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Note

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Oxidation of β-Ketoamides: The Synthesis of Vicinal Tricarbonyl Amides

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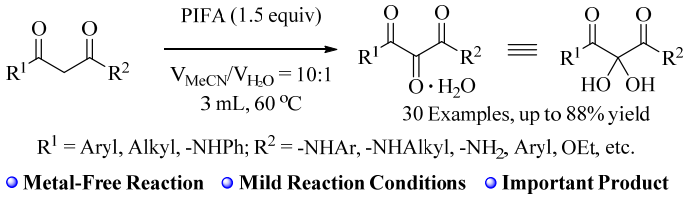


Abstract: A facile and direct oxidative reaction for the synthesis of vicinal tricarbonyl amides (VTAs) in moderate to excellent yields (53%−88%) was developed starting from readily available β-ketoamides in the presence of phenyliodine(III) bis(trifluoroacetate) (PIFA). The resulting products possess significant synthetic potential, making this approach a valuable addition to the traditional methods already available for the preparation of these molecules.

Keywords: Vicinal tricarbonyl amides (VTAs); β-Dicarbonyl compounds; β-Ketoamides; PIFA; Hypervalent iodine

Vicinal tricarbonyls are an important moiety that appears in biologically and pharmaceutically significant compounds, such as the elastase inhibitors YM−47141 and YM−47142 (Figure 1).[1] They are also a key synthon[2] that plays an important role in the construction of some natural products[3] and useful small molecules.[4] Commonly, vicinal tricarbonyl compounds (VTCs) are usually obtained in a mixture of the keto and dihydroxy forms,[5] and the *gem*-diol can be easily dehydrated to provide the original free vicinal tricarbonyls under certain conditions,[6] which is indicative of the reversible nature of this system (Figure 2, right box).[7] Recent research has indicated that the reversible addition

of alcohols, amines and thiols can also occur to the central carbonyl group of the VTCs to afford hemiketal, hemiaminal, and hemithioketal formation, respectively.[8] Generally, three strategies are utilized for the synthesis of VTCs, in which β-ketoamides are always employed as a special case of β-dicarbonyl compounds. First, starting with α-unfunctionalized β-dicarbonyl compounds has been the most efficient way to obtain VTCs in the presence of various oxidation catalytic systems, including DDQ/TEMPO,[9] CAN,[10] *m*-CPBA/$Cu(OAc)_2$,[11] Dess–Martin periodinane (DMP),[12] SeO_2,[13] and $^1O_2$/Bu_4NF[14] over the past several decades (Scheme 1, path a). Second, the conversion of α-mono- and disubstituted β-dicarbonyl derivatives to the desired VTCs constitutes another important route (Figure 2, path b).[13, 15] Third, oxidative cleavage of the C=C, C=N, C=S, C=P, and C=I double bonds of some α-methylene functionalized β-dicarbonyl compounds such as α-diazo-β-dicarbonyls, can also afford VTCs.[2, 10, 16] This involves a two-step procedure consisting of functionalizing the central carbon followed by oxidation with suitable reagents such as ^{t}BuOCl/HCO_2H,[6] 2-iodoxybenzoic acid (IBX),[2] O_2 or O_3,[17] Oxone,[18] DMP,[19] and $NaIO_4$ (Figure 2, path c).[20] Although numerous, efficient approaches have been established to date, a literature review showed a limited number of existing works addressing the systematic construction of vicinal tricarbonyl amides (VTAs) directly using β-ketoamides through a one-step reaction,[12] except for several examples using the strategy of α-methylene-functionalized β-ketoamides by multi-step reactions.[17b, 19-21] At the time we prepared this manuscript, Zhang and co-workers[22] reported a complementary approach to VTCs by an iodosobenzene-mediated direct oxidation of β-dicarbonyls C−H activation/annulation cascade using electrophilic α-halo and α-pseudohalo ketones assisted by $Fe(NO_3)_3 \cdot 9H_2O$ under mild and environmentally friendly conditions. In their work, only two types of secondary amides were employed, and the desired VTAs were obtained in 67% and 68% yields, respectively. Thus, as it can be seen, the synthesis of a VTA series using a simple catalytic system with a high yield of the target products is largely unexplored. Here, we present our recent efforts regarding the PIFA-mediated α-C–H bond oxidative reaction of β-ketoamide derivatives for the

synthesis of VTAs.[23]

Figure 1. Structure of YM−47141 and YM−47142.

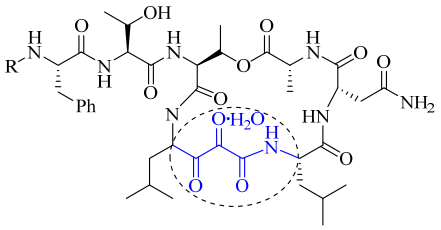
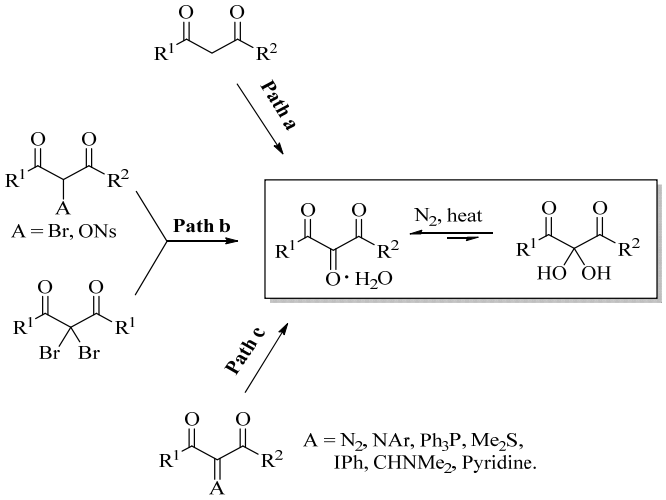


Figure 2. Representative routes to the VTCs and the equilibrium of the dihydroxyl and keto forms.

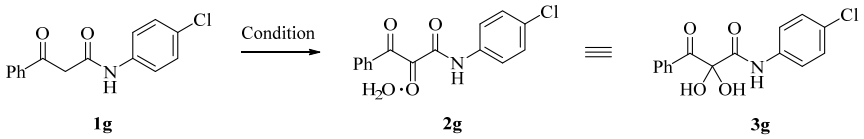


Hypervalent iodine reagents are advanced oxidants and advantageous because of their ready availability, nontoxicity, ease of handling and environmentally benign characteristics; they have been vastly utilized in many useful organic transformations.[24] Previous works[25] have demonstrated that, in the presence of PIFA and water,[26] the oxidization of amides bearing more active α-positions can generate alcohols, which are easily oxidized to α-diketones.[27] Very recently, we developed two reliable, efficient, green oxidative C–N bond formation reactions in the presence of hypervalent iodine reagents for the synthesis of 1*H*-indazoles[28] and spirocyclopropane quinolinediones under mild conditions.[29] These metal-free reactions inspired us to synthesize other useful synthons, such as VTAs, via α-C–H bond oxidative reactions starting from readily available β-ketoamides in the presence of organoiodine reagents.

With this assumption in mind, *N*-(4-chlorophenyl)-3-oxo-3-phenylpropanamide (**1g**) was selected

as the model substrate to explore the optimal conditions for the oxidative reaction. A portion of the key results are summarized in Table 1. At the beginning, we treated **1g** with 1.5 equiv. of PIFA in MeCN (3 mL) at 60 °C. After 36 h, compound **2g**, which was identified by ^{1}H, ^{13}C NMR, and MS, could be obtained in 82% yield after work-up followed by column chromatography (Table 1, entry 1). The spectroscopic analysis showed product **2g** was a mixture of the dihydroxy and keto forms; the keto form was the major one. This spectral evidence corresponds with those available in the literature.[2, 10] It is worth noting that the ratio of compounds **2** and **3** could be determined based on ^{1}H NMR, but the ratio will vary with the amount of water. Further investigation of the solvent indicated that a certain proportion of water can shorten the reaction time greatly (Table 1, entry 2 vs entry 1). And after many attempts, the ratio of acetonitrile and water was finally identified as 10 to 1 (Table 1, entry 2). The yield of **2g** decreased slightly if 1.0 and 2.0 equiv. of PIFA was loaded or a lower or higher reaction temperature was employed (Table 1, entries 3-6). Other organoiodine reagents including diacetoxyiodobenzene (PIDA), PhIO, IBX, and DMP, were screened and they were found to be not as efficient as PIFA (Table 1, entries 7-10). Several other solvents, such as PEG-400, EtOH, dioxane, DCE, DMSO, DMF, and THF resulted in lower yields of **2g** compared with those in the mixed-solvent of acetonitrile and water ($V_{CH3CN/H2O}$ = 10:1) (Table 1, entries 11–17).

Table 1. Survey of the Reaction Conditions[a]



1g **2g** **3g**

entry	oxidant (equiv)	solvent	time/h	yield/%
1	PIFA (1.5)	MeCN	36	82
2	PIFA (1.5)	MeCN/H_2O (10:1)	10	84
3	PIFA (1.0)	MeCN/H_2O (10:1)	13	74
4	PIFA (2.0)	MeCN/H_2O (10:1)	12	71

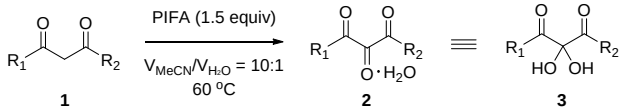
5	PIFA (1.5)/40 °C	MeCN/H_2O (10:1)	12	69
6	PIFA (1.5)/80 °C	MeCN/H_2O (10:1)	10	74
7	PIDA (1.5)	MeCN/H_2O (10:1)	13	58
8	PhIO (1.5)	MeCN/H_2O (10:1)	13	63
9	IBX (1.5)	MeCN/H_2O (10:1)	13	49
10	DMP (1.5)	MeCN/H_2O (10:1)	13	55
11	PIFA (1.5)	PEG-400	72	72
12	PIFA (1.5)	EtOH	48	58
13	PIFA (1.5)	Dioxane	72	Trace[b]
14	PIFA (1.5)	DCE	72	20[c]
15	PIFA (1.5)	DMSO	46	73
16	PIFA (1.5)	DMF	48	74
17	PIFA (1.5)	THF	60	0[d]

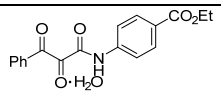
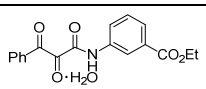
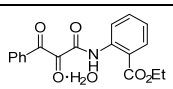
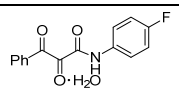
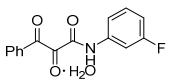
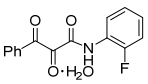
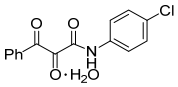
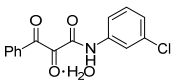
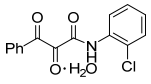
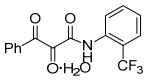
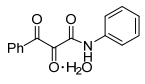
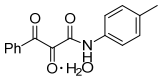
[a] Unless otherwise indicated, all reactions were carried out with **1** (0.5 mmol) in 3 mL solvent at 60 °C. [b] 71% of **1g** was recovered. [c] 61% of **1g** was recovered. [d] 93% of **1g** was recovered.

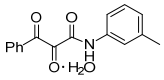
After having optimized the reaction conditions (Table 1, entry 2), the substrate scope of this oxidative reaction was investigated (Table 2). Initially, various β-ketoamides were investigated (R^2): a number of functional aromatic amine groups bearing -CO_2Et, -CF_3, -F, -Cl, -Me, or -MeO at the -*ortho*, -*meta* or -*para* positions were tolerated well (products **2a**–**q**). The ester group, which can be converted easily to other useful functional groups, was suitable for the oxidative reaction and gave **2a**–**c** in good yields (70%−88%). Importantly, the chloro and fluoro substituents could be tolerated well in this reaction, thereby facilitating additional modifications at these positions (**2d**–**i**). Furthermore, the CF_3 group also showed high reactivity leading to **2j** in good yield (84%). Gratifyingly, the starting materials **1k**−**q** bearing electron-donating groups on the aromatic ring were also viable for the construction of **2k**−**q** in high yields (71%−86%). Subsequently, the aliphatic

amine substituent cyclohexyl was employed inthe reaction and gave a satisfying yield of **2r** (81%). The investigation using β-keto ester (**1s**: R^2 = OMe) resulted in an incomplete oxidative reaction. Compound **2s** was isolated in 72% yield along with the recovered starting material **1s** (12%), and the yield of **2s** could not be increased further by prolonging the reaction times. It was found that the dibenzoylmethane compound (**1t**: R^2 = Ph) only gave product **2t** in a yield of 53%. The reaction toward the benzoyl group (R^1) bearing a –Me at the -*ortho*, -*meta* or -*para* position on the phenyl ring was also carried out with **1u**−**w** under the optimized conditions, and they gave the corresponding VTAs **2u**−**w** in 77%–81% yields. However, fewer experiments were conducted toward varying other arylcarbonyl groups because of the limited number of available substrates at this position. To our delight, diamide **1x** also afforded the desired compound **2x** in 53% yield, along with some unidentified complex mixture. This case suggested that the present method might be utilized in oxidative reactions containing a plurality of amino groups.[30] It should be emphasized that all of the synthesized VTAs are stable enough for storage at room temperature.

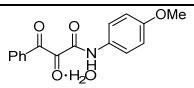
Table 2. Reaction Extension[a]



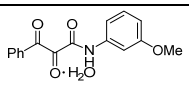
			
2a: 13 h, 88% (3:1)	**2b**: 13 h, 76% (4:1)	**2c**: 13 h, 70% (10:1)	**2d**: 10 h, 79% (3:1)
			
2e: 15 h, 86% (2:1)	**2f**: 11 h, 83% (2:1)	**2g**: 12 h, 84% (14:1)	**2h**: 12 h, 84% (9:1)
			
2i: 11 h, 85% (2:1)	**2j**: 15 h, 84% (2:1)	**2k**: 14 h, 72% (5:1)	**2l**: 13 h, 71% (3:1)



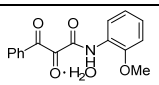
2m: 11 h, 71% (4:1)



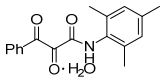
2n: 12 h, 80% (5:1)



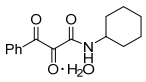
2o: 14 h, 86% (6:1)



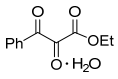
2p: 15 h, 83% (10:1)



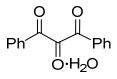
2q: 20 h, 71% (2:1)



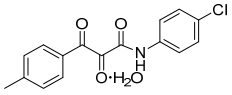
2r: 12 h, 81% (2:1)



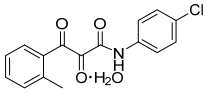
2s: 6 h, 72% (6:1)[b]



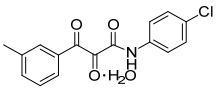
2t: 2 h, 88% (7:1)[c]



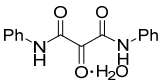
2u: 12 h, 81% (3:1)



2v: 11 h, 77% (>95:5)



2w: 20 h, 77% (20:1)



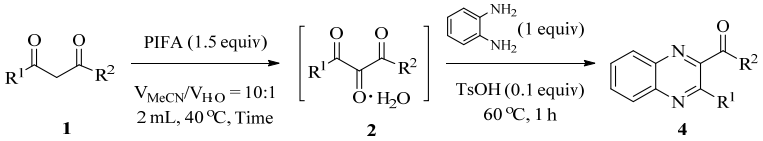
2x: 10 h, 53%

(>95:5)

[a] Unless otherwise indicated, all reactions were carried out with **1** (0.5 mmol) and PIFA (1.5 equiv) in 3 mL mixed solvents of CH_3CN and H_2O (V_{CH3CN}:V_{H2O} = 10:1) at 60 °C, and the ratio of **2** and **3** in parentheses is based on current ^{1}H NMR. [b] 12% of **1s** was recovered, and the yield of **2s** could not be increased by adding 2.5 equivalent of PIFA. [c] Reaction was performed at room temperature.

It should be noted that, similar to Deng's[9] work in 2014, we also failed to purify the aliphatic VTC product **2y** by flash chromatography on silica gel, although a high yield was observed on the thin-layer chromatography (TLC) plate. Accordingly, after producing **2y** in situ at 40 °C under the optimal conditions, further derivatization was carried out with benzene-1,2-diamine in the presence of 4-methylbenzenesulfonic acid at 60 °C in one-pot. As expected, the quinoxaline derivative **4y** was isolated in 70% yield after 1 h, which proved the formation of **2y** (Table 3, entry 1). To our delight, four types of other aliphatic β-ketoamides, including **1z**−**c'** and aliphatic β-keto ester **1d'**, could also afford the derivatives **4z**−**d'** in 41%−87% total yields (Table 3, entries 2-5).

Table 3. One-pot Synthesis of Quinoxaline Derivative 4.



1 2 4

Entry	R^1	R^2	Temperature/°C	Time/h	Yield of **4**/%

1	Me	NHPh	40	4	**4y**: 70
2	Me	NH_2	r.t.	15 min	**4z**: 41
3	Me	$N(Me)_2$	40	4	**4a'**: 83
4	^{t}Bu	NHPh	60	8	**4b'**: 85
5	^{n}Bu	NHPh	60	5	**4c'**: 87
6	^{n}Bu	OMe	60	5	**4d'**: 75

In summary, we have demonstrated a facile method for the direct synthesis of VTAs from readily available β-ketoamides in moderate to excellent yields through PIFA-mediated oxidative activation of the sp^3 C–H bond. The advantage of this protocol is associated with readily available starting materials, excellent yields, dense and flexible substituted patterns, and important synthetic potential of the products. It is noted that different from previous literature reports on the synthesis of VTCs from 1,3-dicarbonyls, the present method focused on the preparation of VTA series. Moreover, as an alternative and valuable route, it may be more practical for the construction of VTA analogue-containing biomolecules.[1, 3a, 3e, 31]

Experimental Section

General Remarks. All reactions were carried out under air atmosphere, unless otherwise indicated. Other all reagents were purchased from commercial sources and used without further treatment, unless otherwise indicated. Petroleum ether (PE) used refers to the 60-90 °C boiling point fraction of petroleum. Ethyl acetate is abbreviated as EA. ^{1}H NMR and ^{13}C{^{1}H} NMR spectra were recorded on Bruker Avance/600 (^{1}H: 600 MHz, ^{13}C{^{1}H}: 150 MHz at 25 °C) or Bruker Avance/400 (^{1}H: 400 MHz, ^{13}C{^{1}H}: 100 MHz at 25 °C) and TMS as internal standard. Data are represented as follows: chemical shift, integration, multiplicity (br = broad, s = singlet, d = doublet, dd = double doublet, t = triplet, q = quartet, m = multiplet), coupling constants in Hertz (Hz). All high-resolution mass spectra (HRMS) were measured on a mass spectrometer by using electrospray ionization (ESI-oa-TOF), and the purity of all samples used for HRMS (>95%) were confirmed by ^{1}H NMR and ^{13}C{^{1}H} NMR spectroscopic analysis. Melting points were measured on a melting point apparatus equipped with a

thermometer and were uncorrected. All reactions were monitored by TLC with GF254 silica gel coated plates. Flash chromatography was carried out on SiO_2 (silica gel 200−300 mesh).

Typical Experimental Procedure For 2 (2g as an example): To a round-bottom flask (25 mL) **1g** (137 mg, 0.5 mmol) and PIFA (323 mg, 0.75 mmol) were added, and the mixture was well stirred in CH_3CN/H_2O (3 mL) at 60 °C (the whole process was closely monitored by TLC). After 12 h, the residue was purified by a short flash silica gel column chromatography (eluent: EA/PE = 3/10) to give *N*-(4-chlorophenyl)-2,3-dioxo-3-phenylpropanamide **2g** as white solid (128 mg, 84%).

Ethyl 4-(2,3-dioxo-3-phenylpropanamido)benzoate (2a). The product was isolated by flash chromatography (eluent: EA/PE = 3/10) as a white solid (151 mg, 88%) with the ratio of **2a** and **3a** was 3:1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (s, 1H), 8.09 (d, J = 8.4 Hz, 2H), 7.93 (d, J = 7.6 Hz, 2H), 7.76 (d, J = 8.8 Hz, 2H), 7.56 (t, J = 7.6 Hz, 2H), 4.37 (t, J = 7.0 Hz, 2H), 1.40 (t, J = 7.2 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 193.6, 193.1, 188.5, 167.4, 166.0, 165.9, 156.8, 140.6, 139.7, 135.7, 134.9, 132.0, 131.3, 131.0, 130.84, 130.8, 130.77, 130.6, 129.6, 129.2, 128.8, 127.6, 127.0, 119.4, 119.3, 61.2, 61.1, 14.3; IR (KBr, neat): v = 3503, 3408, 3343, 1713, 1688, 1597, 1525, 1411, 1288, 1182, 1115, 1008, 856, 769 cm^{-1}; HRMS (ESI), *m/z* calcd. for $C_{18}H_{15}NO_5$ ($[M+Na]^+$) 348.0842, found: 348.0845.

Ethyl 3-(2,3-dioxo-3-phenylpropanamido)benzoate (2b). The product was isolated by flash chromatography (eluent: EA/PE = 3/10) as a white solid (130 mg, 76%) with the ratio of **2b** and **3b** was 4:1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.90 (s, 1H), 8.24 (s, 1H), 8.06-7.99 (m, 1H), 7.90 (t, J = 9.0 Hz, 2H), 7.69 (t, J = 7.6 Hz, 1H), 7.53 (t, J = 7.8 Hz, 2H), 7.34-7.47 (m, 2H), 4.41-4.32 (m, 2H), 1.38 (t, J = 7.2 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 193.2, 188.7, 165.8, 156.7, 136.0, 135.59, 134.9, 132.0, 131.8, 130.8, 129.6, 129.5, 129.3, 129.2, 128.8, 126.9, 126.4, 124.3, 124.1, 120.9, 61.4, 14.3; IR (KBr, neat): v = 3265, 3195, 3126, 1733, 1684, 1597, 1533, 1493, 1403, 1092, 827 cm^{-1}; HRMS (ESI), *m/z* calcd. for $C_{18}H_{15}NO_5$ ($[M+H]^+$)326.1023, found: 326.1023.

Ethyl 2-(2,3-dioxo-3-phenylpropanamido)benzoate (2c). The product was isolated by flash

chromatography (eluent: EA/PE = 3/10) as a white solid (120 mg, 70%) with the ratio of **2c** and **3c** was 10:1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.58 (s, 1H), 8.72 (d, J = 8.4 Hz, 1H), 8.14 (dd, J = 8.0 Hz, 1.6 Hz, 1H), 7.94 (dd, J = 8.4 Hz, 2H), 7.69 (t, J = 7.4 Hz, 1H), 7.57 (m, 3H), 7.27-7.18 (m, 1H), 4.47 (dd, J = 14.4 Hz, 7.2 Hz, 2H), 1.45 (t, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.8, 188.7, 167.8, 157.5, 139.2, 135.4, 134.7, 132.2, 131.3, 129.6, 129.1, 124.4, 120.7, 116.9, 62.0, 14.2; IR (KBr, neat): v = 3234, 3185, 3119, 1697, 1666, 1589, 1529, 1451, 1303, 1281, 1222, 1102, 866, 767, 752 cm^{-1}; HRMS (ESI), *m/z* calcd. for $C_{18}H_{15}NO_5$ ([M+Na]$^+$) 348.0842, found: 348.0843.

***N*-(4-fluorophenyl)-2,3-dioxo-3-phenylpropanamide (2d).** The product was isolated by flash chromatography (eluent: EA/PE = 3/10) as a white solid (114 mg, 79%) with the ratio of **2d** and **3d** was 3:1; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.64 (s, 1H), 7.92 (dd, J = 8.4 Hz, 2H), 7.71 (t, J = 7.5 Hz, 1H), 7.67-7.64 (m, 2H), 7.55 (t, J = 7.8 Hz, 2H), 7.11-7.07 (m, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 193.3, 189.0, 161.0, 159.4, 156.4, 135.6, 135.0, 132.1, 130.8, 129.6, 129.2, 128.8, 122.0, 121.9, 121.7, 121.68, 116.3, 116.1, 116.0, 115.9; IR (KBr, neat): v = 3419, 3352, 3067, 1680, 1658, 1595, 1558, 1509, 1209, 1110, 1090, 834 cm^{-1}; HRMS (ESI), m/z calcd. for $C_{15}H_{10}FNO_3$ ([M+Na]$^+$) 294.0537, found: 294.0541.

***N*-(3-fluorophenyl)-2,3-dioxo-3-phenylpropanamide (2e).** The product was isolated by flash chromatography (eluent: EA/PE = 3/10) as a white solid (124 mg, 86%) with the ratio of **2e** and **3e** was 2:1; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.66 (s, 1H), 7.82 (d, J = 7.8 Hz, 2H), 7.62 (t, J = 7.5 Hz, 1H), 7.52 (d, J = 10.2 Hz, 1H), 7.46 (t, J = 7.8 Hz, 2H), 7.25 (s, 2H), 6.86-6.81 (m, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 193.1, 188.6, 163.8, 162.2, 156.6, 137.2, 137.16, 135.6, 132.0, 130.8, 130.6, 130.55, 129.6, 129.2, 128.8, 115.5, 115.4, 112.9, 112.7, 107.7, 107.5; IR (KBr, neat): v = 3454, 3305, 3210, 1737, 1686, 1671, 1614, 1551, 1493, 1449, 1147, 1095, 967, 775 cm^{-1}; HRMS (ESI), m/z calcd. for $C_{15}H_{10}FNO_3$ ([M+Na]$^+$) 294.0537, found: 294.0538.

***N*-(2-fluorophenyl)-2,3-dioxo-3-phenylpropanamide (2f).** The product was isolated by flash chromatography (eluent: EA/PE = 3/10) as a white solid (120 mg, 83%) with the ratio of **2f** and **3f**

was 2:1; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.93 (s, 1H), 7.93 (d, J = 7.2 Hz, 2H), 7.56 (t, J = 7.8 Hz, 2H), 7.47 (m, 2H), 7.18 (dd, J = 7.8 Hz, 4.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.0, 188.2, 167.2, 156.5, 154.0, 135.6, 134.8, 132.0, 130.8, 129.6, 129.2, 128.7, 126.3, 126.2, 125.7, 124.9, 124.6, 121.8, 121.5, 115.4, 115.2, 115.1; IR (KBr, neat): v = 3386, 3350, 3074, 1696, 1680, 1598, 1530, 1487, 1456, 1412, 1263, 1196, 1116, 992, 925, 846, 780, 754 cm^{-1}; HRMS (ESI), m/z calcd. for $C_{15}H_{10}FNO_3$ ([M+Na]$^+$) 294.0537, found: 294.0539.

***N*-(4-chlorophenyl)-2,3-dioxo-3-phenylpropanamide (2g).** The product was isolated by flash chromatography (eluent: EA/PE = 3/10) as a white solid (128 mg, 84%) with the ratio of **2g** and **3g** was 14:1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 (s, 1H), 7.89 (dd, J = 8.4 Hz, 1.6 Hz, 2H), 7.72-7.67 (m, 1H), 7.65-7.60 (m, 2H), 7.53 (t, J = 7.8 Hz, 2H), 7.36-7.32 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.1, 188.6, 156.4, 135.6, 134.3, 131.9, 131.0, 129.5, 129.4, 129.2, 121.2; IR (KBr, neat): v = 3315, 3115, 3061, 1728, 1694, 1666, 1596, 1539, 1493, 1449, 1403, 1220, 1011, 870, 827, 758 cm^{-1}; HRMS (ESI), *m/z* calcd. for $C_{15}H_{10}ClNO_3$ ([M+Na]$^+$) 310.0241, found: 310.0246.

***N*-(3-chlorophenyl)-2,3-dioxo-3-phenylpropanamide (2h).** The product was isolated by flash chromatography (eluent: EA/PE = 3/10) as a white solid (128 mg, 84%) with the ratio of **2h** and **3h** was 9:1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 (s, 1H), 7.94-7.89 (m, 2H), 7.80 (t, J = 2.0 Hz, 1H), 7.72 (t, J = 7.6 Hz, 1H), 7.59-7.49 (m, 3H), 7.33 (t, J = 8.2 Hz, 1H), 7.23-7.18 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.1, 188.5, 156.5, 136.8, 135.6, 135.0, 131.9, 130.3, 129.5, 129.2, 126.0, 120.1, 117.9; IR (KBr, neat): v = 3300, 3133, 3063, 1734, 1686, 1670, 1597, 1549, 1485, 1449, 1430, 1417, 1225, 1092, 909, 876, 781 cm^{-1}; HRMS (ESI), *m/z* calcd. for $C_{15}H_{10}ClNO_3$ ([M+Na]$^+$) 310.0241, found: 310.0240.

***N*-(2-chlorophenyl)-2,3-dioxo-3-phenylpropanamide (2i).** The product was isolated by flash chromatography (eluent: EA/PE = 3/10) as a white solid (130 mg, 85%) with the ratio of **2i** and **3i** was 2:1; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.11 (s, 1H), 8.21 (d, J = 8.4 Hz, 1H), 7.93 (d, J = 7.8 Hz, 1H), 7.71 (t, J = 9.0 Hz, 1H), 7.61 (t, J = 6.6 Hz, 2H), 7.55 (dd, J = 16.5 Hz, 8.7 Hz, 2H), 7.46 (t, J =

7.8 Hz, 1H), 7.27 (t, *J* = 6.6 Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 193.4, 192.7, 188.1, 167.5, 156.6, 135.6, 134.9, 133.3, 133.0, 132.0, 131.2, 130.7, 129.6, 129.2, 128.8, 126.6, 126.5, 126.3, 125.8, 125.5, 124.2, 123.2; IR (KBr, neat): *v* = 3384, 1743, 1700, 1594, 1537, 1462, 1321, 1289, 1190, 1130, 1098, 1037, 765 cm^{-1}; HRMS (ESI), *m/z* calcd. for $C_{15}H_{10}ClNO_3$ ($[M+Na]^+$) 310.0241, found: 310.0241.

***N*-(2-trifluoromethyl)- 2,3-dioxo-3-phenylpropanamide (2j).** The product was isolated by flash chromatography (eluent: EA/PE = 3/10) as a white solid (142 mg, 84%) with the ratio of **2j** and **3j** was 2:1; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.12 (s, 1H), 8.21 (d, *J* = 7.8 Hz, 1H), 7.93 (d, *J* = 7.8 Hz, 1H), 7.71 (t, *J* = 10.2 Hz, 1H), 7.61 (t, *J* = 8.1 Hz, 2H), 7.58-7.52 (m, 2H), 7.45 (t, *J* = 7.8 Hz, 1H), 7.27 (t, *J* = 7.5 Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 193.4, 192.7, 188.1, 167.5, 156.6, 135.6, 134.9, 133.3, 133.0, 132.0, 131.2, 130.7, 129.6, 129.2, 128.8, 126.6, 126.5, 126.3, 125.8, 125.5, 124.2, 123.2; IR (KBr, neat): *v* = 3396, 1709, 1594, 1537, 1456, 1321, 1293, 1174, 1120, 1035, 937, 866, 766 cm^{-1}; HRMS (ESI), *m/z* calcd. for $C_{16}H_{10}F_3NO_3$ ($[M+Na]^+$) 344.0505, found: 344.0521.

***N*-2,3-dioxo-3-diphenylpropanamide (2k).** The product was isolated by flash chromatography (eluent: EA/PE = 3/10) as a white solid (98 mg, 72%) with the ratio of **2k** and **3k** was 5:1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.82 (s, 1H), 7.96 (d, *J* = 7.2 Hz, 2H), 7.73 (d, *J* = 7.6 Hz, 3H), 7.57 (t, *J* = 7.4 Hz, 2H), 7.42 (t, *J* = 7.6 Hz, 2H), 7.26 (t, *J* = 7.2 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.5, 189.0, 156.5, 135.7, 135.4, 132.0, 130.7, 129.5, 129.3, 129.1, 129.0, 128.6, 125.8, 125.3, 120.0, 119.9; IR (KBr, neat): *v* = 3345, 3284, 3194, 1689, 1648, 1596, 1532, 1492, 1395, 1325, 1315, 1244, 1164, 1006, 935, 828, 816 cm^{-1}; HRMS (ESI), *m/z* calcd. for $C_{15}H_{11}NO_3$ ($[M+H]^+$) 254.0812, found: 254.0810.

2,3-dioxo-3-phenyl-*N*-(*p*-tolyl)propanamide (2l). The product was isolated by flash chromatography (eluent: EA/PE = 3/10) as a white solid (101 mg, 71%) with the ratio of **2l** and **3l** was 3:1; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.63 (s, 1H), 7.91 (d, *J* = 7.8 Hz, 2H), 7.54 (dd, *J* = 15.3 Hz, 7.5 Hz, 4H), 7.44 (t, *J* = 7.2 Hz, 1H), 7.18 (d, *J* = 7.8 Hz, 2H), 2.34 (s, 3H); ^{13}C NMR (151 MHz,

$CDCl_3$) δ 193.9, 193.6, 189.3, 166.9, 156.4, 135.8, 135.5, 134.8, 133.9, 133.3, 132.2, 131.4, 130.8, 129.9, 129.6, 129.5, 129.2, 128.8, 120.2, 119.9, 21.0; IR (KBr, neat): v = 3343, 3033, 2921, 1679, 1598, 1530, 1453, 1403, 1242, 1113, 996, 925, 811, 763 cm^{-1}; HRMS (ESI), *m/z* calcd. for $C_{16}H_{13}NO_3$ ($[M+Na]^+$) 290.0788, found: 290.0788.

2,3-dioxo-3-phenyl-*N*-(*m*-tolyl)propanamide (2m). The product was isolated by flash chromatography (eluent: EA/PE = 3/10) as a white solid (101 mg, 71%) with the ratio of **2m** and **3m** was 4:1; ^1H NMR (600 MHz, $CDCl_3$) δ 8.59 (s, 1H), 7.91 (d, J = 8.4 Hz, 2H), 7.70 (t, J = 7.5 Hz, 1H), 7.54 (t, J = 7.8 Hz, 3H), 7.28 (d, J = 7.8 Hz, 1H), 7.03 (d, J = 7.8 Hz, 1H), 2.36 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 193.6, 189.3, 156.4, 139.5, 135.7, 135.5, 134.9, 132.2, 130.8, 129.5, 129.2, 129.18, 129.0, 128.8, 126.8, 126.2, 120.5, 117.0, 21.5; IR (KBr, neat): v = 3357, 3066, 2923, 1680, 1614, 1546, 1538, 1491, 1451, 1257, 1113, 1003, 988, 932, 849, 777 cm^{-1}; HRMS (ESI), *m/z* calcd. for $C_{16}H_{13}NO_3$ ($[M+H]^+$) 268.0968, found: 268.0968.

***N*-(4-methoxyphenyl)-2,3-dioxo-3-phenylpropanamide (2n).** The product was isolated by flash chromatography (eluent: EA/PE = 3/10) as a white solid (120 mg, 80%) with the ratio of **2n** and **3n** was 5:1; ^1H NMR (600 MHz, $CDCl_3$) δ 8.62 (s, 1H), 7.91 (d, J = 7.8 Hz, 2H), 7.69 (t, J = 7.2 Hz, 1H), 7.60 (d, J = 7.8 Hz, 2H), 7.53 (t, J = 7.5 Hz, 2H), 6.90 (d, J = 7.8 Hz, 2H), 3.81 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 193.6, 189.4, 166.8, 157.4, 156.1, 149.5, 135.4, 129.5, 129.1, 121.4, 114.4, 55.5; IR (KBr, neat): v = 3495, 3323, 3057, 1678, 1598, 1534, 1514, 1448, 1303, 1247, 1125, 1034, 931, 824 cm^{-1}; HRMS (ESI), *m/z* calcd. for $C_{16}H_{13}NO_4$ ($[M+Na]^+$) 306.0737, found: 306.0731.

***N*-(3-methoxyphenyl)-2,3-dioxo-3-phenylpropanamide (2o).** The product was isolated by flash chromatography (eluent: EA/PE = 3/10) as a white solid (130 mg, 86%) with the ratio of **2o** and **3o** was 6:1; ^1H NMR (400 MHz, $CDCl_3$) δ 8.65 (s, 1H), 7.95-7.84 (m, 2H), 7.71-7.65 (m, 1H), 7.52 (t, J = 7.6 Hz, 2H), 7.42 (t, J = 2.2 Hz, 1H), 7.26 (m, 1H), 7.14-7.08 (m, 1H), 6.73-6.77 (m, 1H), 3.78 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.5, 189.0, 160.2, 156.4, 136.9, 135.5, 132.0, 130.7, 130.0, 129.5, 129.1, 128.7, 112.1, 112.0, 105.4, 55.3; IR (KBr, neat): v = 3361, 3072, 2994, 1720, 1700,

1672, 1609, 1552, 1498, 1448, 1420, 1294, 1265, 1202, 1176 ,1156, 1097, 1045, 960, 851, 839, 786 cm^{-1}; HRMS (ESI), *m/z* calcd. for $C_{16}H_{13}NO_4$ ($[M+Na]^+$) 306.0737, found: 306.0738.

***N*-(2-methoxyphenyl)-2,3-dioxo-3-phenylpropanamide (2p).** The product was isolated by flash chromatography (eluent: EA/PE = 3/10) as a white solid (125 mg, 83%) with the ratio of **2p** and **3p** was 10:1; ^1H NMR (400 MHz, $CDCl_3$) δ 9.34 (s, 1H), 8.39 (dd, J = 8.0 Hz, 1H), 7.92 (dd, J = 8.4 Hz, 2H), 7.69 (t, J = 7.4 Hz, 1H), 7.54 (t, J = 7.8 Hz, 2H), 7.16 (m, 1H), 6.99 (t, J = 7.8 Hz, 1H), 6.95 (d, J = 8.4 Hz, 1H), 3.96 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.8, 189.2, 156.4, 148.7, 135.4, 132.2, 129.5, 129.2, 125.8, 125.5, 121.2, 120.1, 110.3, 55.9; IR (KBr, neat): v = 3382, 3025, 2970, 1721, 1688, 1669, 1596, 1535, 1488, 1465, 1450, 1318, 1292, 1254, 1217, 1120, 1082, 1025, 937, 865, 785, 757 cm^{-1}; HRMS (ESI), *m/z* calcd. for $C_{16}H_{13}NO_4$ ($[M+Na]^+$) 306.0737, found: 306.0738.

2,3-dioxo-3-phenyl-*N*-mesitylpropanamide (2q). The product was isolated by flash chromatography (eluent: EA/PE = 3/10) as a white solid (111 mg, 71%) with the ratio of **2q** and **3q** was 2:1; ^1H NMR (400 MHz, $CDCl_3$) δ 8.13 (s, 1H), 7.93 (d, J = 7.2 Hz, 2H), 7.70 (t, J = 7.6 Hz, 1H), 7.55 (t, J = 7.8 Hz, 2H), 6.93 (s, 2H), 2.29 (s, 3H), 2.24 (s, 6H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 193.2, 189.1, 157.5, 137.9, 135.4, 134.9, 134.7, 132.1, 130.9, 129.6, 129.2, 129.1, 129.0, 128.7, 21.0, 20.9, 18.4, 17.7; IR (KBr, neat): v = 3335, 3229, 3061, 1660, 1598, 1520, 1449, 1255, 1121, 1006, 927, 854 cm^{-1}; HRMS (ESI), *m/z* calcd. for $C_{18}H_{17}NO_3$ ($[M+H]^+$) 296.1281, found: 296.1286.

2,3-dioxo-3-phenyl-*N*-cyclohexyl-propanamide (2r). The product was isolated by flash chromatography (eluent: EA/PE = 3/10) as a white solid (112 mg, 81%) with the ratio of **2r** and **3r** was 2:1; ^1H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, J = 7.2 Hz, 1H), 7.87 (dd, J = 8.4 Hz, 1H), 7.67 (t, J = 7.4 Hz, 1H), 7.51 (t, J = 7.8 Hz, 2H), 3.82 (m ,1H), 1.97 (d, J = 12.0 Hz, 2H), 1.83-1.58 (m, 5H), 1.44-1.00 (m, 7H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.8, 189.2, 168.2, 158.1, 135.2, 130.5, 129.5, 129.0, 128.6, 49.4, 48.7, 32.5, 32.3, 25.2, 24.6; IR (KBr, neat): v = 3305, 3064, 2932, 2855, 1651, 1530, 1450, 1385, 1253, 1178, 1151, 1099, 1062, 1028, 892 cm^{-1}; HRMS (ESI), *m/z* calcd. for $C_{15}H_{17}NO_3$ ($[M+Na]^+$) 282.1101, found: 282.1100.

2,3-dioxo-3-phenyl-ethylpropanoate (2s).[10] The product was isolated by flash chromatography (eluent: EA/PE = 3/10) as a yellow solid (81 mg, 72%) with the ratio of **2s** and **3s** was 6:1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, J = 7.2 Hz, 2H), 7.62 (t, J = 7.4 Hz, 1H), 7.47 (t, J = 7.8 Hz, 2H), 4.21 (q, J = 7.2 Hz, 2H), 1.08 (t, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.5, 169.9, 134.6, 131.4, 130.1, 130.0, 129.1, 128.8, 63.2, 13.6; HRMS (ESI), *m/z* calcd. for $C_{11}H_{10}O_4$ ($[M+Na]^+$) 229.0471, found: 229.0468.

1,3-diphenylpropane-1,2,3-trione (2t).[10] The product was isolated by flash chromatography (eluent: EA/PE = 3/10) as a white solid (113 mg, 88%) with the ratio of **2t** and **3t** was 7:1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07-8.02 (dd, J = 7.2 Hz, 4H), 7.52 (t, J = 7.4 Hz, 2H), 7.42 (d, J = 7.0 Hz, 1H), 7.38 (t, J = 7.8 Hz, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.2, 192.5, 188.3, 172.3, 135.4, 134.6, 133.8, 132.1, 130.3, 130.2, 129.4, 129.1, 128.8, 128.5; HRMS (ESI), *m/z* calcd. for $C_{15}H_{10}O_3$ ($[M+Na]^+$) 261.0522, found: 261.0517.

***N*-(4-chlorophenyl)-2,3-dioxo-3-(*p*-tolyl)propanamide (2u).** The product was isolated by flash chromatography (eluent: EA/PE = 3/10) as a white solid (129 mg, 81%) with the ratio of **2u** and **3u** was 3:1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67 (s, 1H), 7.81 (d, J = 8.4 Hz, 2H), 7.63 (d, J = 8.8 Hz, 2H), 7.35 (dd, J = 8.8 Hz, 6.4 Hz, 4H), 2.46 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.6, 188.8, 156.5, 147.1, 134.4, 131.0, 129.9, 129.7, 129.5, 129.2, 121.1, 22.1; IR (KBr, neat): ν = 3400, 3348, 3072, 1656, 1605, 1551, 1492, 1404, 1307, 1263, 1090, 1013, 830, 765 cm^{-1}; HRMS (ESI), *m/z* calcd. for $C_{16}H_{12}ClNO_3$ ($[M+H]^+$) 302.0578, found: 302.0576.

***N*-(4-chlorophenyl)-2,3-dioxo-3-(*o*-tolyl)propanamide (2v).** The product was isolated by flash chromatography (eluent: EA/PE = 3/10) as a white solid (123 mg, 77%) with the ratio of **2v** and **3v** was >95:5; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.64 (s, 1H), 7.62 (dd, J = 14.0 Hz, 9.2 Hz, 3H), 7.55 (t, J = 7.4 Hz, 1H), 7.39-7.31 (m, 4H), 2.69 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.2, 188.2, 156.5, 141.4, 134.5, 134.4, 132.7, 132.6, 131.0, 130.5, 129.4, 126.1, 121.1, 21.7; IR (KBr, neat): ν = 3316, 3189, 3127, 1733, 1683, 1668, 1600, 1545, 1494, 1403, 1290, 1237, 1176, 1084, 1012, 833, 767 cm^{-1};

HRMS (ESI), *m/z* calcd. for $C_{16}H_{12}ClNO_3$ ($[M+H]^+$) 302.0578, found: 302.0573.

***N*-(4-chlorophenyl)-2,3-dioxo-3-(*m*-tolyl)propanamide (2w).** The product was isolated by flash chromatography (eluent: EA/PE = 3/10) as a white solid (123 mg, 77%) with the ratio of **2w** and **3w** was 20:1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80 (s, 1H), 7.68 (d, J = 12.4 Hz, 2H), 7.62 (d, J = 8.8 Hz, 2H), 7.49 (d, J = 7.2 Hz, 1H), 7.40 (t, J = 7.6 Hz, 1H), 7.31 (d, J = 8.4 Hz, 2H), 2.40 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.4, 188.7, 156.5, 139.2, 136.4, 134.3, 131.9, 131.0, 129.8, 129.3, 129.0, 126.9, 121.2, 21.2; IR (KBr, neat): v = 3308, 3195, 3060, 1734, 1685, 1666, 1602, 1545, 1494, 1404, 1222, 1078, 1014, 937, 870, 833, 748, 725 cm^{-1}; HRMS (ESI), *m/z* calcd. for $C_{16}H_{12}ClNO_3$ ($[M+H]^+$) 302.0578, found: 302.0574.

2-oxo-N^1,N^3-diphenylmalonamide (2x). The product was isolated by flash chromatography (eluent: EA/PE = 3/10) as a white solid (76 mg, 53%) with the ratio of **2x** and **3x** was >95:5; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.08 (s, 2H), 7.57 (d, J = 7.6 Hz, 4H), 7.37 (t, J = 7.8 Hz, 4H), 7.17 (t, J = 7.4 Hz, 2H), 4.85 (d, J = 2.8 Hz, 1H), 4.75 (d, J = 2.8 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.4, 136.5, 129.2, 125.3, 120.0, 70.6; IR (KBr, neat): v = 3355, 3307, 3055, 1694, 1599, 1536, 1443, 1312, 1196, 1123, 983, 930, 897 cm^{-1}; HRMS (ESI), *m/z* calcd. for $C_{15}H_{12}N_2O_3$ ($[M+Na]^+$) 291.0740, found: 291.0743.

3-methyl-*N*-phenylquinoxaline-2-carboxamide (4y).[32] The product was isolated by the precipitate filtered, washed with ethyl acetate and ether as a yellow solid (92 mg, 70%): mp 177-179 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.02 (s, 1H), 8.16-8.08 (m, 2H), 7.86 (m, 1H), 7.82-7.78 (m, 3H), 7.42 (t, J = 8.0 Hz, 2H), 7.19 (t, J = 7.4 Hz, 1H), 3.22 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.2, 154.6, 143.1, 142.8, 138.9, 137.7, 131.9, 130.0, 129.2, 128.6, 124.7, 120.0, 25.1; IR (KBr, neat): v = 3349, 3055, 2991, 1694, 1595, 1526, 1482, 1441, 1423, 1373, 1315, 1137, 1067, 1008, 912, 881, 779, 758 cm^{-1}; HRMS (ESI), *m/z* calcd. for $C_{16}H_{13}N_3O$ ($[M+Na]^+$) 286.0951, found: 286.0940.

3-methylquinoxaline-2-carboxamide (4z).[33] The product was isolated by the precipitate filtered, washed with ethyl acetate and ether as a yellow solid (38 mg, 41%): mp 192-194 ^{o}C; ^{1}H NMR (400

MHz, $CDCl_3$) δ 8.09-8.05 (m, 2H), 7.89 (d, J = 6.8 Hz, 1H), 7.86-7.81 (m, 1H), 7.74-7.78 (m, 1H), 5.70 (s, 1H), 3.14 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.2, 154.3, 143.1, 142.7, 139.2, 131.8, 129.7, 129.3, 128.5, 24.8; IR (KBr, neat): v = 3449, 3264, 3180, 1703, 1583, 1566, 1467, 1412, 1369, 1342, 1211, 1139, 1030, 956, 821 ,787, 754 cm^{-1}; HRMS (ESI), *m/z* calcd. for $C_{10}H_9N_3O$ ($[M+H]^+$) 188.0818, found: 188.0817.

***N,N*,3-trimethylquinoxaline-2-carboxamide (4a').**[34] The product was isolated by flash chromatography (eluent: EA/PE = 1/2)as a yellow liquid (89 mg, 83%); ^1H NMR (400 MHz, $CDCl_3$) δ 8.04 (m, 2H), 7.80-7.70 (m, 2H), 3.22 (s, 3H), 2.94 (s, 3H), 2.76 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.5, 151.3, 149.7, 141.6, 139.7, 130.8, 129.7, 129.0, 128.4, 38.2, 34.9, 21.9; IR (KBr, neat): v = 3449, 3068, 2995, 1642, 1502, 1485, 1410, 1321, 1260, 1184, 1123, 1061, 1007, 886, 765 cm-1; HRMS (ESI), m/z calcd. for $C_{12}H_{13}N_3O$ ([M+H]+) 216.1131, found: 216.1127.

3-(*tert*-butyl)-*N*-phenylquinoxaline-2-carboxamide (4b'). The product was isolated by the precipitate filtered, washed with ether as a yellow solid (78 mg, 85%): mp 217-219 ºC; ^1H NMR (600 MHz, DMSO) δ 10.82 (s, 1H), 8.14 (d, J = 7.8 Hz, 1H), 8.10 (d, J = 7.8 Hz, 1H), 7.94-7.86 (m, 2H), 7.73 (d, J = 7.8 Hz, 2H), 7.40 (t, J = 7.8 Hz, 2H), 7.16 (t, J = 7.5 Hz, 1H), 1.52 (s, 9H); ^{13}C NMR (151 MHz, DMSO) δ 167.1, 160.4, 149.7, 140.8, 139.2, 138.8, 131.5, 130.8, 129.5, 129.2, 128.8, 124.6, 120.0, 39.2, 30.0; IR (KBr, neat): v = 3283, 3254, 1655, 1607, 1561, 1445, 1330, 1166, 1113, 1057, 767, 756 cm^{-1}; HRMS (ESI), *m/z* calcd. for $C_{19}H_{19}N_3O$ ($[M+H]^+$) 306.1601, found: 306.1600.

3-butyl-*N*-phenylquinoxaline-2-carboxamide (4c'). The product was isolated by flash chromatography (eluent: EA/PE = 3/10) as a white solid (133 mg, 87%) : mp 119-121 ºC; ^1H NMR (600 MHz, $CDCl_3$) δ 10.00 (s, 1H), 8.12 (t, J = 7.5 Hz, 2H), 7.85 (t, J = 7.5 Hz, 1H), 7.79 (t, J = 8.7 Hz, 3H), 7.42 (t, J = 7.8 Hz, 2H), 7.19 (t, J = 7.5 Hz, 1H), 3.62 (t, J = 7.8 Hz, 2H), 1.91-1.83 (m, 2H), 1.54 (m, 2H), 0.99 (t, J = 7.2 Hz, 3H); ^{13}C NMR (151 MHz, CDC_{l3}) δ 162.2, 158.5, 143.2, 142.8, 138.7, 137.7, 131.7, 129.9, 129.2, 129.1, 128.8, 124.6, 120.0, 36.8, 31.8, 23.0, 14.1; IR (KBr, neat): v

= 3349, 2956, 1689, 1599, 1531, 1446, 1361, 1315, 1131, 1070, 913, 777, 755 cm^{-1}; HRMS (ESI), *m/z* calcd. for $C_{19}H_{19}N_3O$ ($[M+H]^+$) 306.1601, found: 306.1588.

Methyl 3-butylquinoxaline-2-carboxylate (4d'). The product was isolated by flash chromatography (eluent: EA/PE = 3/10) as a colorless oil (92 mg, 75%); ^1H NMR (600 MHz, $CDCl_3$) δ 8.17 (d, J = 8.4 Hz, 1H), 8.07 (d, J = 8.4 Hz, 1H), 7.83 (t, J = 7.5 Hz, 1H), 7.76 (t, J = 7.5 Hz, 1H), 4.08 (s, 3H), 3.25 (t, J = 7.8 Hz, 2H), 1.85-1.77 (m, 2H), 1.48 (m, 2H), 0.98 (t, J = 7.2 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 166.2, 156.6, 144.2, 142.7, 139.7, 131.7, 129.8, 129.7, 128.7, 53.3, 35.8, 31.5, 22.8, 13.9; IR (KBr, neat): v = 3443, 2957, 2872, 1732, 1560, 1483, 1465, 1438, 1324, 1263, 1235, 1193, 1125, 1080, 850, 762 cm^{-1}; HRMS (ESI), *m/z* calcd. for $C_{14}H_{16}N_2O_2$ ($[M+H]^+$) 245.1285, found: 245.1274.

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Supporting Information

Experimental procedure, ^1H and ^{13}C NMR spectra of all compounds. Crystallographic data in CIF or other electronic format. This material is available free of charge via the internet at http://pubs.acs.org.

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