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As we Graphical Abstract

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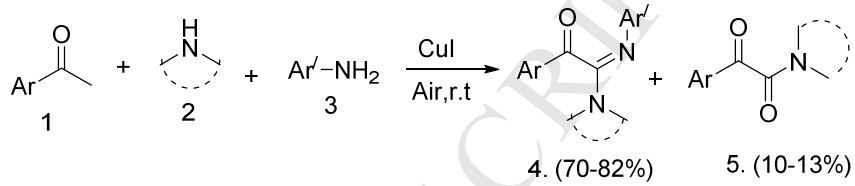

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ABSTRACT

Some novel 2-oxo-acetamidines were synthesized *via* one-pot three-component reaction of acetophenones, secondary amines and anilines in presence of CuI as catalyst. The reaction involved in a oxidation process of C(sp^3)-H bonds of acetophenones in presence of air followed by aminations, and products were obtained in good to excellent yields (70-82%) in simple work-up procedure.

1. Introduction

Organic synthesis aims in building new valuable structures/C-C or C-heteroatom bond. Now a days, researchers find α-amination of C=O group as an interesting area due to the ability of such linkage as versatile scaffold to approach a diverse spectrum of complex molecular scaffolds.[1] In organic research area, amidines are considered as important functional groups for their structural similarity with guanidines and as they can form water soluble salts.[2] Amidines/2-oxo-acetamidines constitute the core functional group of diverse drugs and pharmaceutical which is reviewed in the book series "*Progress in Medicinal Chemistry*".[3] A few of such amidine bearing drugs are shown in figure 1 (I, II, III, IV). Compounds containing *N*-arylamidines also serves as active molecule in the treatment of inflammation and pain.[4]

Carbonyls bearing α-amino group are widely considered among pharmaceutically active compounds and bioactive molecules.[5] α-Amino ketones also serve as important precursors to numerous natural products and pharmaceutically relevant compounds.[6] Some bioactive molecules possessing α-amino carbonyl moiety are shown in figure 1 (**V**, **VI**).

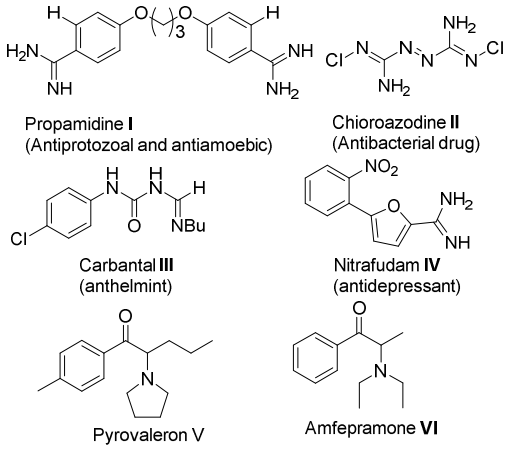

Figure 1

Considering the importance of amidines/2-oxo-acetamidines and α-amino ketones, lot of efforts has been diverted towards the development of method for the preparation of these compounds. The synthesis of amidines, particularly 2-oxo-acetamidines usually involves the construction of a carbon-nitrogen double bond and a carbon-nitrogen single bond whereas the synthesis of α-amino ketones involves the construction of a carbon-nitrogen single bond. In the present times, significant progress has been achieved in developing

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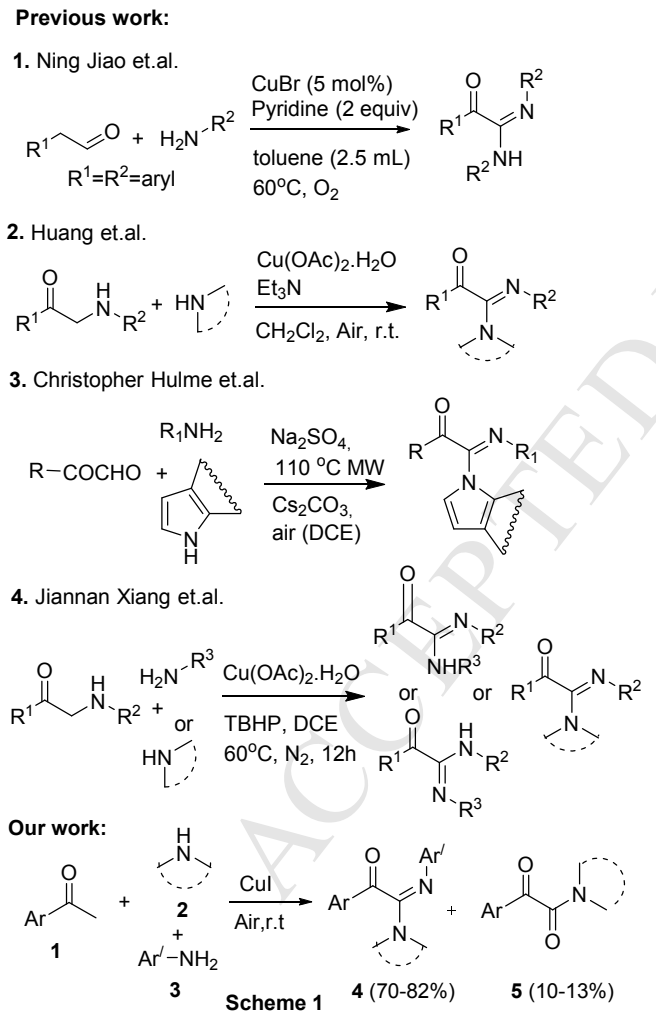
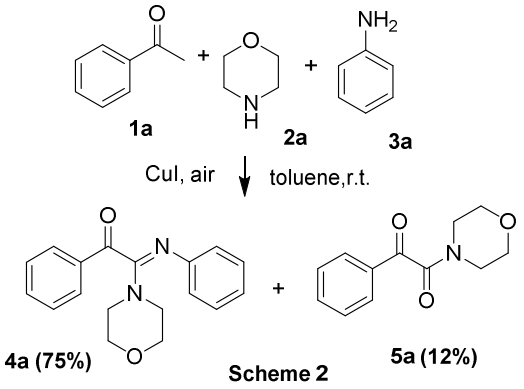
various functionalization of C-H bonds adjacent to a carbonyl group by utilizing different methodology.[7] In this regard, although, the formation of C-C bonds has been reported largely, but the cleavage of a C(sp^3)-H bonds adjacent to the carbonyl group leading to C-N bond formation has rarely been studied. The literature survey revealed a number of reports for the preparation of amidines/2-oxo-acetamidines from the reaction of carbonyl compounds and amines under various catalytic and reaction conditions all of which involved in a carbon-nitrogen single as well as double bond formation process. However, all these methods have some limitations in terms of the reaction conditions, substrate scope and the catalyst used. In 2012, Ning Jiao and his group reported the synthesis of 2-oxo-acetamidines utilizing aryl-acetaldehydes with primary amines in presence of copper bromide as catalyst.[8] But the reaction



has the limitation of substrate scope as they used only aryl acetaldehydes and aromatic amines in the reaction process. Moreover, the reaction required the use of two equivalents of pyridine and took long reaction time. In 2016, G-H. Huang and his group[9] described the synthesis of 2-oxo-acetamidines *via* α-amination of α-amino-carbonyl compounds using copper catalyst. Another method for the synthesis of 2-oxo-acetamidines was reported by C. Hulme by utilizing aryl glyoxal with amines and anilines in presence of $CsCO_3$ as base.[10] However, the reaction used only nitrogen bearing heterocyclic compounds for *N*-1 addition and the reaction was performed at 110 °C. Recently, Jiannan Xiang [11] reported the synthesis of 2-oxo-acetamidines *via* a copper catalyzed oxidative cross coupling of amines with α-amino carbonyl compounds. But, the reaction required the use of excess base and took long reaction time at 60 °C. Considering the importance of 2-oxo-acetamidines and our continued work on the synthesis of heterocyclic compounds of biological importance,[12] in the present paper, we report the synthesis of some new 2-oxo-acetamidines **4** from aryl methyl ketones **1**, secondary amines **2** and aryl amines **3** using CuI as oxidant, which involved in a oxidation process of C(sp^3)-H bond followed by the formation of a carbon-nitrogen double bond and a carbon-nitrogen single bond (Scheme 1). During the reaction process, small amount of α-amino ketones **5** also formed which is also an important class of compounds.

2. Results and discussion

Synthesis of 2-oxo-acetamidines 4 and α-amino ketones 5



The study was initiated by conducting the reaction of acetophenone **1a (**1mmol), morpholine **2a** (3 mmol) and aniline **3a** (1 mmol) in the presence of CuI as catalyst using toluene as solvent at 50 °C under oxygen atmosphere (Scheme 2). In fact, CuI was utilized earlier for oxidation of C(Sp^3)H bond in a method of preparation of α-ketoamides from the reaction of aryl methyl ketones and secondary amines in presence of an oxygen atmosphere.[13] It was expected that utilization of anilines with aryl methyl ketones and secondary amines in the presence of CuI as catalyst in a similar reaction protocol will produce predominantly our desired 2-oxo-acetamidines derivative **4a**. But, after the completion of

the reaction, as checked by TLC and further analyzed with the help of column chromatography, we found that the reaction produced the desired compound **4a** only in 28 % yield and the α-amino ketone **5a** in 62% yield (Table 1, Entry 1). Then we optimized the temperature of the reaction by performing the reaction at various temperatures. It was very interesting to note that the yield of the product **4a** increases with the decrease of the undesired compound **5a** with the lowering of reaction temperature, and 25 ^{o}C is found to be sufficient

Table 1: Optimisation of temperature, catalyst and Amines 2a & 3a

Ent.	Comp. 2a	Comp. 3a	T ^{o}C	Cat. mol%	Yd.4a (%)	Yd. 5a (%)
1[a]	3 mmol	1 mmol	50	20	28	62
2[a]	3 mmol	1 mmol	40	20	30	50
3[a]	3 mmol	1 mmol	25	20	33	42
4 [a]	2 mmol	1 mmol	25	20	35	40
5 [a]	1.5 mmol	1 mmol	25	20	74	17
6[a]	1 mmol	1 mmol	25	20	60	14
7[a]	1.5 mmol	1 mmol	25	15	75	13
8[b]	1.5 mmol	1 mmol	25	15	75	13
9[b]	1.5 mmol	1 mmol	25	10	75	12
10[a]	1.5 mmol	1 mmol	70	10	25	65
11 [a]	1.5 mmol	1 mmol	20	10	60	20

Ent = Entry; [a] = oxygen ballon; [b] = air; Comp. = Compound; T = Temperature; Cat. = Catalyst; Yd. = Yield.

to produce maximum yield of the product **4a** (Table 1, Entry 7). On the other hand increase in the reaction temperature above 50 ^{o}C decreases the yield of the desired compound **4a** (Table 1, Entry 10), and lowering the temperature to 20 ^{o}C lowers the yield of both the compound **4a** & **5a** (Table 1, Entry 11). Hence, all other reactions were carried out at 25 ^{o}C. It was also observed that when the reaction was carried out at 25 ^{o}C additional oxygen is not required and atmospheric oxygen is sufficient to produce the product in maximum yield (Table 1, Entry 8). To explore the utility of oxygen in the reaction, we also performed the reaction in an inert atmosphere. But, as expected, it did not proceed to afford our desired product. Then we optimized the load of the catalyst, and 10 mol% of CuI was found to be sufficient for the reaction process at optimized reaction temperature (Table 1, Entry 9). The reaction was also studied taking different molar ratio of morpholine **2a** and aniline **3a**. Equimolar amounts of both morpholine **2a** and aniline **3a** produced only 60% of the desired compound **4a** and 14% of the compound **5a** (Table 1, Entry 6). With the increase in the amount of morpholine with respect to aniline, the

Table 2: Scope of the product 4 with respect to 1 and 3

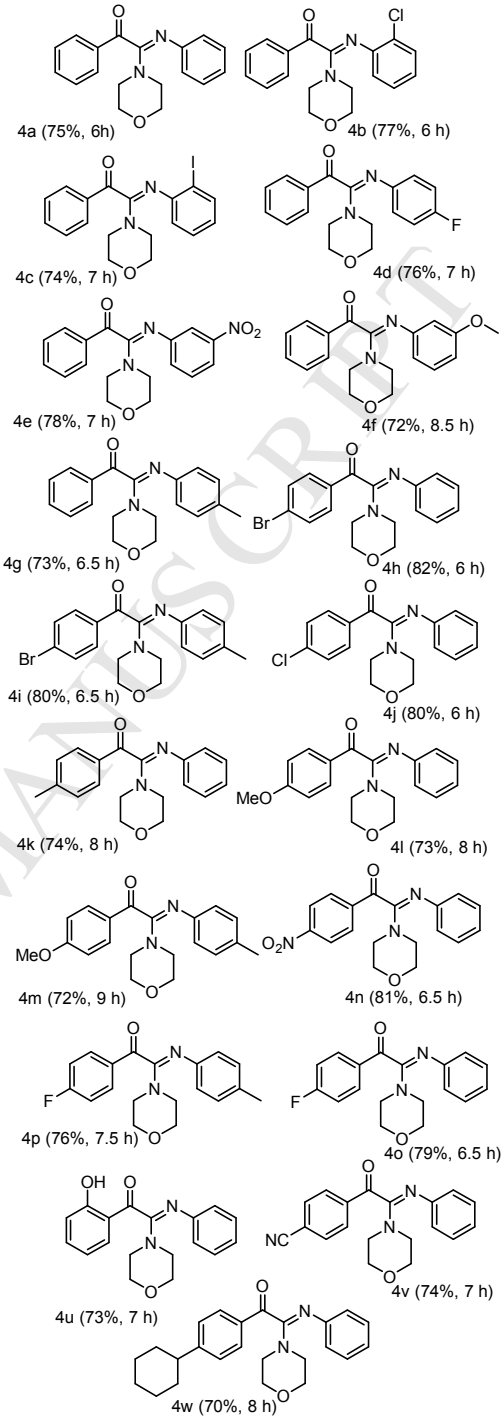
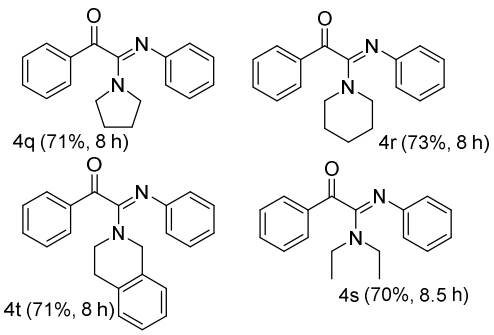


Table 3: Scope of the product 4 with respect to 2

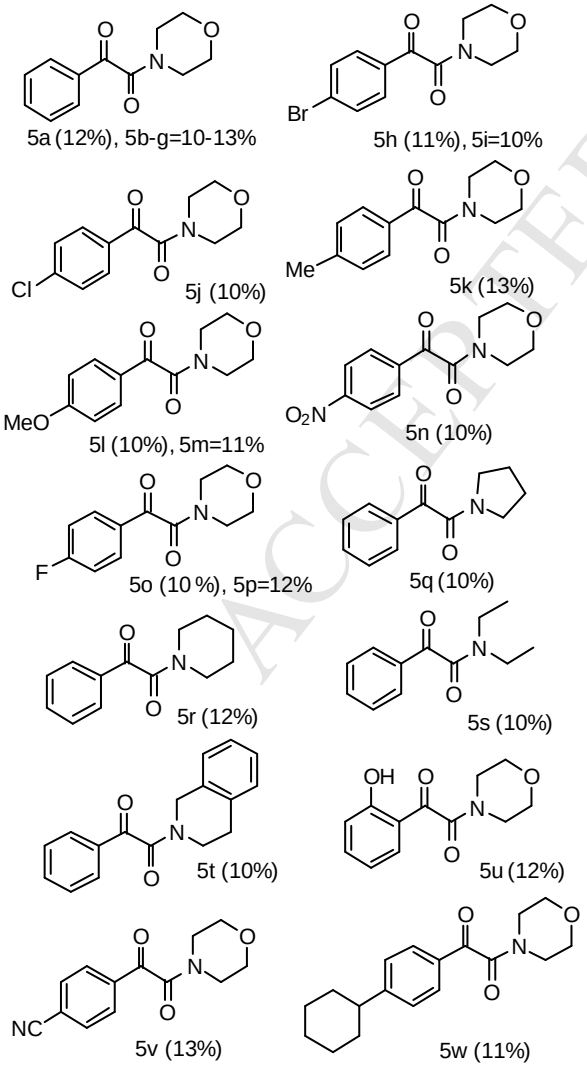


yield of the desired product **4a** also increases. Finally, 1.5 equivalent of morpholine and 1.0 equivalent of aniline were found to be the best for the formation of the desired product **4a** in high yield (Table 1, Entry 5 & 9).

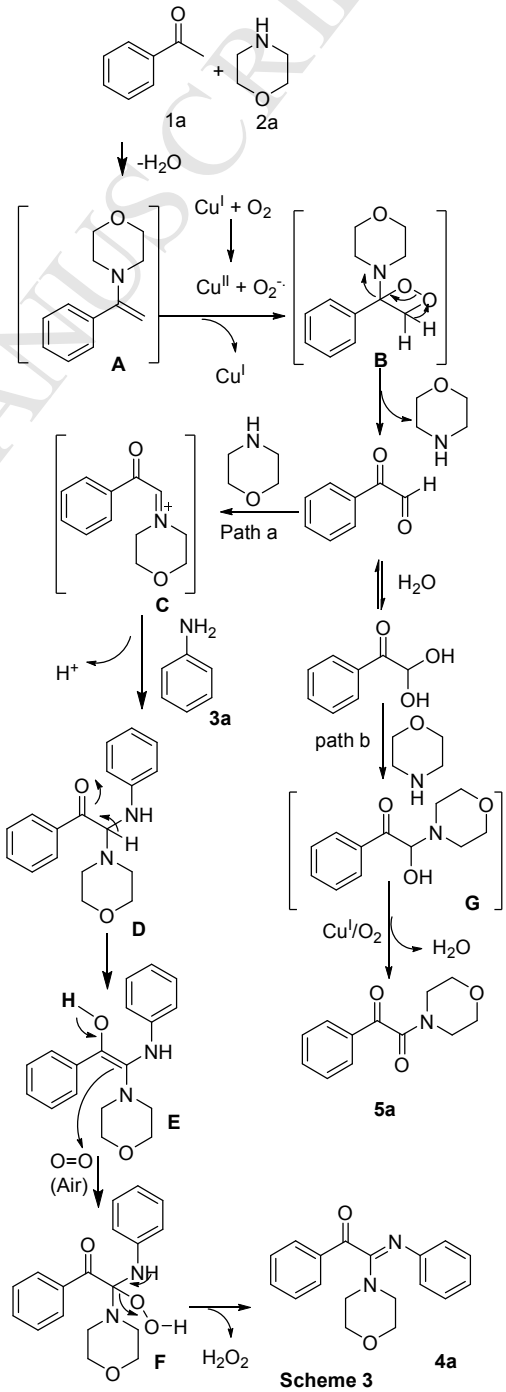
After optimization of the reaction conditions 1.0 equivalent of acetophenone **1a**, 1.5 equivalent of morpholine **2a** and 1.0 equivalent of aniline **3a** were treated in the presence of CuI (10 mol%) as catalyst using toluene as solvent at room temperature (25 ^{o}C) under stirring conditions. Progress of the reaction was monitored by thin layer chromatographic study. After completion of the reaction, the compounds formed were separated and purified with the help of column chromatography. The spectroscopic and analytical data confirmed the formation of 2-oxo-acetamide **4a** and ketoamide **5a** in 75% and 12% isolated yield respectively. The generality of the reaction was established by synthesizing the compounds **4a-w** and **5a-w** by using various substituted acetophenones **1**, secondary amine **2** and anilines **3 (Table 2, 3 and 4)** and characterizing them. The reaction was not satisfactory with the application aliphatic primary amine in place of aniline as it produced only a small amount of the compound **5** only which was not desirable.

In general, we observed that irrespective of the substitution pattern on the substrate **1, 2** and **3** all the reactions afforded satisfactory yield of the products. However, the reactions were smooth and products were obtained in higher yield in case of the aryl methyl ketones possessing electron withdrawing group at the aromatic ring.

Table 4: Formation of compound 5



Mechanism for the formation of 4 and 5



Scheme 3

On the basis of above results and previous studies,[13,14] we proposed the probable mechanistic pathway for the

formation of **4a** and **5a** as shown in scheme 3. Initially, an enamine **A** was generated from acetophenone **1a** and morpholine **2a.** This enamine interacted with the superoxide radical ($O_2^{\cdot-}$) and Cu (II) which was formed through the aerial oxidation of CuI in the presence of morpholine, to produce aminodioxetane **B**. Then, **B** underwent ring opening and gave the phenylglyoxal. The formation of phenylglyoxal was detected in TLC study of the reaction mixture during the reaction process. This *in situ* generated phenyl glyoxal reacted with morpholine to form the intermediate 2-oxo iminium ion **C**. It was followed by the reaction with aniline **3a** that produced the intermediate **D** and then **E** which on interaction with air formed the intermediate **F.** Finally, this intermediate **F** underwent intramolecular rearrangement and afforded the required product **4a** by losing one molecule of hydrogen peroxide (path a). On the other hand the addition of morpholine reacted with phenylglyoxal also to form hemiaminal intermediate **G** (path b) which on oxidation by air and copper iodide resulted the formation of side product **5a**. From the effect of temperature in the reaction process it could be concluded that higher temperature favored the path b and hence the formation of compound **5**. On the other hand, room temperature (25 ^{o}C) is sufficient for the formation of arylglyoxal and to produce the desired product **4** through path a. In case of aliphatic primary amines the localized lone pair of electrons of the secondary amine of the intermediate type **E** might have disfavored the oxidation step, and hence the product **4** was not formed. We also studied the reaction using arylglyoxal in place of acetophenone in a similar reaction condition and observed the formation of the products **4** and **5** as expected which further supported the proposed mechanism.

3. Conclusion

In conclusion, we have developed a new synthetic method for the preparation of 2-oxo-acetamidines from one-pot three-component reactions of acetophenones, secondary amines and anilines in the presence of CuI as catalyst and air as oxidizing agent. The reaction occurred *via* oxidation of C(sp^3)-H bonds of aryl methyl ketones followed by double amination process. The reaction protocol involved a simple and cheap catalyst, readily available starting materials and mild reaction conditions that gave a new and highly attractive approach towards acetamidines. The small amount of α-amino ketones which were formed during the reaction process is also an important class of compounds.

4. Experimental

General information: All chemicals were purchased from Merck and Aldrich chemical companies. The reagents and solvents were used without drying. The IR spectra were recorded on Perkin Elmer system 2000 FTIR spectrometer. ^{1}H NMR and ^{13}C NMR Spectra were recorded on Bruker AV500 Avance–III 500 MHz and 125 MHz FT NMR in $CDCl_3$ using TMS as an internal standard. NMR chemical shifts were measured relative to the signals of residual $CDCl_3$ at δ_H 7.26 ppm, δ_C 76.65-77.16 ppm and δ_H 1.5 ppm (water contamination). Mass spectra were recorded in Waters Xevo G2-XS QT of mass spectrometer. Analytical thin layer chromatography (TLC) was performed using E-Merck aluminium-backed silica gel plates coated with 0.2 mm thickness of silica gel. Melting points (uncorrected) were determined in open capillary tubes on a Buchi B-540 apparatus.

General procedure for the synthesis of 4 and 5: Aryl methyl ketone **1** (Methyl phenyl ketone, 0.120 g, 1 mmol), secondary amine **2** (Morpholine, 0.131g 1.5 mmol), aryl amine **3** (Aniline, 0.093 g, 1 mmol) and CuI (10 mol %) were taken in a 25 mL round bottomed flask. To this added 2 mL of toluene and the reaction mixture was stirred at 25 ^{o}C until the completion of the reaction (as confirmed by TLC). Then, the reaction mixture was concentrated under reduced pressure to give a crude product which was purified by column chromatography (silica gel 100-200#, hexane/ EtOAc, 9:1) to yield the compounds **4a** and **5a**. Similarly, compounds **4a-w** and **5a-w** were synthesized by using various substituted acetophenones **1**, secondary amine **2** and anilines **3** and characterized.

4a. (Z)-2-morpholino-1-phenyl-2-(phenylimino)ethanone: Yield: 220 mg, 75%; Yellow solid, m.p. 131.9-133.8 °C; R_f = 0.21 (EtOAc/Hexane = 2:8); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 (dt, *J* = 8.4, 1.5 Hz, 2H), 7.56 – 7.51 (m, 1H), 7.43 – 7.37 (m, 2H), 7.04 – 6.98 (m,2H), 6.78 (tt, *J* = 7.6, 1.2 Hz, 1H), 6.73 – 6.68 (m, 2H), 3.76 (s, 4H), 3.53 (s, 4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.98, 156.00, 148.02, 134.51, 134.33, 129.11, 128.80, 128.30, 122.44, 122.11, 66.48; **IR** (cm^{-1}): 3586, 2920, 2854, 1775, 1606, 1597, 1497, 503; **HRMS** $(M+H)^+$ calcd for $C_{18}H_{18}N_2O_2$= 295.1447, found = 295.1448.

4b. (Z)-2-((2-chlorophenyl)imino)-2-morpholino-1-phenylethanone: Yield: 252 mg, 77%; Yellow solid, m.p. 121.6-122.6 °C; R_f = 0.41 (EtOAc/Hexane = 2:8); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 – 7.83 (m, 2H), 7.55

(ddd, *J* = 8.7, 2.5, 1.3 Hz, 1H), 7.45 – 7.38 (m, 2H), 7.11 (dd, *J* = 7.9, 1.4 Hz, 1H), 6.92 (td, *J* = 7.7, 1.4 Hz, 1H), 6.76 – 6.65 (m, 2H), 3.78 (s, 8H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.12, 155.93, 144.87, 134.76, 133.75, 129.18, 129.01, 128.79, 126.96, 126.66, 123.39, 123.31, 66.51; **IR** (cm^{-1}): 3414, 2922, 2851, 2100, 1679, 1600, 769; **HRMS** $(M+H)^+$ calcd for $C_{18}H_{17}ClN_2O_2$= 329.1057, found = 329.1055.

4c. (**Z)-2-((2-iodophenyl)imino)-2-morpholino-1-phenylethanone:** Yield: 310 mg, 74%; Yellow solid; m.p. 106.8-108.9 °C; R_f = 0.54 (EtOAc/Hexane = 2:8); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 – 7.85 (m, 2H), 7.60 – 7.52 (m, 2H), 7.43 – 7.39 (m, 2H), 7.02 – 6.98 (m, 1H), 6.67 (dd, *J* = 7.9, 1.5 Hz, 1H), 6.52 – 6.47 (m, 1H), 3.80 (s, 8H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.21, 155.33, 148.28, 138.32, 134.79, 133.77, 129.13, 128.82, 128.39, 123.93, 121.48, 95.29, 66.64; **IR** (cm^{-1}): 3412, 2920, 2853, 2101, 1678, 1609, 505; **HRMS** $(M+H)^+$ calcd for $C_{18}H_{17}N_2O_2I$= 421.0413, found = 421.0416.

4d. (Z)-2-((4-fluorophenyl)imino)-2-morpholino-1-phenylethanone: Yield: 236.5 mg, 76%; Yellow solid, m.p. 136-137 °C ; R_f = 0.18 (EtOAc/Hexane = 2:8); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 – 7.77 (m, 2H), 7.56 (dd, *J* = 10.6, 4.3 Hz, 1H), 7.42 (t, *J* = 7.8 Hz, 2H), 6.78 – 6.62 (m, 4H), 3.77 (s, 4H), 3.54 (s, 4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.98, 157.69, 156.52, 144.11, 134.71, 134.16, 129.07, 128.92, 123.24, 123.17, 115.03, 114.85, 66.46; **IR** (cm^{-1}): 3419, 2922, 2850, 1680, 1610, 1451, 1219, 510; **HRMS** $(M+H)^+$ calcd for $C_{18}H_{17}N_2O_2F$= 313.1352, found = 313.1356

4e. (Z)-2-morpholino-2-((3-nitrophenyl)imino)-1-phenylethanone: Yield: 264.1mg, 78%; Yellow solid; m.p. 113.4-114.8°C; R_f = 0.42 (EtOAc/Hexane = 2:8); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 (dd, *J* = 8.4, 1.2 Hz, 2H), 7.64 (ddd, *J* = 8.1, 2.2, 0.9 Hz, 1H), 7.60 – 7.53 (m, 2H), 7.44 (t, *J* = 7.8 Hz, 2H), 7.17 (t, *J* = 8.1 Hz, 1H), 7.01 (ddd, *J* = 7.9, 2.1, 1.0 Hz, 1H), 3.81 (s, 4H), 3.32 (s, 4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 192.69, 156.59, 149.66, 148.12, 135.14, 133.87, 129.17, 129.04, 128.96, 128.38, 117.17, 66.42; **IR** (cm^{-1}): 3425, 2354, 2100, 1678, 1455, 1116, 769, 521; **HRMS** $(M+H)^+$ calcd for $C_{18}H_{17}N_3O_4$= 340.1297, found = 340.1299.

4f. (Z)-2-((3-methoxyphenyl)imino)-2-morpholino-1-phenylethanone: Yield: 232 mg, 72%; Yellow solid; m.p. 87-88°C; R_f = 0.61 (EtOAc/Hexane = 2:8); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 (dd, *J* = 8.3, 1.2 Hz, 2H), 7.56 – 7.52 (m, 1H), 7.41 (t, *J* = 7.8 Hz, 2H), 6.68 – 6.62 (m, 2H), 6.60 – 6.55 (m, 2H), 3.76 (s, 4H), 3.64 (s, 3H), 3.49 (s, 4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.68, 156.35, 155.07, 141.14, 134.26, 133.77, 129.10, 128.83, 122.94, 113.64, 66.48, 55.12; **IR** (cm^{-1}): 3415, 2924, 2085, 1689, 1643, 1179, 763; **HRMS** $(M+H)^+$ calcd for $C_{19}H_{20}N_2O_3$= 325.1552, found = 325.1554.

4g. (Z)-2-morpholino-1-phenyl-2-(p-tolylimino)-ethanone: Yield: 224.2 mg, 73%; Yellow solid; m.p. 124-126 °C °C; R_f = 0.55 (EtOAc/Hexane= 2:8); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 – 7.80 (m, 2H), 7.54 (t, *J* = 7.3 Hz, 1H), 7.41 (t, *J* = 7.8 Hz, 2H), 6.81 (d, *J* = 8.3 Hz, 2H), 6.60 (d, *J* = 8.2 Hz, 2H), 3.75 (s, 4H), 3.52 (s, 4H), 2.12 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.29, 156.03, 145.23, 134.49, 134.33, 131.73, 129.14, 128.95, 128.81, 121.88, 66.48, 20.56; **IR** (cm^{-1}): 3429, 2966, 2854, 2098, 1682, 1450, 1211, 1177; **HRMS** $(M+H)^+$ calcd for $C_{19}H_{20}N_2O_2$= 309.1603, found = 309.1606

4h. (Z)-1-(4-bromophenyl)-2-morpholino-2-(phenylimino)ethanone: Yield: 304.3 mg, 82%; yellow solid, m.p. 139.2-141.4 °C.; R_f = 0.36 (EtOAc/Hexane= 2:8), ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 – 7.63 (m, 2H), 7.59 – 7.50 (m, 2H), 7.08 – 6.99 (m, 2H), 6.81 (dd, *J* = 10.6, 4.2 Hz, 1H), 6.68 (dd, *J* = 8.4, 1.1 Hz, 2H), 3.76 (s, 4H), 3.52 (s, 4H).^{13}C NMR (126 MHz, $CDCl_3$) δ 193.08, 155.50, 147.76, 133.00, 132.26, 130.44, 130.08, 128.44, 122.65, 122.02, 66.45; **IR** (cm^{-1}): 3340, 2949, 2922, 1679, 1609, 1266, 1116, 751; **HRMS** $(M+H)^+$ calcd for $C_{18}H_{17}BrN_2O_2$= 373.0552, found = 373.0554

4i. (Z)-1-(4-bromophenyl)-2-morpholino-2-(p-tolylimino)ethanone: Yield: 307.8 mg, 80%; Yellow solid, m.p. 130.2-131.9 °C; R_f = 0.32 (EtOAc/Hexane= 2:8); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 – 7.64 (m, 2H), 7.57 – 7.52 (m, 2H), 6.83 (d, *J* = 8.0 Hz, 2H), 6.61 – 6.56 (m, 2H), 3.75 (s, 4H), 3.49 (s, 4H), 2.14 (s, *J* = 6.6 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.43, 155.52, 145.04, 133.01, 132.26, 131.95, 130.48, 130.02, 129.08, 121.79, 66.45, 20.58; **IR** (cm^{-1}): 3398, 2950, 2854, 1680, 1609, 1213, 1116, 505; **HRMS** $(M+H)^+$ calcd for $C_{19}H_{19}N_2O_2Br$= 387.0708, found = 387.0706

4j. (Z)-1-(4-chlorophenyl)-2-morpholino-2-(phenylimino)ethanone: Yield: 262.5 mg, 80%; Yellow solid, m.p. 145-146.3 °C; R_f = 0.24 (EtOAc/Hexane= 2:8); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 – 7.71 (m, 2H), 7.40 – 7.34 (m, 2H), 7.06 – 7.00 (m, 2H), 6.84 – 6.77 (m, 1H), 6.73 – 6.66 (m, 2H), 3.76 (s, 4H), 3.52 (s,4H);^{13}C NMR (126 MHz, $CDCl_3$) δ 192.84, 155.56, 147.79, 141.14, 132.62, 130.42, 129.27, 128.43, 122.63, 122.02, 66.45; **IR** (cm^{-1}): 3412, 2923, 2855, 2108, 1663, 1598, 984; **HRMS** $(M+H)^+$ calcd for $C_{18}H_{17}N_2O_2Cl$= 329.1057, found = 329.1055

4k. (Z)-2-morpholino-2-(phenylimino)-1-(p-tolyl)ethanone: Yield: 227.2 mg, 74%; yellow solid, m.p. 114.6-116.8 °C.; R_f = 0.35(EtOAc/Hexane= 2:8), ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 – 7.67 (m, 2H), 7.23 – 7.16 (m, 2H), 7.05 – 6.98 (m, 2H), 6.78 (tt, *J* = 7.6, 1.1 Hz, 1H), 6.74 – 6.68 (m, 2H), 3.76 (s, 4H), 3.53 (s, 4H), 2.36 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.47, 156.15, 148.16, 145.79, 131.97, 129.57, 129.29, 128.29, 122.36, 122.11,66.49, 21.74; **IR** (cm^{-1}): 3006, 2944, 2883, 1773, 1663, 1598, 1226, 755; **HRMS** (M+H) $^+$ calcd for $C_{19}H_{20}N_2O_2$= 309.1603, found = 309.1605

4l. (Z)-1-(4-methoxyphenyl)-2-morpholino-2-(phenylimino)ethanone: Yield: 236 mg, 73%; Yellow solid; m.p. 109.4-111.7 °C; R_f = 0.38 (EtOAc/Hexane= 2:8); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 (dd, *J* = 8.3, 1.2 Hz,2H), 7.56 – 7.52 (m, 1H), 7.41 (t, *J* = 7.8 Hz, 2H), 6.67 – 6.62 (m, 2H), 6.59 – 6.55 (m, 2H), 3.76 (s, 4H), 3.64 (s, 3H), 3.49 (s, 4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 192.13, 164.57, 156.28, 148.28, 131.69, 128.30, 127.52, 122.34, 122.07, 114.11, 66.51, 55.45; **IR** (cm^{-1}): 3412, 2921, 2087, 1776, 1648, 1188, 765; **HRMS** (M+H) $^+$ calcd for $C_{19}H_{20}N_2O_3$= 325.1552, found = 325.1556.

4m. (Z)-1-(4-methoxyphenyl)-2-morpholino-2-(p-tolylimino)ethanone: Yield: 236 mg, 70%; Yellow solid; m.p.108.9-109.6°C; R_f = 0.39(EtOAc/Hexane= 2:8); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 – 7.77 (m, 2H), 6.91 – 6.80 (m, 4H), 6.62 (d, *J* = 7.2 Hz, 2H), 3.84 (s, 3H), 3.75 (s, 4H), 3.52 (s, 4H), 2.13 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 192.49, 164.53, 156.29, 145.57, 131.69, 131.55, 128.95, 127.58, 121.81, 114.10, 66.51, 55.45, 20.5; **IR** (cm^{-1}): 3411, 2921, 2086, 1775, 1649, 1191, 503; **HRMS** (M+H) $^+$ calcd for $C_{20}H_{22}N_2O_3$= 339.1709, found = 339.1708

4n. (Z)-2-morpholino-1-(4-nitrophenyl)-2-(phenylimino)ethanone: Yield: 274 mg, 81%; Yellow solid; m.p.138.0-139.0.6°C; R_f = 0.15 (EtOAc/Hexane= 2:8); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.25 – 8.19 (m, 2H), 7.96 – 7.89 (m, 2H), 7.05 – 6.97 (m, 2H), 6.83 – 6.76 (m, 1H), 6.70 – 6.63 (m, 2H), 3.78 (s,4H), 3.53 (s, 4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 192.91, 154.99, 150.73, 147.31, 138.33, 129.94, 128.57, 124.02, 122.95, 122.02, 66.42. **IR** (cm^{-1}): 3420, 2354, 2098, 1643, 1515, 1455, 1116, 770; **HRMS** (M+H)$^+$ calcd for $C_{18}H_{17}N_3O_4$= 340.1297, found = 340.1295

4o. (Z)-1-(4-fluorophenyl)-2-morpholino-2-(phenylimino)ethanone: Yield: 246.1 mg, 79 %; Yellow solid; m.p.133.8-136.2°C; R_f = 0.21(EtOAc/ Hexane= 2:8); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 (dd, *J* = 8.6, 5.4 Hz, 2H), 7.04 (dt, *J* = 15.6, 8.1 Hz, 4H), 6.79 (t, *J* = 7.3 Hz, 1H), 6.69 (d, *J* = 7.6 Hz, 2H), 3.77 (s, 4H), 3.53 (s, 4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 192.32, 167.39, 165.34, 155.72, 147.90, 131.97, 131.89, 130.85, 128.39, 122.57, 122.02, 116.27, 116.09, 66.47; **IR** (cm^{-1}): 3361, 2921, 2853, 1675, 1598, 983, 615; **HRMS** (M+H) $^+$ calcd for $C_{18}H_{17}N_2O_2F$= 313.1352, found = 313.1353

4p. (Z)-1-(4-fluorophenyl)-2-morpholino-2-(p-tolylimino)ethanone: Yield: 247 mg, 76%; Yellow solid; m.p.1112.5-113.8°C; R_f = 0.24 (EtOAc/Hexane= 2:8); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (ddd, *J* = 8.2, 5.1, 2.5 Hz, 2H), 7.10 – 7.04 (m, 2H), 6.82 (d, *J* = 8.0 Hz, 2H), 6.61 – 6.57 (m, 2H), 3.76 (s, 4H), 3.51 (s, 4H), 2.13 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 192.69, 167.38, 165.33, 155.74, 145.18, 131.99, 131.91, 131.86, 130.86, 130.84, 129.03, 121.78, 116.27, 116.09, 66.47, 20.57; **IR** (cm^{-1}): 3427, 2933, 2851, 2099, 1681, 1448, 1215, 965; **HRMS** (M+H) $^+$ calcd for $C_{19}H_{19}N_2O_2F$= 327.1509, found = 327.1505

4q. (Z)-1-phenyl-2-(phenylimino)-2-(pyrrolidin-1-yl)ethanone: Yield: 191.2 mg, 69%; Yellow solid; m.p. 179.1-180.2°C; R_f = 0.27(EtOAc/Hexane= 2:8); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 (d, *J* = 7.6 Hz, 2H), 7.51 (t, *J* = 7.4 Hz, 1H), 7.38 (t, *J* = 7.7 Hz, 2H), 7.00 (t, *J* = 7.7 Hz, 2H), 6.81 – 6.70 (m, 3H), 3.70 (s, 2H), 3.32 (s, 2H), 1.96 (d, *J* = 23.7 Hz, 4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.44, 154.61,148.81, 134.23, 133.86, 129.29, 128.71, 128.20, 122.72, 122.04, 46.78; **IR** (cm^{-1}): 3422, 2923, 2354, 2100, 1645, 1515, 754, 662; **HRMS** (M+H) $^+$ calcd for $C_{18}H_{18}N_2O$= 279.1497, found = 279.1494

4r. (Z)-1-phenyl-2-(phenylimino)-2-(piperidin-1-yl)ethanone: Yield: 213 mg, 73%; Yellow solid; m.p. 129.6-132.0°C; R_f = 0.35(EtOAc/Hexane= 2:8); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (dd, *J* = 8.3, 1.1 Hz, 2H), 7.57 – 7.51 (m, 1H), 7.42 (t, *J* = 7.6 Hz, 2H), 7.01 (dd, *J* = 11.7, 4.1 Hz, 2H), 6.77 (td, *J* = 7.4, 1.0 Hz, 1H), 6.74 – 6.68 (m, 2H), 3.49 (s, 4H), 1.71 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.42, 155.95, 148.54, 134.59, 134.24, 129.11, 128.68, 128.19, 122.42, 121.99, 24.53; **IR** (cm^{-1}): 3424, 2933, 2852, 2098, 1671, 1599, 1276, 973; **HRMS** (M+H) $^+$ calcd for $C_{19}H_{20}N_2O$= 293.1654, found = 293.1656

4s. (Z)-N,N-diethyl-2-oxo-N',2-diphenylacetimidamide: Yield: 181.8 mg, 65%; Yellow solid; m.p. 88.0-89.8°C; R_f = 0.63(EtOAc/Hexane= 2:8); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 (d, *J* = 7.1 Hz, 2H), 7.54 – 7.48 (m, 1H), 7.38 (t, *J* = 7.8 Hz, 2H), 7.00 – 6.95 (m, 2H), 6.71

(ddd, *J* = 11.5, 9.5, 4.2 Hz, 3H), 3.64 (d, *J* = 85.9 Hz, 2H), 3.15 (s, 2H), 1.36 (s, 3H), 1.11 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.98, 155.33, 148.78, 134.55, 134.11, 129.16, 128.60, 128.46, 128.11, 122.56, 121.78, 77.16, 76.90, 76.65, 29.59; **IR** (cm^{-1}): 3431, 2094, 1648, 1632, 1224, 766; **HRMS** $(M+H)^+$ calcd for $C_{18}H_{20}N_2O$= 281.1654, found = 281.1652

4t. (Z)-2-(3,4-dihydroisoquinolin-2(1H)-yl)-1-phenyl-2-(phenylimino)ethanone: Yield: 227 mg, 67%; Yellow solid; m.p. 130.0-131.6°C; R_f = 0.45(EtOAc/ Hexane= 2:8); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (d, *J* = 6.9 Hz, 2H), 7.53 (t, *J* = 7.2 Hz, 1H), 7.38 (t, *J* = 7.4 Hz, 2H), 7.24 – 7.12 (m, 4H), 7.01 (t, *J* = 7.7 Hz, 2H), 6.81 – 6.70 (m, 3H), 4.88 (s, 2H), 3.55 (s, 2H), 2.92 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.04, 155.83, 148.30, 134.45, 132.82, 129.18, 128.79, 128.63, 128.27, 126.40, 122.37, 122.28; **IR** (cm^{-1}): 3583, 3411, 2920, 2851, 1647, 1019, 503; **HRMS** $(M+H)^+$ calcd for $C_{23}H_{20}N_2O$= 341.1654, found = 341.1656

4u. (Z)-1-(2-hydroxyphenyl)-2-morpholino-2-(phenylimino)ethanone: Yield: 226 mg, 73%; Yellow solid, m.p. 127.4-128.4°C; R_f = 0.60(EtOAc/Hexane= 2:8); ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.30 (s, 1H), 7.61 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.46 – 7.42 (m, 1H), 7.05 (t, *J* = 7.9 Hz, 2H), 6.92 – 6.81 (m, 3H), 6.72 (d, *J* = 7.4 Hz, 2H), 3.78 (s, 4H), 3.55 (s, 4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 198.87, 162.36, 153.96, 147.74, 137.79, 132.04, 128.43, 122.72, 121.86, 119.59, 118.26, 118.10, 66.43; **IR** (cm^{-1}): 3416, 2917, 2856, 1678, 1597, 1450, 1220, 941; **HRMS** $(M+H)^+$ calcd for $C_{18}H_{18}N_2O_3$= 311.1396, found = 311.1391.

4v. (Z)-4-(2-morpholino-2-(phenylimino)acetyl)-benzonitrile: Yield: 236 mg, 74%; Yellow solid; m.p. 103.5-109.5°C; R_f = 0.42(EtOAc/Hexane= 2:8); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 – 7.83 (m, 2H), 7.70 – 7.66 (m, 2H), 7.01 (td, *J* = 7.5, 1.9 Hz, 2H), 6.82 – 6.77 (m, 1H), 6.65 (dd, *J* = 8.4, 1.1 Hz, 2H), 3.77 (s, 4H), 3.51 (s, 4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.08, 155.01, 147.36, 136.97, 132.61, 129.23, 128.54, 122.90, 122.01, 117.45, 117.42, 66.42; **IR** (cm^{-1}): 3058, 2968, 2919, 2855, 2231, 1683, 1607, 1590, 1438,1267, 983; .**HRMS** $(M+H)^+$ calcd for $C_{19}H_{17}N_3O_2$= 320.1399, found = 320.1397

4w. (Z)-1-(4-cyclohexylphenyl)-2-morpholino-2-(phenylimino)ethanone: Yield: 263 mg, 70%; Yellow solid; m.p. 133.2-136.1°C; R_f = 0.54(EtOAc/Hexane= 2:8); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66 (d, *J* = 7.1 Hz, 2H), 7.15 (d, *J* = 7.4 Hz, 2H), 6.95 (t, *J* = 7.2 Hz, 2H), 6.71 (t, *J* = 6.9 Hz, 1H), 6.64 (d, *J* = 8.1 Hz, 2H), 3.69 (s, 4H), 3.46 (s, 4H), 2.44 (s,1H), 1.77 (s, 4H), 1.68 (d, *J* = 12.5 Hz, 1H), 1.30 (t, *J* = 9.9 Hz, 4H), 1.22 – 1.14 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.49, 156.19, 155.47, 148.16, 132.21, 129.38, 128.28, 127.35, 122.33, 122.13, 66.50, 44.66, 33.77, 26.50, 25.84; **IR** (cm^{-1}): 3484, 2918, 2852, 1650, 1623, 1596, 1470; **HRMS** $(M+H)^+$ calcd for $C_{24}H_{28}N_2O_2$= 377.2229, found = 377.2226

5a. 1-morpholino-2-phenylethane-1,2-dione: Yield: 26 mg, 12%; Yellow oil; R_f = 0.24 (EtOAc/Hexane= 2:8); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 (dt, *J* = 8.5, 1.4 Hz, 1H), 7.67 (tdd, *J* = 7.1, 4.2, 2.9 Hz, 1H), 7.56 – 7.51 (m, 1H), 7.27 (s, 1H), 3.85 – 3.77 (m, 2H), 3.70 – 3.63 (m, 1H), 3.42 – 3.36 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 191.06, 165.35, 134.87, 132.91, 129.69, 129.57, 129.01, 66.63, 66.56, 46.15, 41.51; **IR** (cm^{-1}): 3336, 2971, 2920, 2855, 1681, 1644, 11595, 1114; **HRMS** $(M+H)^+$ calcd for $C_{12}H_{13}NO_3$= 220.0974, found = 220.0972.

5h. 1-(4-bromophenyl)-2-morpholinoethane-1,2-dione: Yield: 32 mg, 11 %; Light Yellow solid; m.p. 126.0-126.5 °C; R_f = 0.12 (EtOAc/Hexane= 2:8); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 – 7.81 (m, 2H), 7.70 – 7.66 (m, 2H), 3.83 – 3.77 (m, 4H), 3.68 – 3.65 (m, 2H), 3.39 (dd, *J* = 6.1, 3.5 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 189.82, 164.76, 132.41, 131.79, 131.56, 130.97, 130.45, 66.64, 66.55, 46.18, 41.60; **IR** (cm^{-1}): 2970, 2921, 2856, 1680, 1644, 1596, 1114, 665; **HRMS** $(M+H)^+$ calcd for $C_{12}H_{12}$ Br NO_3= 298.0079, found = 298.0078.

5j. 1-(4-chlorophenyl)-2-morpholinoethane-1,2-dione : Yield: 25.4 mg, 10 %; Yellow solid; m.p. 115.6.0-116.4 °C; R_f = 0.30 (EtOAc/Hexane= 2:8); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 – 7.90 (m, 2H), 7.52 – 7.49 (m, 2H), 3.82 – 3.77 (m, 4H), 3.68 – 3.65 (m, 2H), 3.40 – 3.37 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 189.60, 164.80, 141.54, 131.33, 130.94, 129.41, 66.64, 66.54, 46.18, 41.60; **IR** (cm^{-1}): 2918, 2850, 1674, 1628, 1587, 1466, 1216, 765; **HRMS** $(M+H)^+$ calcd for $C_{12}H_{12}$ Cl NO_3= 254.0584, found = 254.0587.

5k. 1-morpholino-2-(p-tolyl)ethane-1,2-dione: Yield: 30.3 mg, 13 %; Colorless solid; m.p. 80.5-81.2°C; R_f = 0.27 (EtOAc/Hexane= 2:8); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.2 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 3.80 (d, *J* = 1.6 Hz, 4H), 3.67 – 3.63 (m, 2H), 3.37 (dd, *J* = 6.1, 3.6 Hz, 2H), 2.45 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 190.82, 165.57, 146.25, 130.48, 130.06, 129.74, 129.69, 129.07, 66.64, 66.57, 46.15, 41.45, 21.84; **IR** (cm^{-1}): 3332, 2968, 2922, 2857, 1715, 1676,

1650, 1444, 757; **HRMS** (M+H) $^{+}$ calcd for $C_{13}H_{15}NO_3$= 234.1130, found = 234.1137.

5l. 1-(4-methoxyphenyl)-2-morpholinoethane-1,2-dione: Yield: 23.2 mg, 10 %; Yellow solid; m.p. 112.9-113.4°C; R_f = 0.24 (EtOAc/Hexane= 2:8);^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 (dd, *J* = 9.3, 2.4 Hz ,2H), 7.27 (s, 1H), 6.99 (d, *J* = 8.9 Hz, 2H), 3.90 (s, 3H), 3.80 (t, *J* = 4.6 Hz, 4H), 3.68 – 3.63 (m, 2H), 3.41 – 3.37 (m, 2H).^{13}C NMR (126 MHz, $CDCl_3$) δ 189.73, 165.70, 164.92, 132.07, 125.99, 114.32, 66.68, 66.59, 55.59, 46.19, 41.44; **IR** (cm^{-1}): 2970, 2919, 2855, 1638, 1599, 1507, 1443, 1264, 980; **HRMS** (M+H) $^{+}$ calcd for $C_{13}H_{15}NO_3$= 234.1130, found = 234.1137.

5n. 1-morpholino-2-(4-nitrophenyl)ethane-1,2-dione: Yield: 26.5 mg, 10 %; Yellow solid; m.p. 140.0-141.5°C; R_f = 0.18 (EtOAc/Hexane= 2:8); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.38 – 8.35 (m, 2H), 8.19 – 8.15 (m, 2H), 7.27 (s, 1H), 3.82 (s, 4H), 3.72 – 3.68 (m, 2H), 3.45 – 3.42 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 188.56, 163.90, 151.06, 137.33, 130.74, 124.07, 66.63, 66.52, 46.24, 41.83; **IR** (cm^{-1}): 2918, 2850, 1687, 1643, 1524, 1347, 1208, 981; **HRMS** (M+H) $^{+}$ calcd for $C_{12}H_{12}N_2O_5$= 265.0824, found = 265.0823.

5o. 1-(4-fluorophenyl)-2-morpholinoethane-1,2-dione : Yield: 24 mg, 10 %; Light yellow solid; m.p. 86.2-86.6°C; R_f = 0.21 (EtOAc/Hexane= 2:8); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (d, *J* = 5.2 Hz, 2H), 7.20 (d, *J* = 3.1 Hz, 2H), 3.80 (s, 4H), 3.73 – 3.60 (m, 2H), 3.54 – 3.31 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 189.39, 167.83, 165.78, 165.09, 132.60, 132.52, 129.63, 116.55, 116.38, 77.29, 77.04, 76.78, 66.75, 66.66, 46.31, 41.70; **IR** (cm^{-1}): 2958, 2923, 2852, 1682, 1638, 1597, 1506, 1442, 981; **HRMS** (M+H) $^{+}$ calcd for $C_{12}H_{12}NO_3F$= 238.0879, found = 238.0876.

5q. 1-phenyl-2-(pyrrolidin-1-yl)ethane-1,2-dione: Yield: 20 mg, 10 %; Oily ; R_f = 0.18 (EtOAc/Hexane= 2:8); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 (d, *J* = 7.3 Hz, 2H), 7.64 (t, *J* = 7.4 Hz, 1H), 7.51 (t, *J* = 7.8 Hz, 2H), 7.29 (s, 1H), 3.67 (dd, *J* = 14.5, 7.7 Hz, 2H), 3.42 (t, *J* = 6.4 Hz, 2H), 1.95 (dq, *J* = 9.4, 7.0 Hz, 4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 191.51, 164.85, 134.56, 132.72, 129.77, 128.84, 46.57, 45.14, 25.78, 23.90; **IR** (cm^{-1}): 3361, 2921, 2854, 1757, 1661, 1598, 1515, 754; **HRMS** (M+H)$^{+}$ calcd for $C_{12}H_{13}NO_2$= 204.1025, found = 204.1029.

5r. 1-phenyl-2-(piperidin-1-yl)ethane-1,2-dione: Yield: 26.2 mg, 12 %; Yellow solid; m.p. 104.1-104.8°C; R_f = 0..29 (EtOAc/Hexane= 2:8); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (d, *J* = 7.1 Hz, 2H), 7.67 – 7.59 (m, 1H), 7.51 (dd, *J* = 10.7, 4.8 Hz, 2H), 7.28 (s, 1H), 3.71 (s, *J* = 5.0 Hz, 2H), 3.29 (dd, *J* = 6.3, 4.8 Hz, 2H), 1.70 (dd, *J* = 5.7, 2.7 Hz, 4H), 1.54 (d, *J* = 4.6 Hz, 2H).^{13}C NMR (126 MHz, $CDCl_3$) δ 191.89, 165.33, 134.60, 133.07, 129.45, 128.91, 46.92, 42.02, 26.07, 25.32, 24.24; **IR** (cm^{-1}): 2964, 2881, 1683, 1627, 1552; **HRMS** (M+H) $^{+}$ calcd for $C_{13}H_{15}NO_2$= 218.1181, found = 218.1185.

5s. *N,N*-diethyl-2-oxo-2-phenylacetamide: Yield: 21 mg, 10 %; Gummy ; R_f = 0.33 (EtOAc/Hexane= 2:8); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 – 7.93 (m, 2H), 7.66 – 7.62 (m, 1H), 7.51 (dd, *J* = 10.7, 4.8 Hz, 2H), 7.27 (s, 1H), 3.57 (q, *J* = 7.2 Hz, 2H), 3.25 (q, *J* = 7.1 Hz, 2H), 1.29 (t, *J* = 7.2 Hz, 3H), 1.16 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 191.52, 166.63, 134.51, 133.09, 129.53, 128.87, 42.00, 38.67, 14.00, 12.74; **IR** (cm^{-1}): 3363, 2919, 2851, 1687, 1647, 1595, 1450; **HRMS** (M+H) $^{+}$ calcd for $C_{12}H_{15}NO_2$= 206.1181, found = 206.1180.

5t. 1-(3,4-dihydroisoquinolin-2(1H)-yl)-2-phenyl-ethane-1,2-dione: Yield: 26.4 mg, 10 %; Colorless solid; m.p. 105.8-107.2°C; R_f = 0.30 (EtOAc/Hexane= 2:8); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 (ddd, *J* = 16.4, 8.3, 1.1 Hz, 2H), 7.69 – 7.61 (m, 1H), 7.51 (dt, *J* = 15.8, 7.8 Hz, 2H), 7.18 (ddd, *J* = 25.0, 15.2, 7.1 Hz, 4H), 4.73 (d, *J* = 187.2 Hz, 2H), 4.04 – 3.50 (m, 2H), 3.06 – 2.70 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 191.45, 191.30, 165.99, 165.68, 134.79, 134.75, 134.08, 133.31, 132.98, 132.91, 131.71, 131.43, 129.65, 129.64, 128.99, 128.96, 128.90, 128.73, 127.13, 126.79, 126.75, 126.60, 126.53, 126.00, 47.24, 43.43, 43.34, 39.26, 29.13, 28.17; **IR** (cm^{-1}): 3027, 2943, 2881, 2166, 1643, 1597, 1474, 1226, 720; **HRMS** (M+H)$^{+}$calcd for $C_{17}H_{15}NO_2$= 266.1181, found = 266.1182.

5u. 1-(2-hydroxyphenyl)-2-morpholinoethane-1,2-dione: Yield: 28 mg, 12 %; Colorless solid; m.p. 108.2-109.4°C; R_f = 0.30 (EtOAc/Hexane= 2:8); ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.26 (s, 1H), 7.60 – 7.54 (m, 2H), 7.06 – 7.02 (m, 1H), 6.97 (td, *J* = 7.7, 1.0 Hz, 1H), 3.83 – 3.77 (m, 4H), 3.70 – 3.66 (m, 2H), 3.43 – 3.39 (m, 2H);^{13}C NMR (126 MHz, $CDCl_3$) δ 195.92, 163.42, 163.24, 138.08, 131.88, 119.81, 118.59, 116.66, 66.58, 66.50, 46.27, 41.54; **IR** (cm^{-1}): 3417, 2941, 2122, 1717, 1638, 1598, 1470, 1191; **HRMS** (M+H)$^{+}$ calcd for $C_{12}H_{13}NO_4$= 236.0923, found = 236.0924.

5v. 4-(2-morpholino-2-oxoacetyl)benzonitrile: Yield: 31.4 mg, 13 %; Colorless solid; m.p. 118.2-119.9°C; R_f = 0.21 (EtOAc/Hexane= 2:8); 34B =^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10 – 8.07 (m, 2H), 7.84 – 7.82 (m,

2H), 3.84 – 3.78 (m, 4H), 3.70 – 3.67 (m, 2H), 3.43 – 3.40 (m, 2H).^{13}C NMR (126 MHz, $CDCl_3$) δ 188.90, 163.99, 135.91, 132.70, 129.98, 117.81, 117.46, 66.63, 66.51, 46.21, 41.78; **IR** (cm^{-1}): 3317, 2924, 2853, 1724, 1650, 1598, 1467, 1227; **HRMS** $(M+H)^+$ calcd for $C_{13}H_{12}N_2O_3$= 245.0926 found = 245.0927.

5w. 1-(4-cyclohexylphenyl)-2-morpholinoethane-1,2-dione: Yield: 33 mg, 11 %; Yellow oily; R_f = 0.27 (EtOAc/Hexane= 2:8); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 (d, *J* = 8.1 Hz, 2H), 7.35 (d, *J* = 8.3 Hz, 2H), 3.80 (s, 4H), 3.67 – 3.64 (m, 2H), 3.40 – 3.36 (m, 2H), 2.68 – 2.50 (m, 1H), 1.87 (d, *J* = 7.0 Hz, 4H), 1.77 (d, *J* = 12.3 Hz, 1H), 1.66 (s, 1H), 1.48 – 1.35 (m, 4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 190.82, 165.62, 155.98, 130.77, 129.83, 127.57, 66.68, 66.58, 46.16, 44.81, 41.46, 33.85, 26.51, 25.83; **IR** (cm^{-1}): 2970, 2924, 1938, 1719, 1463, 1208; **HRMS** $(M+H)^+$ calcd for $C_{18}H_{23}NO_3$= 302.1756 found = 302.1757.

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5. References

1. (a) Kumar, A.; Battani, N.; Kumar, R. R. *Eur. J. Org. Chem*. **2016**, *20*, 3344; (b) Evans, R. W.; Zbieg, J. R.; Zhu, S.; Li, W.; MacMillan, D. W. C. *J. Am. Chem.Soc.* **2013**, *135*, 16074; (c) Meltzer, P. C.; Butler, D.; Deschamps, J. R.; Madras, B. K. *J. Med. Chem.* **2006**, *49*, 1420; (d) Carrol, F. I.; Blough, B. E.; Abraham, P.; Mills, A. C.; Holleman, J. A.; Wolchenhauer, S. A.; Decker, A. M.; Landavazo, A. K.; McElroy, T.; Navarro, H. A.; Gatch, M. B.; Forster, M. J. *J. Med. Chem.* **2009**, *52*, 6768; (e) Bouteiller, C.; Becerril-Ortega, J.; Marchand, P.; Nicole, O.; Barré, L.; Buisson, A.; Perrio, C. *Org. Biomol.Chem.* **2010**, *8*, 1111; (f) Meyers, M. C.; Wang, J. L.; Iera, J. A.; Bang, J. K.; Hara, T.; Saito, S.; Zambetti, G. P.; Appella, G. H. *J. Am. Chem. Soc.* **2005**, *127*, 6152; (g) Tokumasu, K.; Yazaki, R.; Ohshima, T. *J. Am.Chem. Soc.* **2016**, *138*, 2664.
2. Kort, M. E.; Drizin, I.; Gregg, R. J.; Scanio, M. J. C.; Shi, L.; Gross, M. F.; Atkinson, R. N.; Johnson, M. S.; Pacofsky, G. L.; Thomas, J. B.; Carroll, W. A.; Krambis, M. J.; Liu, D.; Shieh, C. C.; Zhang, X.; Hernandez, G.; Mikusa, J. P.; Zhong, C.; Joshi, S.; Honore, P.; Roeloffs, R.; Marsh, K. C.; Murray, B. P.; Liu, J.; Werness, S.; Faltynek, C. R.; Krafte, D. S.; Jarvis, M. F.; Chapman, M. L.; Marron, B. E. *J. Med.Chem.* **2008**, *51*, 407.
3. Greenhill, J. V.; Lue, L. In: Ellis G.P.; Luscombe, D.K., Eds.; *Progress in Medicinal Chemistry*, New York, **1993**, *3*.
4. (a) Annedi, S. C.; Ramnauth, J.; Maddaford, S. P.; Renton, P.; Rakhit, S.; Mladenova, G.; Dove, P.; Silverman, S.; Andrews, J. S.; Felice, M. D.; Porreca, F. *J. Med. Chem*. **2011**, *54*, 7408; (b) Klingler, F. D. *Acc. Chem. Res*. **2007**, *40*, 1367; (c) Guile, S. D.; Alcaraz, L.; Birkinshaw, T. N.; Bowers, K. C.; Ebden, M. R.; Furber, M.; Stocks, M. J. *J. Med. Chem*. **2009**, *52*, 3123.
5. Evans, R.; Zbieg, J. R.; Zhu, S.; Li, W.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2013**, *135*, 16074
6. Concellón, J. M.; Rodríguez-Solla, H. *Current Organic Chemistry*, **2008**, *12*, 524.
7. (a) Zhao, L.; Basle, O.; Li, C-J. *Proc. Natl. Acad. Sci. USA*, **2009**, *106*, 4106; (b) Zhang, G.; Zhang, Y.; Wang, R. *Angew. Chem.* **2011**, *123*, 10613; *Angew. Chem. Int. Ed.* **2011**, **50**, 10429; (c) Xie, J.; Huang, Z.-Z.; *Angew. Chem.* **2010**, *122*, 10379; (d) Jia, X.; Wang, Y.; Peng, F.; Huo, C.; Yu, L.; Liu, J.; Wang, X. *J. Org. Chem.* **2013**, *78*, 9450; (e) Rohlmann, R.; Stopka, T.; Richter, H.; Mancheno, O. G. *J. Org. Chem.* **2013**, *78*, 6050; (f) Liu, P.; Wang, Z.; Lin, J.; Hu, X. *Eur. J. Org. Chem.* **2012**, 1583; (g) Liu, P.; Li, Y.; Wang, H.; Wang, Z.; Hu, X. *Tetrahedron Lett*. **2012**, *53*, 6654; (h) Zhu, S.; Rueping, M. *Chem. Commun*. **2012**, *48*, 11960; (i) Huo, C.; Wang, C.; Wu, M.; Jia, X.; Xie, H.; Yuan, Y. *Adv. Synth. Catal.* **2014**, *356*, 411; (j) Huo, C.; Wang, C.; Sun, C.; Jia, X.; Wang, X.; Chang, W.; Wu, M. *Adv. Synth. Catal*. **2013**, *355*, 1911; (k) Jia, X.; Peng, F.; Qing, C.; Huo, C.; Wang, X. *Org. Lett*. **2012**, *14*, 4030; (l) Richter, H.; Mancheno, O. G. *Org. Lett*. **2011**, *13*, 6066.
8. Zhang, C.; Zhang, L.; Jiao, N. *Adv. Synth. Catal*., **2012**, *354*, 1293.
9. Liu, X. X.; Wu, Z. Y.; He, Y. Q.; Zhou, X. Q.; Hu, T.; Ma, C. W.; Huang, G. S.; *Adv. Synth. Catal*., **2016**, *358*, 2385.
10. Martinez-Ariza, G.; McConnell, N.; Hulme, C. *Org. Lett*., **2016**, *18*, 1864
11. Chen, C.; Zhu, M.; Jiang, L.; Zeng, Z.; Yi, N.; Xiang, J. *Org. Biomol. Chem*., **2017**, *15*, 8134.
12. (a) Naidu, P. S.; Kolita, S.; Sharma, M.; Bhuyan, P. J. *J. Org. Chem*. **2015**, *18*, 6381; (b) Kolita, S.; Borah, P.; Naidu, P. S.; Bhuyan, P. J. *Tetrahedron* **2016**, *72*, 532; (c) Dutta, L.; Sharma, M.; Bhuyan, P. J. *Tetrahedron* **2016**, *72*, 6654,; (d) Dutta, L.; Bhuyan, P. J. *Chemistry Select* **2016**, *1*, 5944.
13. Du, F. T..; Ji, J. *Chem. Sci.* **2012**, *3*, 460.
14. Nekkanti, S.; Veeramani, K.; Kumar, N. P.; Shankaraiah, N. *Green Chem*., **2016**, *18*, 3439.