.0 Hz, 1H), 3.06−3.00 (m, 1H), 2.65−2.58 (m, 2H), 2.53−2.46 (m, 1H), 2.33−2.27 (m, 1H), 1.36 (t, J = 7.2 Hz, 3H), 1.20 (d, J = 6.4 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 191.4, 167.3, 161.0, 140.2 (d, J_{C-F} = 43.2 Hz), 119.8, 119.7, 118.1 (d J_{C-F} = 2.4 Hz), 117.1, 62.6, 46.4, 31.3, 30.5, 21.0, 14.0, ^{19}F NMR (377 MHz, $CDCl_3$) δ −62.9 IR (KBr) ν 2361, 1669, 1595, 1580, 1559, 1496, 1449, 1405, 1350, 1317, 1237, 1206, 1177, 1119, 1077, 1015, 953, 900, 773, 761, 731, 710, 692, 673, 657, 616, 578, 544, 484 cm^{-1}; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{13}H_{14}F_3O_4$ 291.0839; found 291.0831.

*1-(4-Benzoyl-2-methyl-5-phenylfuran-3-yl)ethan-1-one (**7a**).* The title compound was prepared from 3-diazopentane-2,4-dione and 1,3-diphenylpropane-1,3-dione according to the general procedures and purified by column chromatography (petroleum ether/ethyl acetate 6:1, R_f = 0.5) to afford a yellow solid in 87% yield (266 mg); mp 152−154 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, J = 7.2 Hz, 2H), 7.57−7.52 (m, 3H), 7.42 (t, J = 7.6 Hz, 2H), 7.30−7.25 (m, 3H), 2.73 (s, 3H), 3.28 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 193.6, 192.8, 157.1, 149.5, 137.5, 133.8, 129.4, 128.9, 128.7, 128.7, 125.8, 125.1, 120.3, 30.0, 14.9; IR (KBr) ν 2968, 2366, 1719, 1672, 1559, 1542, 1508, 1490, 1325, 1220, 1050, 618, 419 cm^{-1}; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{20}H_{17}O_3$ 305.1172; found 305.1167.

*1-(4-Benzoyl-2,5-dimethylfuran-3-yl)ethanone (**7b**).* The title compound was prepared from 3-diazopentane-2,4-dione and 1-phenylbutane-1,3-dione according to the general procedures and purified by column chromatography (petroleum ether/ethyl acetate

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6:1, R_f = 0.5) to afford a white solid in 79% yield (191 mg); mp 86−87 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (dd, J = 4.2 Hz, 1.0 Hz, 2H), 7.42−7.36 (m, 3H), 2.63 (s, 3H), 2.45 (s, 3H), 2.41 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 200.0, 193.5, 156.2, 149.3, 129.2, 129.1, 128.9, 126.5, 124.3, 123.5, 31.9, 30.0, 14.8; IR (KBr) ν 2364, 2337, 1730, 1714, 1683, 1653, 1633, 1560, 1543, 1506, 1456, 1431, 1415, 1396, 1377, 1336, 1023, 669 cm^{-1}; HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{15}H_{15}O_3$ 243.1016; found 243.1021.

General Procedure for the Synthesis of 7,7-Dimethyl-3,4-diphenyl-7,8-dihydro-6*H*-furo[4,3,2-*de*]cinnoline 8. A mixture of 3-benzoyl-6,6-dimethyl-2-phenyl-6,7-dihydrobenzofuran-4(5*H*)-one **3f** (344 mg, 1 mmol) and hydrazine hydrate (0.3 mL) in acetonitrile (3 mL) was heated to 80 °C in an oil bath for 3 h. After the reaction completed (as determined using TLC), the reaction mixture was cooled to room temperature, and the solvent was removed under reduced pressure. The residue was purified using flash column chromatography with a silica gel (200−300 mesh), using petroleum ether, ethyl acetate, and triethylamine (300:100:5, v/v) as the elution solvent to give the desired product **8** in 67% yield.

*7,7-Dimethyl-3,4-diphenyl-7,8-dihydro-6H-furo[4,3,2-de]-cinnoline (**8**).* Yellow solid (228 mg, 67%); R_f = 0.4 (petroleum ether/ethyl acetate/triethylamine 300:100:5); mp 67−68 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (dd, 2H, J = 4.3 Hz, J = 0.9 Hz), 7.42 (t, J = 4.0 Hz, 1H), 7.31 (t, J = 5.0 Hz, 2H), 7.24 (q, J = 1.4 Hz, 1H), 7.18 (m, 4H), 3.00 (s, 2H), 2.93 (s, 2H), 1.24 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 157.0, 154.6, 154.2, 148.8, 136.9, 129.8, 129.7, 129.3, 128.6, 128.5, 128.4, 128.1, 116.7, 108.4, 41.7, 37.9, 36.7, 29.2; IR (KBr) ν 3418, 2957, 2925, 2854, 2360,2341, 1732, 1652, 1634, 1558, 1541, 1506, 1489, 1445, 1385, 1728, 1160, 1122, 1067, 1021, 925, 766, 728, 692, 668, 659, 517 cm^{-1}; HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{23}H_{21}N_2O$ 341.1648; found 341.1641.

General Procedure for the Synthesis of 3-(Hydroxy-(phenyl)methyl)-6,6-dimethyl-2-phenyl-6,7-dihydro-benzofuran-4(5*H*)-one 9. A mixture of 3-benzoyl-6,6-dimethyl-2-phenyl-6,7-dihydrobenzofuran-4(5*H*)-one **3f** (344 mg, 1 mmol), and sodium borohydride (76 mg, 2 mmol) in tetrahydrofuran (3 mL) was stirred at room temperature under a nitrogen atmosphere for 30 min. After the reaction completed (as determined using TLC), the reaction mixture was concentrated under reduced pressure. The residue was purified using flash column chromatography with a silica gel (200−300 mesh), using petroleum ether and ethyl acetate (8:1, v/v) as the elution solvent to give the desired product **9** in 65% yield.

*3-(Hydroxy(phenyl)methyl)-6,6-dimethyl-2-phenyl-6,7-dihydro-benzofuran-4(5H)-one (**9**).* White solid (226 mg, 65%); R_f = 0.5 (petroleum ether/ethyl acetate 8:1); mp 53−55 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, J = 6.8 Hz, 2H), 7.44−7.38 (m, 5H), 7.34 (t, J = 7.2 Hz, 2H), 7.29 (t, J = 3.6 Hz, 2H), 6.02 (d, J = 12.0 Hz, 1H), 5.93 (d, J = 12.0 Hz, 1H), 2.89 (s, 2H), 2.46 (q, J = 16.0 Hz, 2H), 1.21 (d, J = 3.2 Hz, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 196.4, 167.9, 150.2, 143.4, 129.7, 128.9, 128.7, 128.6, 127.5, 126.8, 126.4, 121.2, 120.6, 68.0, 51.9, 37.7,35.7, 29.0, 28.4; IR (KBr) ν 2982, 2359, 1714, 1675, 1583, 1563, 1494, 1438, 1405, 1367, 1325, 1289, 1224, 1185, 1089, 1063, 1037, 825, 773, 754, 689, 665, 597, 526 cm^{-1}; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{23}H_{23}O_3$ 347.1642; found 347.1635.

General Procedure for the Synthesis of Compounds 10 and 11. A mixture of 3-benzoyl-2-phenyl-6,7-dihydrobenzofuran-4(5*H*)-one **3r** (316 mg, 1 mmol), or 3-benzoyl-2-isopropyl-6,6-dimethyl-6,7-dihydrobenzofuran-4(5*H*)-one **3v** (310 mg, 1 mmol), hydroxylamine hydrochloride (209 mg, 1.5 mmol), and sodium bicarbonate (252 mg, 1.5 mmol) in ethanol (3 mL) was heated to 80 °C in an oil bath for 2 h. After the reaction completed (as determined using TLC), the reaction mixture was cooled to room temperature, and the solvent was removed under reduced pressure. The residue was purified using flash column chromatography with silica gel (200−300 mesh), using petroleum ether and ethyl acetate (3:1, v/v) as the elution solvent to give the desired product **10** and **11** in 85% and 82% yield, respectively.

*(E)-3-((Hydroxyimino)(phenyl)methyl)-2-phenyl-6,7-dihydro-benzofuran-4(5H)-one (**10**).* White solid (282 mg, 85%); R_f = 0.4 (petroleum ether/ethyl acetate 3:1); mp 228−229 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 7.2 Hz, 2H), 7.54−7.49 (m, 3H), 7.40 (t, J = 8.0 Hz, 3H), 7.25−7.21 (m, 3H), 6.70 (s, 1H), 2.87 (t, J = 6.2 Hz, 2H), 2.70 (t, J = 6.2 Hz, 2H), 2.09−2.02 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 194.0, 156.0, 150.6, 150.0, 137.1, 133.3, 129.4, 128.5, 128.3, 125.3, 117.0, 116.6, 23.0, 21.7, 21.2; IR (KBr) ν 2950, 2365, 1660, 1638, 1596, 1561, 1489, 1445, 1410, 1341, 1230, 1192, 1071, 932, 901, 767, 751, 710, 690 cm^{-1}; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{21}H_{18}NO_3$ 332.1281; found 332.1273.

*(E)-(4-(Hydroxyimino)-2-isopropyl-6,6-dimethyl-4,5,6,7-tetrahydrobenzofuran-3-yl)(phenyl)methanone (**11**).* White solid (110 mg, 68%); R_f = 0.4 (petroleum ether/ethyl acetate 3:1); mp 152−153 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, J = 7.2 Hz, 2H), 7.52 (t, J = 7.2 Hz, 1H), 7.40 (t, J = 7.6 Hz, 2H), 7.15 (s, 1H), 2.94−2.87 (m, 1H), 2.59 (s, 2H), 2.49 (s, 2H), 1.18 (d, J = 6.8 Hz, 6H), 1.11 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.3, 160.7, 154.4, 150.2, 138.4, 133.1, 129.7, 128.3, 115.9, 114.1, 37.2, 35.9, 32.9, 28.9, 27.4, 21.4; IR (KBr) ν 2948, 2352, 1658, 1643, 1601, 1565, 1492, 1463, 1398, 1334, 1226, 1200, 1070, 945, 903, 765, 748, 706, 695 cm^{-1}; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{20}H_{24}NO_3$ 326.1751; found 326.1754.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.1c00259.

Detailed copies of NMR spectra for all compounds; X-ray structures of **3a**, **9**, **10**, and **11** (PDF)

Accession Codes

CCDC 2015794, 2070138, and 2082018−2082019 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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