HETEROCYCLES, Vol. 106, No. 4, 2023, pp. 664 - 679. © 2023 The Japan Institute of Heterocyclic Chemistry
Received, 19th February, 2023, Accepted, 6th March, 2023, Published online, 10th March, 2023
DOI: 10.3987/COM-23-14827

SYNTHESIS OF 1,2-DICARBONYLS FROM FIVE-MEMBERED CYCLIC ENAMINES AND ARYLGLYOXAL HYDRATES UNDER METAL-FREE CONDITIONS

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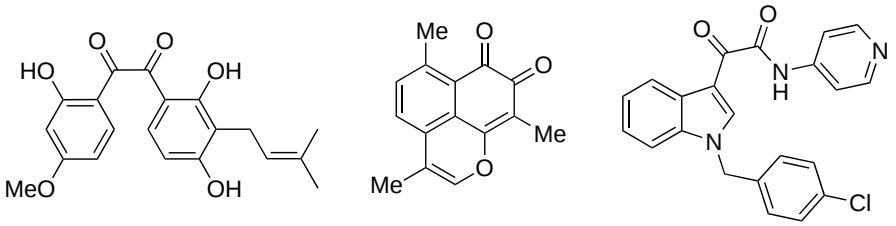
Abstract – An efficient and practical protocol for O_2-enabled oxidative 1,2-dicarbonylation of five-membered cyclic enamines with arylglyoxal hydrates is developed, producing 32 examples of functionalized 1,2-dicarbonyls in good to excellent yields. Notable features of this transformation include wide substrate scope, excellent yields and metal-free conditions as well as O_2 from air as the green oxidant with H_2O as sole by-product.

INTRODUCTION

1,2-Dicarbonyl[1] functionalities are important structural moieties that occur widely in natural products and drug molecules such as licoagrodione,[2] mansonone F,[3] Indibulin,[4] which contain the antimicrobial, antiproliferative, anticancer activity, respectively (Figure 1). Furthermore, 1,2-dicarbonyl compounds can serve as versatile intermediates for the construction of complex molecules.[5,6]



licoagrodione (antimicrobial) | mansonone F (antiproliferative) | Indibulin (anticancer)

Figure 1. Significant Dicarbonyl-Containing Molecules

Consequently, in the past decades, numerous synthetic methodologies for the construction of this important unit have been developed, realizing the 1,2-dicarbonylation of pyridine, indolizine, imidazotriazine and other skeletons (Figure 2).[7-12] However, most of these described methods suffer from limitations such as long reaction time,[7] metal catalysts,[7,9] and stoichiometric oxidants.[12] Therefore, there

is still a need to develop general and simple methods for the synthesis of 1,2-dicarbonyls from inexpensive starting materials and cheap sources of oxygen under metal-free conditions.

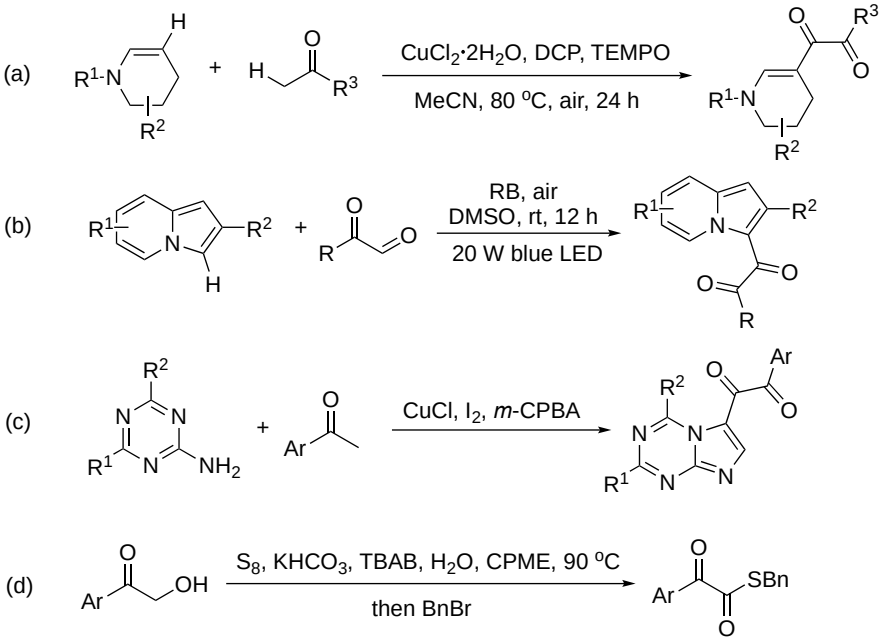


Figure 2. Several Strategies toward 1,2-Dicarbonylation

As important 1,3-bidonors, five-membered cyclic enamines have been extensively applied to the synthesis of heterocycles.[13] On the other hand, arylglyoxal hydrates,[14] possessing two electrophilic centers, have been constructed diverse heterocyclic skeletons by our group such as oxazoloindoles,[14b] pyrazolopyridines,[14e] naphthyridines,[14f-g] and azafluorenone.[14h] Herein, we report an efficient and practical protocol for O_2-enabled oxidative 1,2-dicarbonylation of five-membered cyclic enamines with arylglyoxal hydrates as 1,2-dicarbonyl source (Figure 3). The present protocol features wide substrate scope, excellent yields and metal-free conditions as well as O_2 from air as green oxidant, together with H_2O as sole by-product.

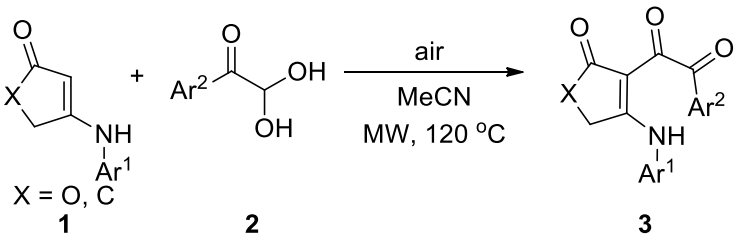


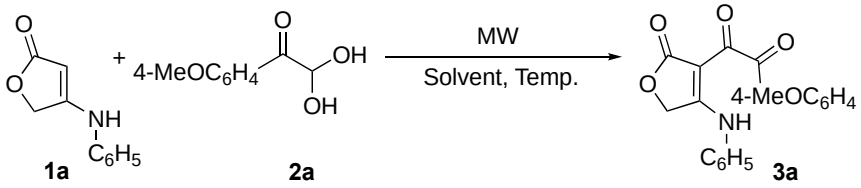
Figure 3. O_2-Enabled Oxidative 1,2-Dicarbonylation of Five-Membered Cyclic Enamines

RESULTS AND DISCUSSION

Our investigation was initiated by evaluating the reaction of 4-(phenylamino)furan-2(5*H*)-one **1a** with 2,2-dihydroxy-1-(4-methoxyphenyl)ethanone **2a**. Representative datas were summarized in Table 1.

Firstly, the reaction was tested under a variety of different solvents such as EtOH, 1,2-dichloroethane (DCE), ethyl acetate (EA), benzene, tetrahydrofuran (THF), 1,4-dioxane and MeCN. It was found that the reaction could proceed at 100 °C using EtOH as a solvent, giving the expected product **3a** with a poor yield of 18% (entry 1). The use of benzene as the solvent completely suppressed the reaction process (entry 2). A higher yield was observed when exchanging EtOH for DCE (21%), EA (25%), 1,4-dioxane (34%), THF (53%) or MeCN (65%) (entries 3-7). Of these solvents, the latter MeCN gave the best result, in which a 65% yield was obtained (entry 7). Next, the reaction temperature was investigated. The higher reaction temperature is beneficial for this reaction (entries 8-10). When increasing the reaction temperature to 120 °C, the reaction gave 76% yield of **3a**. Further increase in the reaction temperature to 130 °C made the reaction system slightly complex, affording a slightly decreased yield (71%, entry 10). Moreover, the identical reaction was investigated under O_2 (1.0 atm) conditions, but the yield of product **3a** could not be improved, suggesting that O_2 from air is enough to oxidize hydroxyl group into carbonyl functionality. In addition, the reaction was conducted at 120 °C under conventional heating for 10 h to provide **3a** in 55% yield (entry 12).

Table 1. Optimization for the Synthesis of Product **3a**[a]



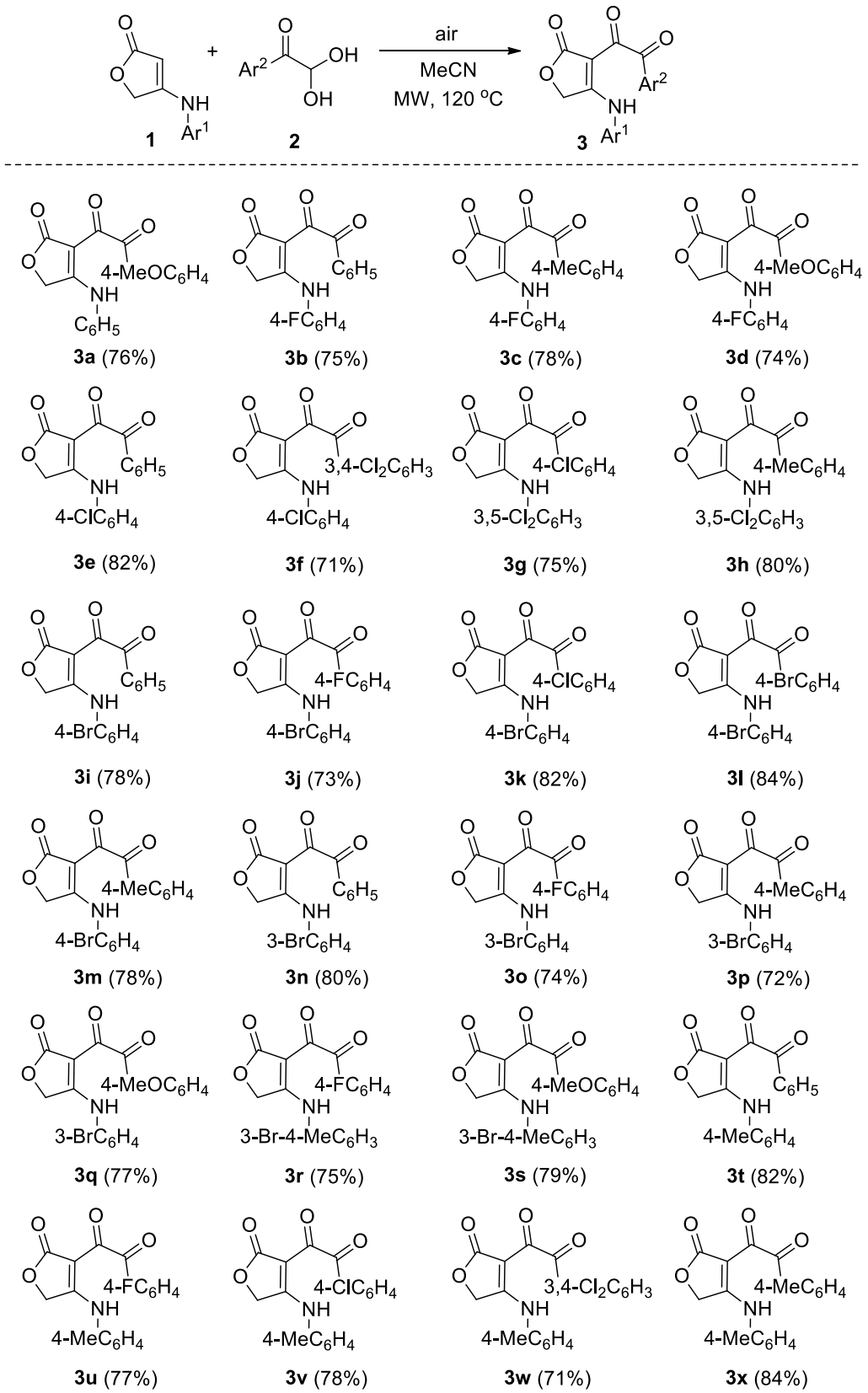
1a **2a** **3a**

Entry	Solvent	Temp. (°C)	Yield/%[b]
1	EtOH	100	18
2	DCE	100	21
3	EA	100	25
4	benzene	100	trace
5	THF	100	53
6	1,4-dioxane	100	34
7	MeCN	100	65
8	MeCN	110	69
9	MeCN	120	76
10	MeCN	130	71
11	MeCN	120	76[c]
12	MeCN	120	55[d]

[a]Reaction conditions: all the reactions were performed with **1a** (0.5 mmol), **2a** (0.5 mmol), solvent (2.0 mL) in the sealed reaction tube under air conditions. [b]Isolated yield. [c]O_2 (1.0 atm) conditions. [d]Conventional heating for 10 h.

With the established optimal conditions, we then set out to explore the scope of this reaction by examining a variety of structurally diverse 4-(arylamino)furan-2(5*H*)-one **1** with arylglyoxal hydrates

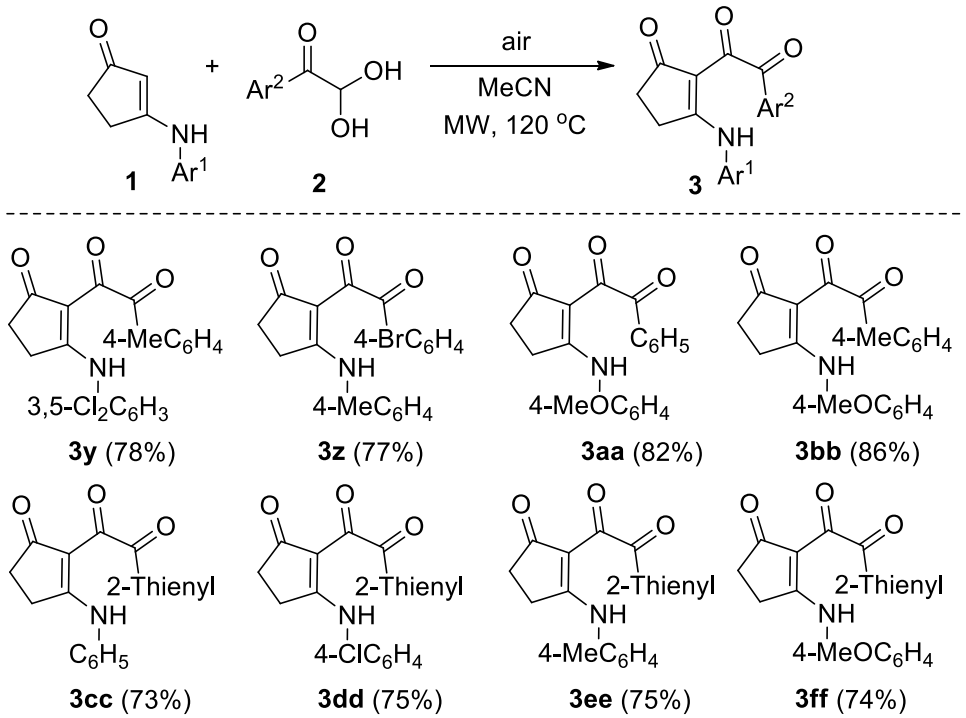
2. As illustrated in Scheme 1, the influence of substituents in the phenyl ring (Ar^1 moiety) of 4-(arylamino)furan-2(5*H*)-one **1** was investigated by employing different aryl groups bearing both



Scheme 1. Substrate Scope for Synthesis of **3a**-**3x**

electron-poor (such as Me) and electron-rich (such as F, Cl and Br) groups. Notably, substituents at 3 and 4 position, and disubstituents at 3, 4 and 3, 5 positions of the aromatic ring were found to have no influence on the course of the reaction. Next, we turned our attention to investigate the electronic properties of Ar^2 moiety of arylglyoxal hydrates **2**. Substrates **2** carrying both electron-donating groups (EDG) groups and electron-withdrawing (EWG) all worked well to provide the corresponding products **3** in moderate to excellent yields.

After our success with 1,2-dicarbonyl derivatives **3a**-**3x**, we attempted to explore the scope of this reaction using 3-(arylamino)cyclopent-2-enone to replace 4-(arylamino)furan-2(5*H*)-one. To our delight, different substituents resided at the phenyl ring (Ar^1) and (Ar^2) were compatible. Both electron-rich and electron-poor groups worked well to provide the desired products **3y**-**3bb** in yields ranging from 73% to 86%. It is worth mentioning that when the Ar^2 is 2-thienyl, it did not hamper the reaction progress, giving the corresponding products **3cc**-**3ff** smoothly (Scheme 2).



Scheme 2. Substrate Scope for Synthesis of **3y**-**3ff**

The structural elucidations were unambiguously determined by their IR, NMR, and HRMS spectroscopic analysis. The structures of **3m** and **3t** were further confirmed by X-ray diffraction analysis (Figure 4 and Figure 5).

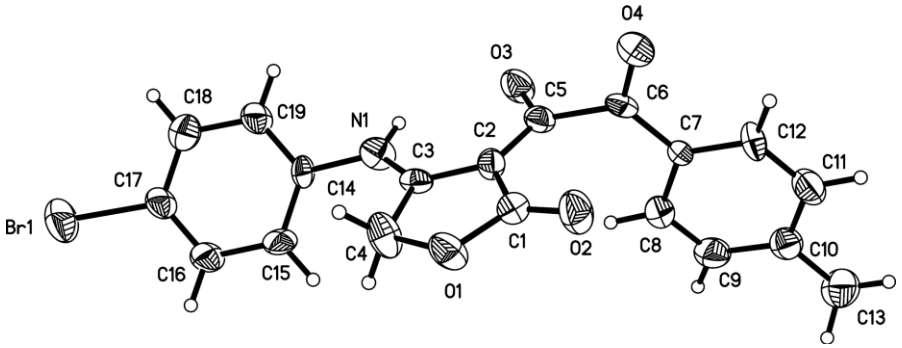


Figure 4. The ORTEP Drawing of **3m**[13]

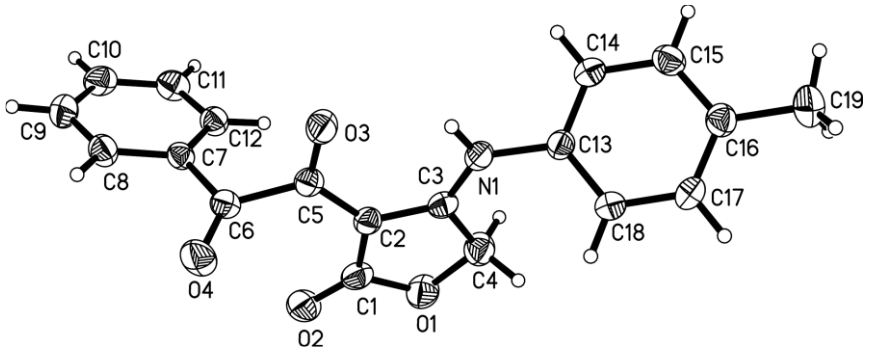
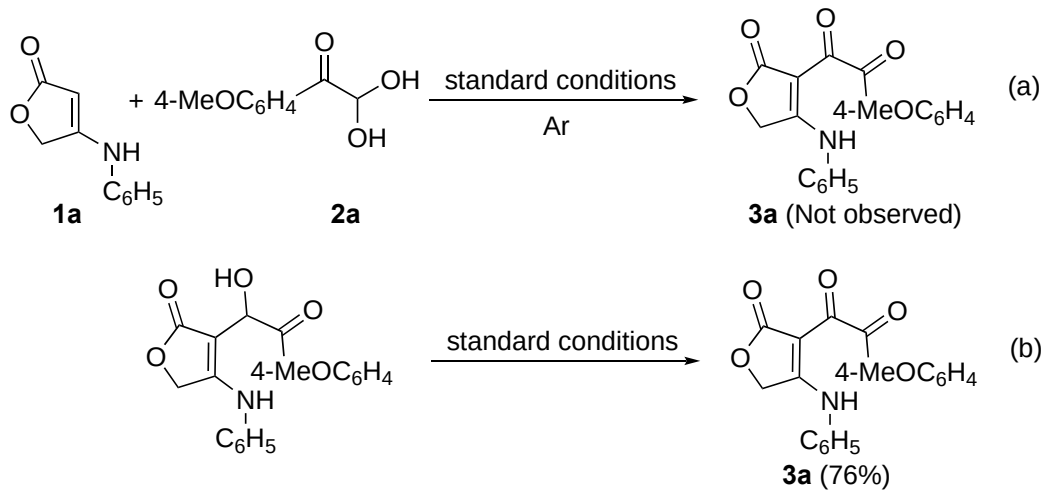


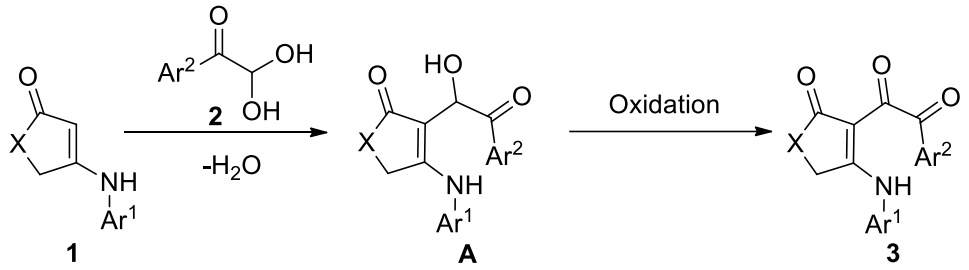
Figure 5. The ORTEP Drawing of **3t**[14]

As shown in Scheme 3, several control reactions were carried out so as to understand the mechanism of this transformation. The desired product 1-(4-methoxyphenyl)-2-(2-oxo-4-(phenylamino)-2,5-dihydrofuran-3-yl)ethane-1,2-dione **3a** was not observed under Ar conditions (Scheme a), indicating that O_2 play a key role in the success of this reaction. The preformed 3-(1-hydroxy-2-(4-methoxyphenyl)-2-oxoethyl)-4-(phenylamino)furan-2(5*H*)-one was reacted under standard conditions, providing **3a** in 76% yield (Scheme b).



Scheme 3. Control Reactions

Based on our above results, a plausible reaction mechanism is presented in Scheme 4. Five-membered cyclic enamine **1** is subjected with arylglyoxal hydrate **2** to give access to intermediate **A**, then the intermediate **A** was oxidized by O_2 to get product **3**. The structure of intermediate **A** was unequivocally confirmed by X-ray diffraction analysis (Figure 6).



Scheme 4. Mechanism Hypothesis for Forming **3**

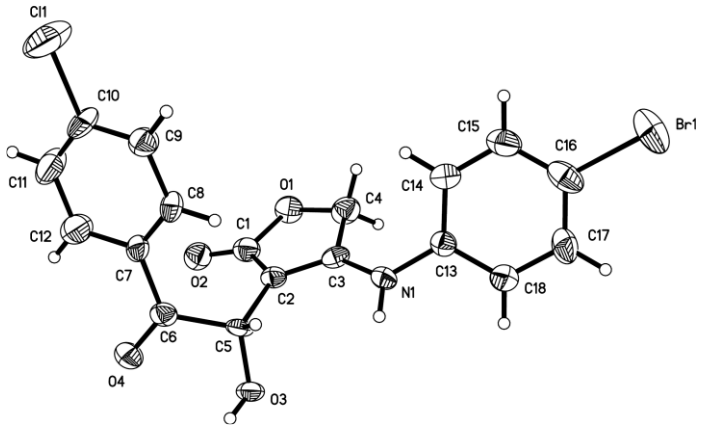


Figure 6. The ORTEP Drawing of Intermediate **A**[15]

In order to explore whether the reaction can be applied to gram-scale, the following experiments were carried out. As shown in Figure 7, 10 mmol 4-(phenylamino)furan-2(5*H*)-one **1a** and 10 mmol 2,2-dihydroxy-1-(4-methoxyphenyl)ethanone **2a** were treated under optimal conditions, then 2.56 g 1-(4-methoxyphenyl)-2-(2-oxo-4-(phenylamino)-2,5-dihydrofuran-3-yl)ethane-1,2-dione **3a** was obtained.

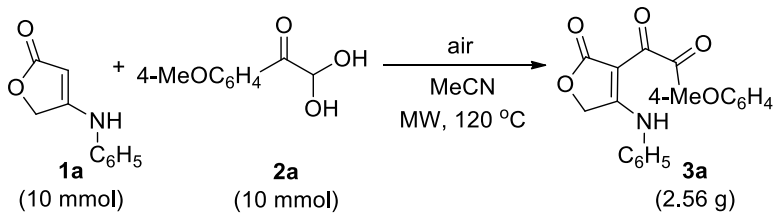


Figure 7. Gram-scale Reaction

CONCLUSION

In summary, we have established a new and versatile protocol for the synthesis of various 1,2-dicarbonyl derivatives in moderate to excellent yield with a broad substrate scopes. This transformation use O_2 as an ideal oxidant and produce H_2O as the only by-product, which is environmentally friendly. Further investigations to understand the mechanism of this reaction and their applications in other organic reactions are ongoing in our laboratory.

EXPERIMENTAL

Microwave irradiation was carried out with Initiator 2.5 Microwave synthesizers obtained from Biotage, Uppsala, Sweden. The reaction temperatures were measured by an infrared detector during microwave heating.

Example for the synthesis of **3a**: In a typical experiment procedure, 4-(phenylamino)furan-2(5*H*)-one **1a** (0.5 mmol) and 2,2-dihydroxy-1-(4-methoxyphenyl)ethanone **2a** (0.5 mmol) were introduced in a 30-mL reaction vial, then MeCN (2.0 mL) was successively added. Subsequently, the mixture was stirred at 120 °C under microwave radiation condition for 30 min. After completion of the reaction (monitored by TLC), the reaction mixture was cooled to room temperature and diluted with cold water, then extracted with EtOAc. The extract was washed with 10% aq. $Na_2S_2O_3$ solution, dried over anhydrous Na_2SO_4 and evaporation. The residue was purified by column chromatography to afford the pure product **3a**.

1-(4-Methoxyphenyl)-2-(2-oxo-4-(phenylamino)-2,5-dihydrofuran-3-yl)ethane-1,2-dione (3a) A yellow solid; 76% yield; Mp 205-207 °C; IR (KBr, *v*, cm^{-1}): 3197, 1755, 1683, 1633, 1599, 1422, 1379, 1264, 1156; ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 11.32 (s, 1H, NH), 7.84 (d, 2H, *J* = 8.8 Hz, ArH), 7.50-7.47 (m, 4H, ArH), 7.41-7.37 (m, 1H, ArH), 7.13 (d, 2H, *J* = 8.8 Hz, ArH), 5.16 (s, 2H, CH_2), 3.88 (s, 3H, OCH_3); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 192.1, 190.5, 173.2, 170.5, 164.6, 137.2, 131.9, 130.0, 128.1, 126.1, 124.5, 115.0, 94.9, 66.8, 56.2; HRMS (ESI): *m*/*z* calcd for: $C_{19}H_{14}NO_5$, 336.0872 $[M-H]^-$; found: 336.0876.

1-(4-((4-Fluorophenyl)amino)-2-oxo-2,5-dihydrofuran-3-yl)-2-phenylethane-1,2-dione (3b) A pink solid; 75% yield; Mp 235-236 °C; IR (KBr, *v*, cm^{-1}): 3189, 1758, 1645, 1637, 1629, 1510, 1255; ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 11.32 (s, 1H, NH), 7.88 (d, 2H, *J* = 7.2 Hz, ArH), 7.75 (t, 1H, *J* = 7.2 Hz, ArH), 7.62 (t, 2H, *J* = 7.6 Hz, ArH), 7.57-7.54 (m, 2H, ArH), 7.34 (t, 2H, *J* = 8.8 Hz, ArH), 5.09 (s, 2H, CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 193.7, 190.0, 173.6, 170.8, 161.5 ($^1J_{CF}$ = 243.6 Hz), 135.0, 133.6 ($^4J_{CF}$ = 2.9 Hz), 133.2, 129.6, 129.5, 127.4 ($^3J_{CF}$ = 8.8 Hz), 116.7 ($^2J_{CF}$ = 22.7 Hz), 94.9, 66.8; HRMS (ESI): *m*/*z* calcd for: $C_{18}H_{11}FNO_4$, 324.0672 $[M-H]^-$; found: 324.0676.

1-(4-((4-Fluorophenyl)amino)-2-oxo-2,5-dihydrofuran-3-yl)-2-(*p*-tolyl)ethane-1,2-dione (3c) A pale yellow solid; 78% yield; Mp 249-250 °C; IR (KBr, *v*, cm^{-1}): 3232, 1758, 1672, 1636, 1509, 1387, 1263,

1160; ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 11.30 (s, 1H, NH), 7.77 (d, 2H, J = 8.4 Hz, ArH), 7.57-7.54 (m, 2H, ArH), 7.42 (d, 2H, J = 8.0 Hz, ArH), 7.34 (t, 2H, J = 8.8 Hz, ArH), 5.08 (s, 2H, CH_2), 2.42 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 193.3, 190.2, 173.5, 170.7, 161.5 ($^1J_{CF}$ = 243.6 Hz), 145.7, 133.6 ($^4J_{CF}$ = 2.8 Hz), 130.8, 130.2, 129.6, 127.4 ($^3J_{CF}$ = 8.8 Hz), 116.7 ($^2J_{CF}$ = 22.7 Hz), 94.9, 66.7, 21.8; HRMS (ESI): *m*/*z* calcd for: $C_{19}H_{13}FNO_4$, 338.0829 [M-H]$^-$; found: 338.0831.

1-(4-((4-Fluorophenyl)amino)-2-oxo-2,5-dihydrofuran-3-yl)-2-(4-methoxyphenyl)ethane-1,2-dione (3d) A pale yellow solid; 74% yield; Mp 205-206 °C; IR (KBr, v, cm^{-1}): 3236, 1766, 1668, 1651, 1516, 1392, 1263, 1151; ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 11.29 (s, 1H, NH), 7.83 (d, 2H, J = 8.8 Hz, ArH), 7.57-7.53 (m, 2H, ArH), 7.33 (t, 2H, J = 8.8 Hz, ArH), 7.13 (d, 2H, J = 7.2 Hz, ArH), 5.08 (s, 2H, CH_2), 3.88 (s, 3H, OCH_3); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 192.2, 190.4, 173.5, 170.6, 164.6, 161.4 ($^1J_{CF}$ = 243.5 Hz), 133.6 ($^4J_{CF}$ = 2.9 Hz), 131.9, 127.3 ($^3J_{CF}$ = 8.7 Hz), 126.1, 116.7 ($^2J_{CF}$ = 22.7 Hz), 115.0, 94.9, 66.7, 56.2; HRMS (ESI): *m*/*z* calcd for: $C_{19}H_{13}FNO_5$, 354.0778 [M-H]$^-$; found: 354.0779.

1-(4-((4-Chlorophenyl)amino)-2-oxo-2,5-dihydrofuran-3-yl)-2-phenylethane-1,2-dione (3e) A white solid; 82% yield; Mp 218-220 °C; IR (KBr, v, cm^{-1}): 3225, 1757, 1670, 1636, 1621, 1487, 1373, 1258, 1158; ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 11.35 (s, 1H, NH), 7.88 (d, 2H, J = 7.2 Hz, ArH), 7.75 (t, 1H, J = 7.6 Hz, ArH), 7.61 (t, 1H, J = 8.0 Hz, ArH), 7.57-7.52 (m, 4H, ArH), 5.15 (s, 2H, CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 193.7, 190.1, 173.3, 170.7, 136.2, 135.0, 133.1, 132.5, 129.9, 129.6, 129.5, 126.7, 95.2, 66.9; HRMS (ESI): *m*/*z* calcd for: $C_{18}H_{11}ClNO_4$, 340.0377 [M-H]$^-$; found: 340.0381.

1-(4-((4-Chlorophenyl)amino)-2-oxo-2,5-dihydrofuran-3-yl)-2-(3,4-dichlorophenyl)ethane-1,2-dione (3f) A pale yellow solid; 71% yield; Mp 230-232 °C; IR (KBr, v, cm^{-1}): 3238, 1753, 1689, 1656, 1639, 1517, 1162; ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 11.38 (s, 1H, NH), 8.04 (d, 1H, J = 1.6 Hz, ArH), 7.91 (d, 1H, J = 8.4 Hz, ArH), 7.85-7.83 (m, 1H, ArH), 7.57-7.51 (m, 4H, ArH), 5.15 (s, 2H, CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 191.7, 188.5, 173.4, 170.8, 138.1, 136.1, 133.2, 132.9, 132.6, 132.3, 130.7, 129.9, 129.4, 126.7, 95.1, 67.2; HRMS (ESI): *m*/*z* calcd for: $C_{18}H_9Cl_3NO_4$, 407.9597 [M-H]$^-$; found: 407.9599.

1-(4-Chlorophenyl)-2-(4-((3,5-dichlorophenyl)amino)-2-oxo-2,5-dihydrofuran-3-yl)ethane-1,2-dione (3g) A white solid; 75% yield; Mp 225-227 °C; IR (KBr, v, cm^{-1}): 3216, 1768, 1651, 1641, 1627, 1518, 1170; ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 11.37 (s, 1H, NH), 7.87 (d, 2H, J = 8.4 Hz, ArH), 7.71-7.65 (m, 5H, ArH), 5.23 (s, 2H, CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 192.5, 189.5, 173.4, 170.6, 140.1, 139.6, 135.0, 131.7, 131.2, 129.9, 127.8, 124.0, 95.7, 67.1; HRMS (ESI): *m*/*z* calcd for: $C_{18}H_9Cl_3NO_4$, 407.9597 [M-H]$^-$; found: 407.9600.

1-(4-((3,5-Dichlorophenyl)amino)-2-oxo-2,5-dihydrofuran-3-yl)-2-(*p*-tolyl)ethane-1,2-dione (3h) A white solid; 80% yield; Mp 216-218 °C; IR (KBr, v, cm^{-1}): 3240, 1759, 1676, 1643, 1628, 1523, 1167; ^{1}H

NMR (400 MHz, DMSO-d_6) (δ, ppm): 11.33 (s, 1H, NH), 7.75 (d, 2H, J = 8.0 Hz, ArH), 7.66 (s, 3H, ArH), 7.42 (d, 2H, J = 7.6 Hz, ArH), 5.22 (s, 2H, CH_2), 2.42 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 193.1, 190.4, 173.3, 170.5, 145.8, 139.6, 135.0, 130.6, 130.2, 129.6, 127.7, 123.9, 95.7, 67.0, 21.8; HRMS (ESI): m/z calcd for: $C_{19}H_{12}Cl_2NO_4$, 388.0144 $[M-H]^-$; found: 388.0147.

1-(4-((4-Bromophenyl)amino)-2-oxo-2,5-dihydrofuran-3-yl)-2-phenylethane-1,2-dione (3i) A brown solid; 78% yield; Mp 190-191 °C; IR (KBr, v, cm^{-1}): 3233, 1749, 1677, 1646, 1628, 1507, 1158; ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 11.34 (s, 1H, NH), 7.89-7.87 (m, 2H, ArH), 7.75 (t, 1H, J = 7.6 Hz, ArH), 7.69 (d, 2H, J = 8.8 Hz, ArH), 7.61 (t, 2H, J = 7.6 Hz, ArH), 7.47 (d, 2H, J = 8.8 Hz, ArH), 5.16 (s, 2H, CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 193.7, 190.1, 173.2, 170.6, 136.6, 135.0, 133.1, 132.8, 129.6, 129.5, 126.9, 120.9, 95.2, 67.0; HRMS (ESI): m/z calcd for: $C_{18}H_{11}BrNO_4$, 383.9872 $[M-H]^-$; found: 383.9873.

1-(4-((4-Bromophenyl)amino)-2-oxo-2,5-dihydrofuran-3-yl)-2-(4-fluorophenyl)ethane-1,2-dione (3j) A pale yellow solid; 73% yield; Mp 198-200 °C; IR (KBr, v, cm^{-1}): 3196, 1752, 1676, 1639, 1596, 1504, 1390, 1259, 1152; ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 11.35 (s, 1H, NH), 7.98-7.94 (m, 2H, ArH), 7.69 (d, 2H, J = 8.8 Hz, ArH), 7.45 (t, 4H, J = 8.8 Hz, ArH), 5.15 (s, 2H, CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 192.2, 189.7, 173.3, 170.7, 166.2 ($^1J_{CF}$ = 252.4 Hz), 136.6, 132.8, 132.5 ($^3J_{CF}$ = 9.9 Hz), 129.9 ($^4J_{CF}$ = 2.6 Hz), 126.9, 120.9, 116.9 ($^2J_{CF}$ = 22.1 Hz), 95.2, 67.0; HRMS (ESI): m/z calcd for: $C_{18}H_{10}BrFNO_4$, 401.9777 $[M-H]^-$; found: 401.9779.

1-(4-((4-Bromophenyl)amino)-2-oxo-2,5-dihydrofuran-3-yl)-2-(4-chlorophenyl)ethane-1,2-dione (3k) A pale yellow solid; 82% yield; Mp 202-204 °C; IR (KBr, v, cm^{-1}): 3290, 1771, 1695, 1646, 1628, 1579, 1388; ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 11.35 (s, 1H, NH), 7.89 (d, 2H, J = 8.4 Hz, ArH), 7.70 (d, 2H, J = 3.2 Hz, ArH), 7.68 (d, 2H, J = 3.6 Hz, ArH), 7.46 (d, 2H, J = 8.8 Hz, ArH), 5.15 (s, 2H, CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 192.6, 189.4, 173.3, 170.7, 140.0, 136.6, 132.8, 131.8, 131.2, 129.9, 127.0, 121.0, 95.2, 67.0; HRMS (ESI): m/z calcd for: $C_{18}H_{10}BrClNO_4$, 417.9482 $[M-H]^-$; found: 417.9485.

1-(4-Bromophenyl)-2-(4-((4-bromophenyl)amino)-2-oxo-2,5-dihydrofuran-3-yl)ethane-1,2-dione (3l) A yellow solid; 84% yield; Mp 190-192 °C; IR (KBr, v, cm^{-1}): 3193, 1759, 1685, 1635, 1620, 1587, 1398, 1253, 1154; ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 11.36 (s, 1H, NH), 7.85-7.79 (m, 4H, ArH), 7.68 (d, 2H, J = 8.8 Hz, ArH), 7.46 (d, 2H, J = 8.8 Hz, ArH), 5.16 (s, 2H, CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 192.9, 189.4, 173.3, 170.7, 136.6, 132.9, 132.8, 132.1, 131.3, 129.3, 127.0, 121.0, 95.2, 67.1; HRMS (ESI): m/z calcd for: $C_{18}H_{10}Br_2NO_4$, 463.8956 $[M-H]^-$; found: 463.8959.

1-(4-((4-Bromophenyl)amino)-2-oxo-2,5-dihydrofuran-3-yl)-2-(*p*-tolyl)ethane-1,2-dione (3m) A white solid; 78% yield; Mp 246-247 °C; IR (KBr, v, cm^{-1}): 3213, 1760, 1671, 1632, 1572, 1487, 1261, 1158; ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 11.32 (s, 1H, NH), 7.77 (d, 2H, J = 8.0 Hz, ArH), 7.68 (d,

2H, *J* = 8.4 Hz, ArH), 7.46 (d, 2H, *J* = 8.8 Hz, ArH), 7.41 (d, 2H, *J* = 8.0 Hz, ArH), 5.15 (s, 2H, CH_2), 2.42 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 193.2, 190.3, 173.2, 170.5, 145.7, 136.7, 132.8, 130.7, 130.2, 129.6, 126.9, 120.9, 95.2, 66.9, 21.8; HRMS (ESI): *m*/*z* calcd for: $C_{19}H_{13}BrNO_4$, 398.0028 $[M-H]^-$; found: 398.0030.

1-(4-((3-Bromophenyl)amino)-2-oxo-2,5-dihydrofuran-3-yl)-2-phenylethane-1,2-dione (3n) A yellow solid; 80% yield; Mp 208-209 °C; IR (KBr, *v*, cm^{-1}): 3233, 1766, 1679, 1651, 1574, 1482, 1267, 1163; ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 11.35 (s, 1H, NH), 7.87 (d, 2H, *J* = 7.6 Hz, ArH), 7.77-7.73 (m, 2H, ArH), 7.64-7.59 (m, 3H, ArH), 7.53 (d, 1H, *J* = 8.0 Hz, ArH), 7.45 (t, 1H, *J* = 8.0 Hz, ArH), 5.18 (s, 2H, CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 193.6, 190.1, 173.3, 170.6, 138.8, 135.0, 133.1, 131.8, 131.0, 129.6, 129.5, 127.7, 123.9, 122.3, 95.3, 67.0; HRMS (ESI): *m*/*z* calcd for: $C_{18}H_{11}BrNO_4$, 383.9872 $[M-H]^-$; found: 383.9875.

1-(4-((3-Bromophenyl)amino)-2-oxo-2,5-dihydrofuran-3-yl)-2-(4-fluorophenyl)ethane-1,2-dione (3o) A yellow solid; 74% yield; Mp 179-180 °C; IR (KBr, *v*, cm^{-1}): 3232, 1768, 1674, 1630, 1578, 1503, 1260; ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 11.36 (s, 1H, NH), 7.97-7.94 (m, 2H, ArH), 7.77 (s, 1H, ArH), 7.60 (d, 1H, *J* = 8.0 Hz, ArH), 7.52 (d, 1H, *J* = 8.0 Hz, ArH), 7.48-7.43 (m, 3H, ArH), 5.18 (s, 2H, CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 192.2, 189.7, 173.4, 170.6, 166.2 ($^1J_{CF}$ = 252.6 Hz), 138.7, 132.5 ($^3J_{CF}$ = 9.9 Hz), 131.8, 131.0, 129.9 ($^4J_{CF}$ = 2.7 Hz), 127.7, 123.9, 122.3, 116.9 ($^2J_{CF}$ = 22.3 Hz), 95.3, 67.0; HRMS (ESI): *m*/*z* calcd for: $C_{18}H_{10}BrFNO_4$, 401.9777 $[M-H]^-$; found: 401.9780.

1-(4-((3-Bromophenyl)amino)-2-oxo-2,5-dihydrofuran-3-yl)-2-(*p*-tolyl)ethane-1,2-dione (3p) A purple solid; 72% yield; Mp 186-188 °C; IR (KBr, *v*, cm^{-1}): 3231, 1749, 1689, 1642, 1578, 1479, 1252, 1151; ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 11.32 (s, 1H, NH), 7.76 (d, 3H, *J* = 8.0 Hz, ArH), 7.59 (d, 1H, *J* = 8.0 Hz, ArH), 7.52 (d, 1H, *J* = 8.4 Hz, ArH), 7.47-7.41 (m, 3H, ArH), 5.18 (s, 2H, CH_2), 2.42 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 193.2, 190.4, 173.3, 170.5, 145.8, 138.8, 131.8, 131.0, 130.7, 130.2, 129.6, 127.7, 123.8, 122.3, 95.3, 66.9, 21.8; HRMS (ESI): *m*/*z* calcd for: $C_{19}H_{13}BrNO_4$, 398.0028 $[M-H]^-$; found: 398.0031.

1-(4-((3-Bromophenyl)amino)-2-oxo-2,5-dihydrofuran-3-yl)-2-(4-methoxyphenyl)ethane-1,2-dione (3q) A pale yellow solid; 77% yield; Mp 175-177 °C; IR (KBr, *v*, cm^{-1}): 3245, 1737, 1683, 1622, 1572, 1474, 1254, 1154; ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 11.31 (s, 1H, NH), 7.82 (d, 2H, *J* = 8.8 Hz, ArH), 7.77 (s, 1H, ArH), 7.59 (d, 1H, *J* = 8.0 Hz, ArH), 7.52 (d, 1H, *J* = 7.6 Hz, ArH), 7.44 (t, 1H, *J* = 8.0 Hz, ArH), 7.13 (d, 2H, *J* = 8.8 Hz, ArH), 5.17 (s, 2H, CH_2), 3.88 (s, 3H, OCH_3); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 192.1, 190.5, 173.3, 170.4, 164.6, 138.9, 131.9, 131.7, 130.9, 127.6, 126.1, 123.7, 122.3, 115.0, 95.4, 66.8, 56.2; HRMS (ESI): *m*/*z* calcd for: $C_{19}H_{13}BrNO_4$, 413.9977 $[M-H]^-$; found: 413.9980.

1-(4-((3-Bromo-4-methylphenyl)amino)-2-oxo-2,5-dihydrofuran-3-yl)-2-(4-fluorophenyl)ethane-1,2-

dione (3r) A white solid; 75% yield; Mp 208-209 °C; IR (KBr, *v*, cm^{-1}): 3196, 1749, 1673, 1623, 1600, 1557, 1261; ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 11.31 (s, 1H, NH), 7.97-7.94 (m, 2H, ArH), 7.77 (d, 1H, *J* = 1.6 Hz, ArH), 7.47-7.43 (m, 4H, ArH), 5.14 (s, 2H, CH_2), 2.38 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 192.2, 189.6, 173.4, 170.7, 166.2 ($^1J_{CF}$ = 252.4 Hz), 137.5, 136.2, 132.5 ($^3J_{CF}$ = 9.8 Hz), 132.0, 129.9 ($^4J_{CF}$ = 2.7 Hz), 128.4, 124.6, 124.1, 116.9 ($^2J_{CF}$ = 22.2 Hz), 95.1, 66.9, 22.4; HRMS (ESI): *m*/*z* calcd for: $C_{19}H_{12}BrFNO_4$, 415.9934 $[M-H]^-$; found: 415.9936.

1-(4-((3-Bromo-4-methylphenyl)amino)-2-oxo-2,5-dihydrofuran-3-yl)-2-(4-methoxyphenyl)ethane-1,2-dione (3s) A pale yellow solid; 79% yield; Mp 231-233 °C; IR (KBr, *v*, cm^{-1}): 3188, 1756, 1665, 1599, 1476, 1355, 1254, 1160; ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 11.27 (s, 1H, NH), 7.83 (d, 2H, *J* = 8.8 Hz, ArH), 7.77 (d, 1H, *J* = 1.6 Hz, ArH), 7.47-7.41 (m, 2H, ArH), 7.13 (d, 2H, *J* = 8.8 Hz, ArH), 5.14 (s, 2H, CH_2), 3.88 (s, 3H, OCH_3), 2.38 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 192.1, 190.5, 173.3, 170.5, 164.6, 137.4, 136.3, 132.0, 131.9, 128.3, 126.1, 124.6, 124.0, 115.0, 95.1, 66.7, 56.2, 22.4; HRMS (ESI): *m*/*z* calcd for: $C_{20}H_{15}BrNO_5$, 428.0134 $[M-H]^-$; found: 428.0138.

1-(2-Oxo-4-(*p*-tolylamino)-2,5-dihydrofuran-3-yl)-2-phenylethane-1,2-dione (3t) A yellow solid; 82% yield; Mp 241-243 °C; IR (KBr, *v*, cm^{-1}): 3238, 1767, 1688, 1630, 1595, 1398, 1246, 1134; ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 11.29 (s, 1H, NH), 7.88-7.86 (m, 2H, ArH), 7.74 (t, 1H, *J* = 7.6 Hz, ArH), 7.61 (t, 2H, *J* = 8.0 Hz, ArH), 7.37 (d, 2H, *J* = 8.4 Hz, ArH), 7.29 (d, 2H, *J* = 8.4 Hz, ArH), 5.13 (s, 2H, CH_2), 2.35 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 193.7, 190.0, 173.2, 170.7, 137.7, 134.9, 134.7, 133.2, 130.4, 129.6, 129.5, 124.5, 124.4, 94.7, 66.9, 21.0; HRMS (ESI): *m*/*z* calcd for: $C_{19}H_{14}NO_4$, 320.0923 $[M-H]^-$; found: 320.0926.

1-(4-Fluorophenyl)-2-(2-oxo-4-(*p*-tolylamino)-2,5-dihydrofuran-3-yl)ethane-1,2-dione (3u) A yellow solid; 77% yield; Mp 193-195 °C; IR (KBr, *v*, cm^{-1}): 3234, 1759, 1686, 1635, 1595, 1398, 1254, 1154; ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 11.30 (s, 1H, NH), 7.98-7.94 (m, 2H, ArH), 7.45 (t, 2H, *J* = 8.8 Hz, ArH), 7.37 (d, 2H, *J* = 8.4 Hz, ArH), 7.29 (d, 2H, *J* = 8.4 Hz, ArH), 5.13 (s, 2H, CH_2), 2.35 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 192.3, 189.5, 173.2, 170.7, 166.1 ($^1J_{CF}$ = 252.3 Hz), 137.8, 134.7, 132.5 ($^3J_{CF}$ = 9.8 Hz), 130.4, 130.0 ($^4J_{CF}$ = 2.7 Hz), 124.5, 116.9 ($^2J_{CF}$ = 22.2 Hz), 94.7, 66.9, 21.0; HRMS (ESI): *m*/*z* calcd for: $C_{19}H_{13}FNO_4$, 338.0829 $[M-H]^-$; found: 338.0830.

1-(4-Chlorophenyl)-2-(2-oxo-4-(*p*-tolylamino)-2,5-dihydrofuran-3-yl)ethane-1,2-dione (3v) A yellow solid; 78% yield; Mp 214-215 °C; IR (KBr, *v*, cm^{-1}): 3237, 1769, 1663, 1621, 1562, 1391, 1238, 1169; ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 11.31 (s, 1H, NH), 7.89 (d, 2H, *J* = 8.4 Hz, ArH), 7.69 (d, 2H, *J* = 8.4 Hz, ArH), 7.37 (d, 2H, *J* = 8.4 Hz, ArH), 7.29 (d, 2H, *J* = 8.4 Hz, ArH), 5.13 (s, 2H, CH_2), 2.35 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 192.7, 189.3, 173.2, 170.8, 139.9, 137.8, 134.7, 131.9, 131.3, 130.4, 129.9, 124.5, 94.7, 67.0, 21.0; HRMS (ESI): *m*/*z* calcd for: $C_{19}H_{13}ClNO_4$, 354.0533 $[M-H]^-$; found: 354.0533.

1-(3,4-Dichlorophenyl)-2-(2-oxo-4-(*p*-tolylamino)-2,5-dihydrofuran-3-yl)ethane-1,2-dione (3w) A white solid; 71% yield; Mp 186-187 °C; IR (KBr, *v*, cm^{-1}): 3213, 1759, 1674, 1633, 1604, 1573, 1388, 1238, 1162; ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 11.32 (s, 1H, NH), 8.04 (d, 1H, *J* = 2.0 Hz, ArH), 7.91 (d, 1H, *J* = 8.4 Hz, ArH), 7.85-7.83 (m, 1H, ArH), 7.37 (d, 2H, *J* = 8.4 Hz, ArH), 7.29 (d, 2H, *J* = 8.4 Hz, ArH), 5.13 (s, 2H, CH_2), 2.35 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 191.7, 188.4, 173.3, 170.9, 138.0, 137.9, 134.7, 133.3, 132.9, 132.3, 130.7, 130.4, 129.4, 124.5, 94.7, 67.1, 21.0; HRMS (ESI): *m*/*z* calcd for: $C_{19}H_{12}Cl_2NO_4$, 388.0144 $[M-H]^-$; found: 388.0146.

1-(2-Oxo-4-(*p*-tolylamino)-2,5-dihydrofuran-3-yl)-2-(*p*-tolyl)ethane-1,2-dione (3x) A brown solid; 84% yield; Mp 203-205 °C; IR (KBr, *v*, cm^{-1}): 3227, 1761, 1682, 1651, 1613, 1581, 1376, 1241, 1160; ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 11.28 (s, 1H, NH), 7.76 (d, 2H, *J* = 8.4 Hz, ArH), 7.41 (d, 2H, *J* = 8.0 Hz, ArH), 7.37 (d, 2H, *J* = 8.4 Hz, ArH), 7.29 (d, 2H, *J* = 8.4 Hz, ArH), 5.12 (s, 2H, CH_2), 2.42 (s, 3H, CH_3), 2.35 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 193.3, 190.2, 173.2, 170.6, 145.7, 137.7, 134.7, 130.8, 130.4, 130.1, 129.6, 124.4, 94.7, 66.8, 21.8, 21.0; HRMS (ESI): *m*/*z* calcd for: $C_{20}H_{16}NO_4$, 334.1080 $[M-H]^-$; found: 334.1082.

1-(2-((3,5-Dichlorophenyl)amino)-5-oxocyclopent-1-en-1-yl)-2-(*p*-tolyl)ethane-1,2-dione (3y) A brown solid; 78% yield; Mp 192-194 °C; IR (KBr, *v*, cm^{-1}): 3275, 1759, 1666, 1598, 1567, 1513, 1372, 1318; ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 11.41 (s, 1H, NH), 7.71-7.67 (m, 5H, ArH), 7.39 (d, 2H, *J* = 8.0 Hz, ArH), 2.97-2.94 (m, 2H, CH_2), 2.41 (s, 3H, CH_3), 2.30-2.27 (m, 2H, CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 199.9, 193.7, 191.3, 181.6, 145.2, 139.9, 134.8, 131.0, 130.0, 129.4, 127.6, 124.9, 110.8, 33.3, 26.8, 21.8; HRMS (ESI): *m*/*z* calcd for: $C_{20}H_{14}Cl_2NO_3$, 386.0351 $[M-H]^-$; found: 386.0355.

1-(4-Bromophenyl)-2-(5-oxo-2-(*p*-tolylamino)cyclopent-1-en-1-yl)ethane-1,2-dione (3z) A brown solid; 77% yield; Mp 185-187 °C; IR (KBr, *v*, cm^{-1}): 3188, 1731, 1748, 1704, 1692, 1682, 1601, 1583, 1565, 1516, 1472, 1417; ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 11.40 (s, 1H, NH), 7.81 (d, 2H, *J* = 8.4 Hz, ArH), 7.75 (d, 2H, *J* = 8.0 Hz, ArH), 7.39 (d, 2H, *J* = 8.4 Hz, ArH), 7.30 (d, 2H, *J* = 8.0 Hz, ArH), 2.89-2.88 (m, 2H, CH_2), 2.35 (s, 3H, CH_3), 2.30-2.27 (m, 2H, CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 199.9, 193.4, 190.0, 181.4, 137.6, 134.8, 132.7, 132.6, 131.1, 130.2, 128.7, 125.2, 110.0, 33.3, 26.9, 21.1; HRMS (ESI): *m*/*z* calcd for: $C_{20}H_{15}BrNO_3$, 396.0236 $[M-H]^-$; found: 396.0239.

1-(2-((4-Methoxyphenyl)amino)-5-oxocyclopent-1-en-1-yl)-2-phenylethane-1,2-dione (3aa) A brown solid; 82% yield; Mp 188-190 °C; IR (KBr, *v*, cm^{-1}): 3218, 1697, 1651, 1606, 1553, 1521, 1401, 1373, 1316; ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 11.34 (s, 1H, NH), 7.82 (d, 2H, *J* = 7.2 Hz, ArH), 7.70 (t, 1H, *J* = 6.8 Hz, ArH), 7.58 (t, 2H, *J* = 7.2 Hz, ArH), 7.44 (d, 2H, *J* = 8.4 Hz, ArH), 7.05 (d, 2H, *J* = 8.4 Hz, ArH), 3.81 (s, 3H, OCH_3), 2.84 (s, 2H, CH_2), 2.27 (s, 2H, CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 199.8, 194.3, 190.7, 181.6, 158.9, 134.5, 133.6, 130.2, 129.4, 129.3, 127.0, 114.9, 109.9, 55.9, 33.3,

26.7; HRMS (ESI): *m*/*z* calcd for: $C_{20}H_{16}NO_4$, 334.1080 [M-H]$^-$; found: 334.1082.

1-(2-((4-Methoxyphenyl)amino)-5-oxocyclopent-1-en-1-yl)-2-(*p*-tolyl)ethane-1,2-dione (3bb) A brown solid; 86% yield; Mp 173-175 °C; IR (KBr, *v*, cm^{-1}): 3227, 1693, 1677, 1618, 1599, 1569, 1514, 1479, 1424, 1382, 1321; ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 11.34 (s, 1H, NH), 7.71 (d, 2H, *J* = 8.0 Hz, ArH), 7.44 (d, 2H, *J* = 8.8 Hz, ArH), 7.38 (d, 2H, *J* = 8.0 Hz, ArH), 7.04 (d, 2H, *J* = 8.8 Hz, ArH), 3.81 (s, 3H, OCH_3), 2.85-2.83 (m, 2H, CH_2), 2.40 (s, 3H, CH_3), 2.28-2.25 (m, 2H, CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 199.7, 193.9, 190.9, 181.6, 158.9, 145.1, 131.2, 130.2, 130.0, 129.4, 126.9, 114.9, 109.9, 55.9, 33.3, 26.6, 21.8; HRMS (ESI): *m*/*z* calcd for: $C_{21}H_{18}NO_4$, 348.1236 [M-H]$^-$; found: 348.1237.

1-(5-Oxo-2-(phenylamino)cyclopent-1-en-1-yl)-2-(thiophen-2-yl)ethane-1,2-dione (3cc) A brown solid; 73% yield; Mp 170-172 °C; IR (KBr, *v*, cm^{-1}): 3275, 1760, 1698, 1667, 1597, 1557, 1513, 1413, 1373, 1342, 1318; ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 11.45 (s, 1H, NH), 8.15 (d, 1H, *J* = 4.4 Hz, ArH), 7.66 (d, 1H, *J* = 3.2 Hz, ArH), 7.51 (m, 4H, *J* = 4.0 Hz, ArH), 7.42-7.39 (m, 1H, ArH), 7.23 (t, 1H, *J* = 4.0 Hz, ArH), 2.92-2.90 (m, 2H, CH_2), 2.31-2.28 (m, 2H, CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 199.5, 188.8, 186.8, 181.8, 140.4, 137.4, 136.6, 135.8, 129.8, 129.4, 128.0, 125.4, 109.5, 33.5, 26.8; HRMS (ESI): *m*/*z* calcd for: $C_{17}H_{12}NO_3S$, 310.0538 [M-H]$^-$; found: 310.0539.

1-(2-((4-Chlorophenyl)amino)-5-oxocyclopent-1-en-1-yl)-2-(thiophen-2-yl)ethane-1,2-dione (3dd) A white solid; 75% yield; Mp 172-174 °C; IR (KBr, *v*, cm^{-1}): 3217, 1752, 1735, 1684, 1652, 1611, 1567, 1513, 1491, 1475, 1410, 1355, 1321; ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 11.41 (s, 1H, NH), 8.16-8.14 (m, 1H, ArH), 7.66-7.65 (m, 1H, ArH), 7.58-7.53 (m, 4H, ArH), 7.28-7.26 (m, 1H, ArH), 2.90-2.87 (m, 2H, CH_2), 2.31-2.28 (m, 2H, CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 199.5, 188.8, 186.8, 181.8, 140.3, 136.6, 136.4, 135.8, 132.4, 129.7, 129.4, 127.5, 109.8, 33.4, 26.8; HRMS (ESI): *m*/*z* calcd for: $C_{17}H_{11}ClNO_3S$, 344.0148 [M-H]$^-$; found: 344.0149.

1-(5-Oxo-2-(*p*-tolylamino)cyclopent-1-en-1-yl)-2-(thiophen-2-yl)ethane-1,2-dione (3ee) A brown solid; 75% yield; Mp 175-177 °C; IR (KBr, *v*, cm^{-1}): 3223, 1680, 1655, 1619, 1570, 1511, 1474, 1410, 1355, 1320; ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 11.39 (s, 1H, NH), 8.14 (d, 1H, *J* = 4.4 Hz, ArH), 7.66 (d, 1H, *J* = 2.8 Hz, ArH), 7.39 (d, 2H, *J* = 8.4 Hz, ArH), 7.30 (d, 2H, *J* = 8.0 Hz, ArH), 7.27 (t, 1H, *J* = 4.0 Hz, ArH), 2.90-2.87 (m, 2H, CH_2), 2.36 (s, 3H, CH_3), 2.30-2.27 (m, 2H, CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 199.4, 188.7, 186.8, 181.8, 140.4, 137.5, 136.5, 135.8, 134.9, 130.3, 129.4, 125.2, 109.4, 33.5, 26.7, 21.1; HRMS (ESI): *m*/*z* calcd for: $C_{18}H_{14}NO_3S$, 324.0695 [M-H]$^-$; found: 324.0697.

1-(2-((4-Methoxyphenyl)amino)-5-oxocyclopent-1-en-1-yl)-2-(thiophen-2-yl)ethane-1,2-dione (3ff) A brown solid; 74% yield; Mp 163-165 °C; IR (KBr, *v*, cm^{-1}): 3282, 1713, 1681, 1589, 1576, 1528, 1376, 1323; ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 11.31 (s, 1H, NH), 8.14 (d, 1H, *J* = 4.8 Hz, ArH), 7.65 (d, 1H, *J* = 3.2 Hz, ArH), 7.43 (d, 2H, *J* = 8.4 Hz, ArH), 7.27 (t, 1H, *J* = 4.0 Hz, ArH), 7.04 (d, 2H, *J* = 8.8

Hz, ArH), 3.81 (s, 3H, OCH_3), 2.83 (s, 2H, CH_2), 2.29-2.26 (m, 2H, CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 199.8, 194.3, 190.7, 181.6, 158.9, 134.5, 133.6, 130.2, 129.4, 129.3, 127.0, 114.9, 109.9, 55.9, 33.3, 26.7; HRMS (ESI): *m*/*z* calcd for: $C_{18}H_{14}NO_4S$, 340.0644 $[M-H]^-$; found: 340.0648.

ACKNOWLEDGEMENTS

We are grateful for the financial support from NSFC (No. 21971090); the horizontal project of Chuzhou City Vocation College (2021hxkt03); the Quality Engineering Project of Anhui Provincial Education Department (2020kfkc362; 2021tszy046).

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15. Crystal data for **3m** (CCDC: 2231949): $C_{19}H_{14}BrNO_4$, *Mr* = 400.22, Monoclinic, *a* = 10.9020(8) Å, *b* = 6.2300(5) Å, *c* = 25.290(2) Å, *U* = 1668.5(2) Å^3, *T* = 293(2) K, space group P2(1)/c, *Z* = 4, 8126 reflections measured, 2943 unique (R_{int} = 0.1963) which were used in all calculation. The final *wR*(F_2) was 0.1296 (all data).
16. Crystal data for **3t** (CCDC: 2231948): $C_{19}H_{15}NO_4$, *Mr* = 321.32, Monoclinic, *a* = 11.0238(9) Å, *b* = 5.9101(4) Å, *c* = 24.313(2) Å, *U* = 1568.4(2) Å^3, *T* = 298(2) K, space group P2(1)/c, *Z* = 4, 7459 reflections measured, 2725 unique (R_{int} = 0.0315) which were used in all calculation. The final *wR*(F_2) was 0.1094 (all data).
17. Crystal data for intermediate **A** (CCDC: 2232494): $C_{18}H_{13}BrClNO_4$, *Mr* = 422.65, Monoclinic, *a* = 25.531(2) Å, *b* = 11.3558(11) Å, *c* = 12.1460(12) Å, *U* = 3478.4(6) Å^3, *T* = 293(2) K, space group C2/c, *Z* = 8, 9003 reflections measured, 3077 unique (R_{int} = 0.1907) which were used in all calculation. The final *wR*(F_2) was 0.2132 (all data).