CHAPTER-3

Synthesis of *N*-Aryl *α*–Ketoamides, *α*–Ketoesters, *α*–Ketothioesters and Their Applications in Quinoxalinone Preparation

3.1 Introduction

α–Ketoamide motifs constitute a wide range of natural and biologically relevant compounds [1]. On the other hand, *α*-ketoamides serve as valuable precursors and intermediates in organic synthesis to prepare medicinally important organic molecules, including heterocyclic compounds [2]. Due to their importance, different synthetic procedures [3,4], including direct amidation of *α*-ketoacids [4c, 4j], oxidative amidation of aryl methyl ketones [4g,4i], oxidation of *α*-hydroxyamides [4p] and palladium-catalyzed double carbonylative amidation of aryl halides [4o] etc., have been developed. Despite the proven efficiency of these protocols, some of these methods suffer from potential drawbacks such as the use of metal catalysts, harsh reaction conditions, complex reagents or ligands and elevated temperature, etc., which limit their practical applicability [3].

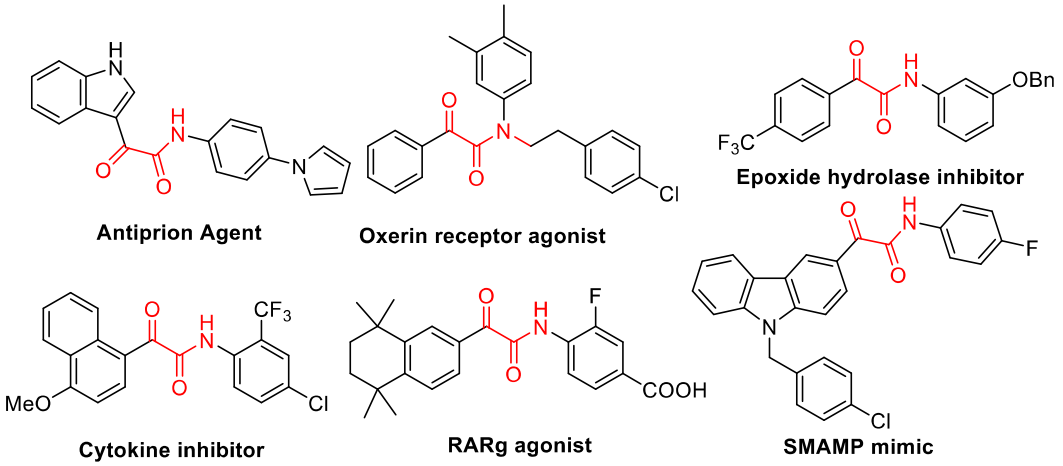
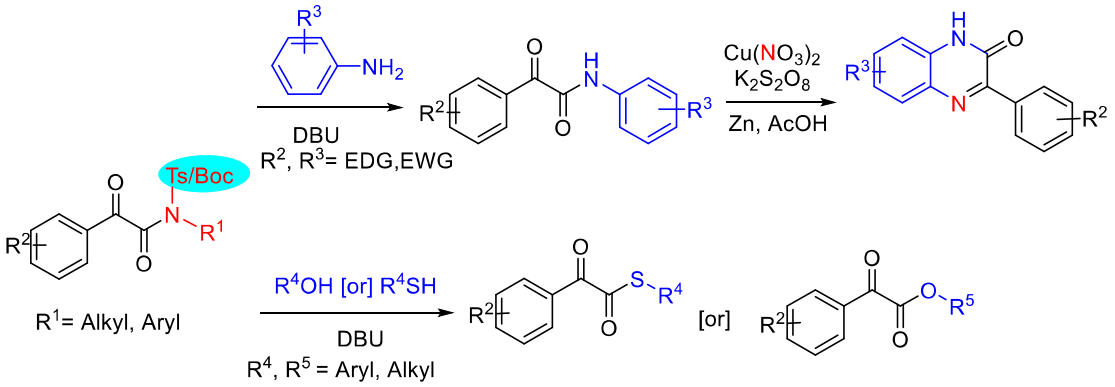


Figure 3.1 Structures of some bioactive aryl α-ketoamides.

Transamidation is an important route widely used for the quick diversification of amides [5]. Recent advancements in the transamidation reactions allow the preparation of the

amides quickly under mild conditions [6]. Over the past few years, our research group has been focusing on the amide activation reactions and reported transamidation of secondary amides *via* *N*-nitroso [7] and *N*-Cbz [8] amide intermediates, syntheses of aryl ketones from *N*-Boc-amides [9], and partial reduction of *N*-Boc and *N*-Ts amides into aldehydes [10]. Moreover, we have recently reported the transamidation approach for the facile synthesis of *N*-alkyl and *N*-benzyl *α*–ketoamides from *N*-tosyl and *N*-Boc *α*–ketoamides at room temperature [11]. Very interestingly, *N*-tosyl *α*-ketoamides underwent transamidation with alkyl amines in the absence of base or catalyst, while Cs_2CO_3 was used to promote the transamidation in *N*-Boc *α*-ketoamides. However, in both cases, arylamines were failed to provide the desired transamidation products. It is not surprising because arylamines are less nucleophilic when compared with alkyl or benzyl amines. It is also worth noting that some of the conventional oxidative amidation methods were also failed to provide the *N*-aryl *α*–ketoamides [3,4e,4f]. Nevertheless, *N*-aryl *α*–ketoamides are important scaffolds in synthetic organic chemistry and medicinal chemistry (**Figure 3.1**) [1-3]. Considering these facts and in continuation of our previous works in transamidation [7-10], here we explored the synthesis of *N*-aryl *α*–ketoamides, *α*–ketoesters and *α*–ketothioesters *via* transamidation reaction in the presence of organic base DBU under metal free conditions (**Scheme 3.1**). In addition, we have also explored the regioselective synthesis of biologically relevant quinoxalinones from *N*-aryl *α*–ketoamides *via* nitration followed by reduction reactions.



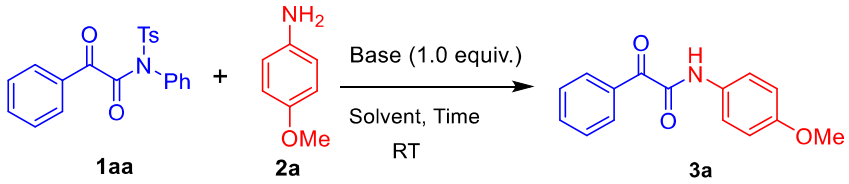
Scheme 3.1 Transamidation of α-ketoamides.

3.2 Results and Discussion

The nucleophilicity of the amine plays an important role in transamidation reactions. In general, arylamines are poor nucleophiles when compared with alkyl amines. In this context, bases can play a key role to facilitate the transamidation process effectively in the case of aryl amines. For instance, it has been shown earlier that the transamidation reaction with aryl amines (anilines) can be achieved in the presence of a strong base (e.g. LiHMDS) [6p] or transition metal catalysts [6b,c,k]. Keeping these facts in mind, at the outset, we have performed the optimization study using *N*-tosyl *N*-phenyl *α*-ketoamide (**1aa**) and 4-methoxyaniline (**2a**) as model substrates. All these reactions were performed in dichloromethane at room temperature. Initially, the reaction was performed in the absence of base (**Table 3.1, entry 1**), which failed to provide any products. Further, the transamidation was investigated in the presence of different organic and inorganic bases including Cs_2CO_3, K_2CO_3, CsF, triethylamine, DABCO, DBU and pyridine (**Table 3.1, entries 2-8**). To our delight, the reaction proceeds with most of the bases and provided the amide **3a** in 5-95% yields. In particular, the reaction with DBU gave the desired product 3a in 95% yield within 30 minutes (**Table 3.1, entry 8**). The high basicity of DBU might be

the reason for better yield. It is also important to mention that the actual basicity of organic and inorganic bases is mainly dependent on their solubility in the reaction medium [12]. In this context, we believe that although Cs_2CO_3 and K_2CO_3 have comparable basicity with DBU [13], their poor solubility in organic solvents would be one of the reasons for observing low yields. Further, the reaction was investigated in different solvents in the presence of DBU (**Table 3.1, entries 9-12**). It was observed that the reaction proceeds better in DCM when compared with other solvents, including THF, toluene, acetonitrile and methanol.

Table 3.1 Optimization of the reaction condition.[a,b]



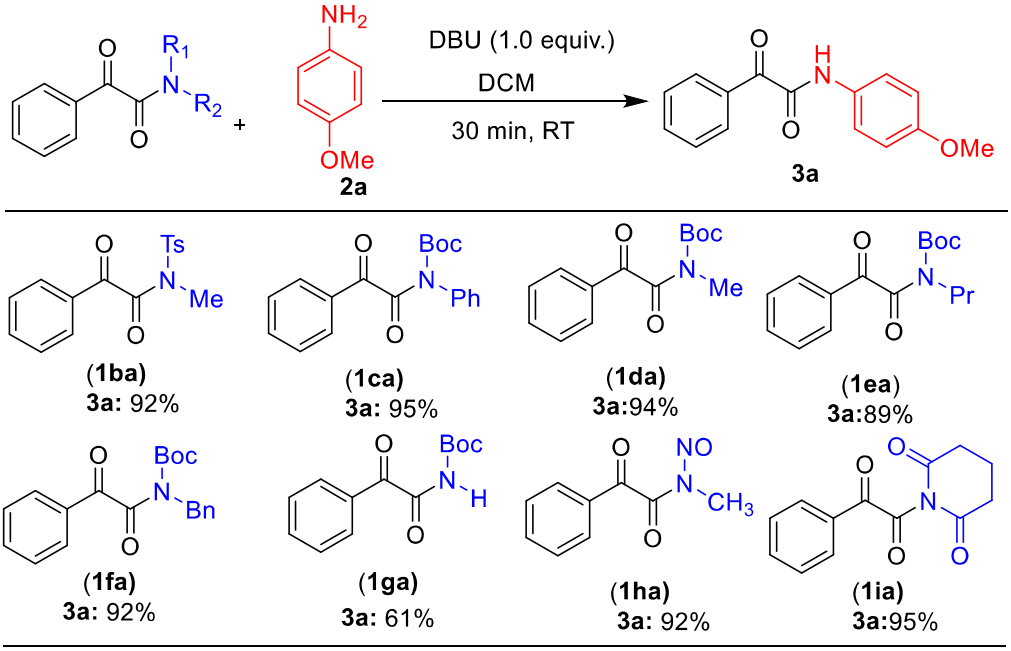
1aa 2a 3a

Entry	Solvent	Base	Time	Yield(%)[b]
1	DCM	-	6 h	nr
2	DCM	Cs_2CO_3	6 h	30
3	DCM	K_2CO_3	6 h	22
4	DCM	CsF	6 h	35
5	DCM	Et_3N	6 h	40
6	DCM	DABCO	6 h	60
7	DCM	Pyridine	6 h	5
8	DCM	DBU	30 min	95
9	THF	DBU	30 min	68
10	Toluene	DBU	30 min	70
11	CH_3CN	DBU	30 min	80
12	CH_3OH	DBU	30 min	30

[a]Reaction conditions: Substrate (**1aa**, 189 mg, 0.5 mmol), 4-methoxyaniline (**2a**, 67 mg, 1.1 equiv.) and base in DCM (3 mL) at room temperature. [b]Isolated yields.

We further investigated the transamidation of various activated α–ketoamides such as *N*-tosyl *N*-methyl α–ketoamide (**1ba**), *N*-Boc *N*-phenyl α–ketoamide (**1ca**), *N*-Boc *N*-methyl α–ketoamide (**1da**), and *N*-Boc *N*-propyl α–ketoamide (**1ea**), *N*-Boc *N*-benzyl α–ketoamide (**1fa**), *N*-Boc α–ketoamide (**1ga**), *N*-nitroso α–ketoamide (**1ha**) as well as 2-oxo *N*-acyl glutarimide (**1ia**) with 4-methoxyaniline in the presence of DBU in dichloromethane (**Table 3.2**). To our delight, all these substrates underwent transamidation and provided the desired product **3a** in 61-95% yields. It was observed that the mono-Boc compound **1ga** showed less reactivity and gave the product **3a** in 66% yield.

Table 3.2 Transamidation of various activated α-ketoamides with 4-methoxyaniline.

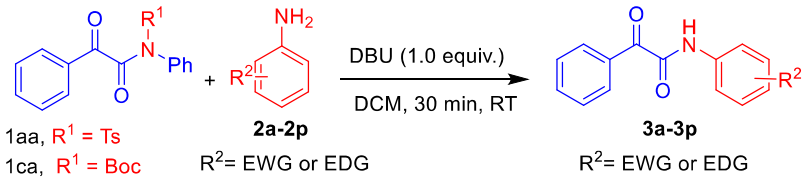


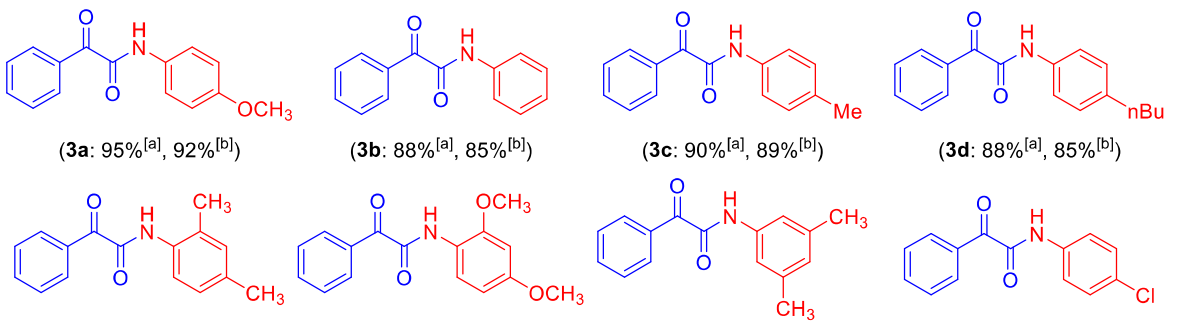
Reaction conditions: Substrate (**1ba-1ia**, 0.5 mmol), DBU (76 µL, 1.0 equiv.), 4-methoxyaniline (67 mg, 1.1 equiv.) in DCM (3 mL) at room temperature. Isolated yields presented.

3.2.1 Substrate scope

Encouraged, the scope of different aryl amines in transamidation was investigated with *N*-tosyl *N*-phenyl *α*–ketoamide (**1aa**) and *N*-Boc *N*-phenyl *α*–ketoamide (**1ca**) under optimized condition (**Table 3.3**).

Table 3.3. Transamidation of *N*-tosyl *N*-phenyl and *N*-Boc *N*-phenyl *α*-ketoamides with different anilines.



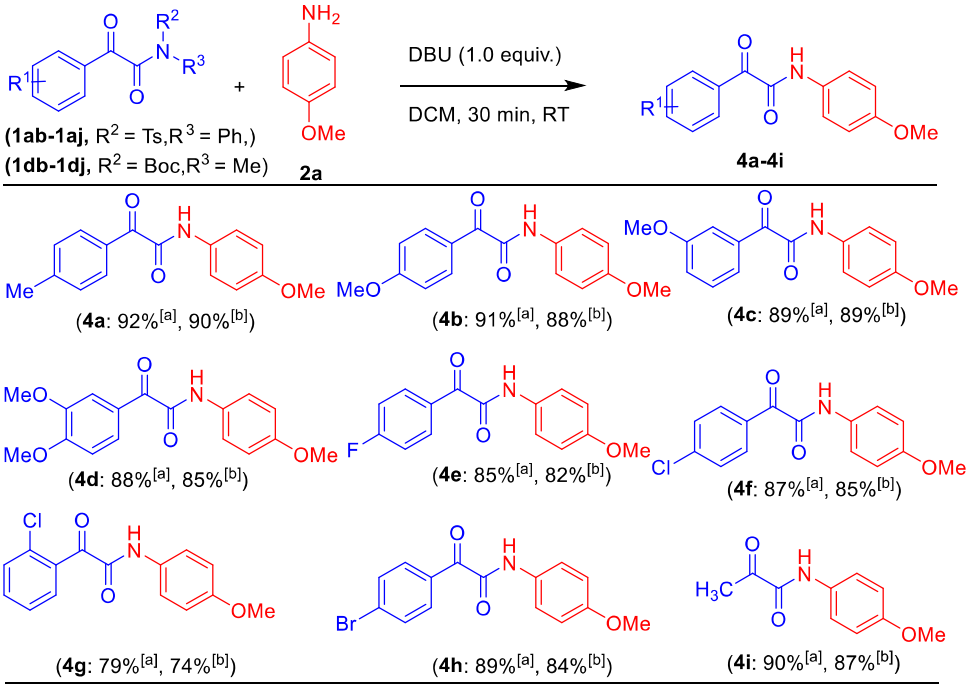


Reaction conditions: Substrate (**1aa, 1ca**: 189 mg, 162 mg, 0.5 mmol), DBU (76 µL, 1.0 equiv.), anilines (**3a-3p**: 1.1 equiv.) in DCM (3 mL) at room temperature. Isolated yields presented. [a] Yield is from **1aa**. [b] Yield is from **1ca**. [c] Reactions were carried out for 6 h.

To our delight, unsubstituted as well as electron-donating groups (e.g. methyl, methoxy, etc.) functionalized anilines participated in the transamidation reactions and gave the desired α-ketoamides **3a-3g** in 85-95% yields within 30 minutes at room temperature.

The yields obtained from *N*-Boc amides are comparable with *N*-Ts amides. On the other hand, transamidation of amides **1aa** and **1ca** with anilines bearing electron-withdrawing groups also gave the corresponding *N*-aryl α–ketoamides (**3h-3n**) in good yields (68-86%) within 30 minutes. However, the strongly electron-withdrawing groups such as nitro and ester functionalized anilines took little longer reaction time (i.e. 6 h) to provide the desired products **3o** and **3p** in 68-74% yields.

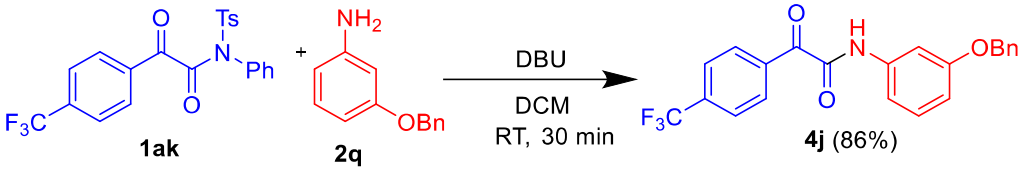
Table 3.4. Transamidation of different *N*-substituted α-ketoamides with 4-methoxyaniline.



Reaction conditions: Substrate (**1ab-1aj** and **1db-1dj** : 0.5 mmol), DBU (76 µL 1.0 equiv.), 4-methoxyaniline (**4a**:67 mg, 1.1 equiv.) in DCM (3 mL) at room temperature. Isolated yields presented. [a] Yield is from *N*-Ts amides. [b] Yield is from *N*-Boc amides.

Further, we have studied the scope of functionalized *N*-Ts and *N*-Boc aryl *α*–ketoamides in transamidation reaction with 4-methoxyaniline (**2a**) under optimized conditions (**Table 3.4**). To our delight, *N*-tosyl *N*-phenyl aryl *α*-ketoamides bearing electron- donating groups and electron-withdrawing groups on the aryl-ring underwent transamidation smoothly. They provided the corresponding *α*–ketoamides **4a-4h** in 79-92% yields. Likewise, various functionalized *N*-Boc *N*-methyl aryl *α*-ketoamides also participated in the transamidation reaction to provide **4a-4h** in 74-90% yields. Similar to aryl *α*–ketoamides, alkyl *α*–ketoamide also gave the desired *N*-aryl *α*–ketoamide **4i** in good yield.

Furthermore, we attempted to obtain a bioactive compound (**4j**), an epoxide hydrolase inhibitor [**1l**], using the developed transamidation protocol. The reaction of *N*-Ts amide **1ak** with aniline **2q** gave the desired product **4j** in 86% yield at room temperature in the presence of DBU (**Scheme 3.2**).

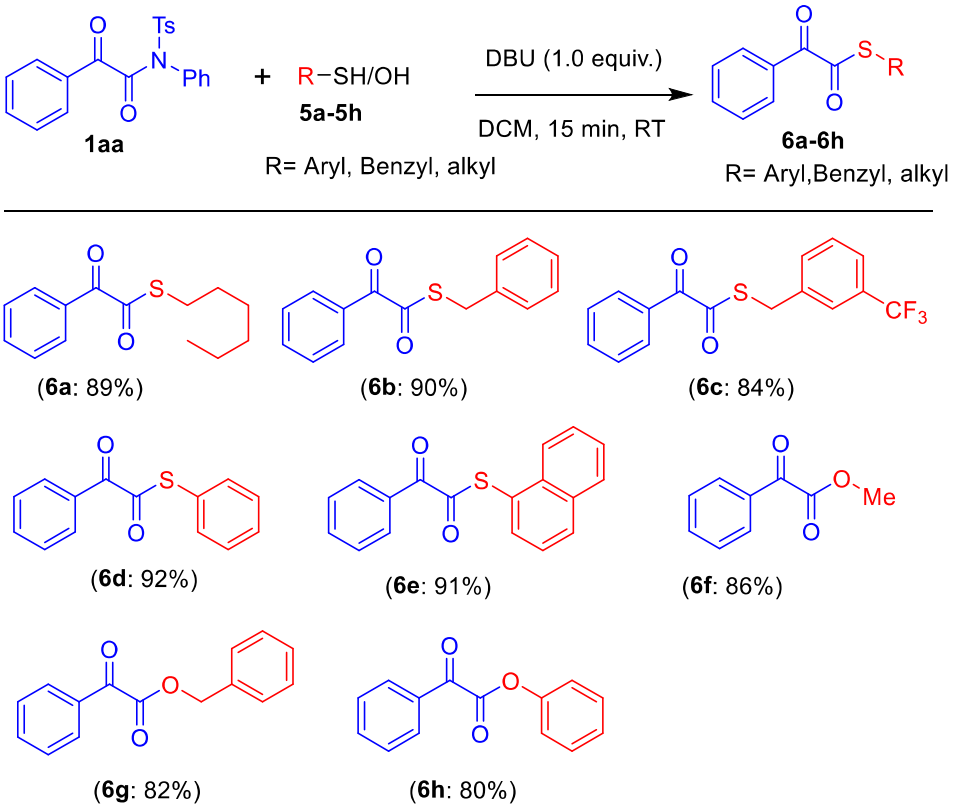


Scheme 3.2. Synthesis of epoxide hydrolase inhibitor (**4j**).

Transformation of carboxylic amides into esters and thioesters are important reactions in organic synthesis. After exploring the transamidation of *α*–ketoamides with various aryl amines, we extended our investigation with the oxygen and sulfur nucleophiles under optimized conditions (**Table 3.5**). The reaction of 1-hexane thiol, benzyl mercaptans (**5a-5c**) and thiophenols (**5d, 5e**) with *N*-tosyl *N*-phenyl *α*–ketoamide (**1aa**) gave the desired

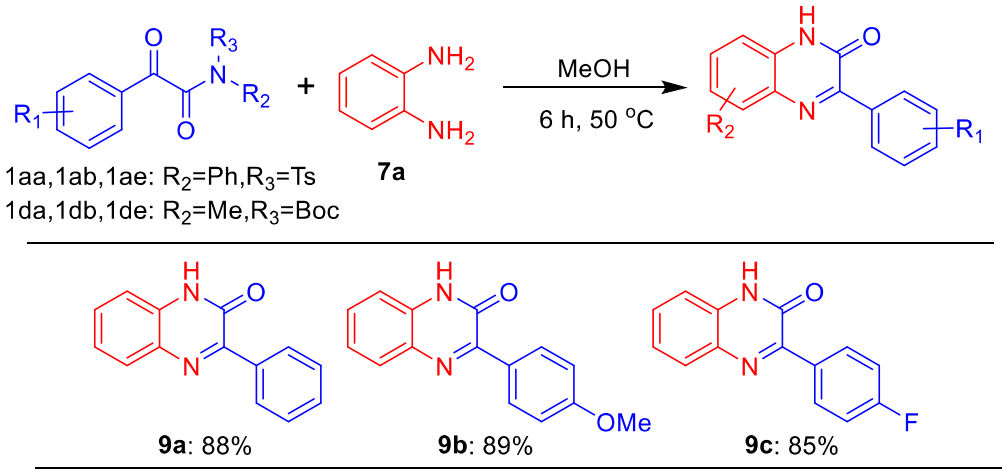
thioesters (**6a-6e**) in excellent yields (84-92%) in a short time. Moreover, methanol, benzyl alcohol and less nucleophilic phenol were also compatible with the reaction conditions and gave the desired transesterification products **6f-6h** in 80-86% yields. In fact, esterification reaction of *N*-tosyl amide was found to be relatively faster than the transamidation reactions. However, the substrates *N*-Boc *N*-phenyl *α*–ketoamide (**1ca**) and *N*-Boc *N*-methyl *α*–ketoamide (**1da**) were found to be inert for the esterification reactions.

Table 3.5 Esterification of *N*-tosyl *N*-phenyl *α*-ketoamide (**1aa**) with different nucleophiles.



Reaction conditions: Substrate (**1aa**: 189 mg, 0.5 mmol), DBU (76 µL, 1.0 equiv.), nucleophiles (**5a-5h**: 1.1 equiv.) in DCM (3 mL) at room temperature. Isolated yields presented.

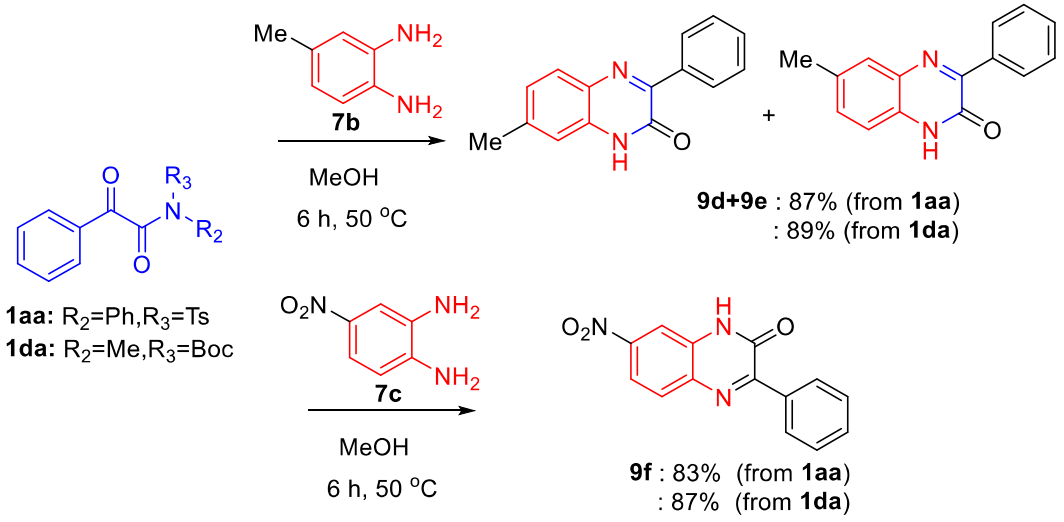
Quinoxalinone nucleus is found in many bioactive molecules and display various medicinal properties, including antimicrobial, analgesic, anti-allergic, anticancer, antiviral and antithrombotic activities [14,15]. Considering their biological potential, we attempted the synthesis of quinoxalinone molecules via transamidation reaction from activated *α*-ketoamides and *o*-phenylenediamines. However, the reaction was not successful under the established transamidation condition (i.e. with DBU in DCM). Hence, the reaction was attempted in methanol at 50 °C in the absence of a base. To our delight, quinoxalinones derivatives, **9a-9c** was obtained in good to excellent yields via transamidation followed by cyclization (**Scheme 3.3**).



Scheme 3.3 Synthesis of quinoxalinones from *N*-Boc *N*-methyl *α*-ketoamides and *ortho*-phenylenediamines. Reaction conditions: Substrate (**1aa and 1da**: 0.5 mmol), *ortho*-phenylenediamines(**7a**: 47 mg) in methanol (3 mL) at 50 °C. Isolated yields presented.

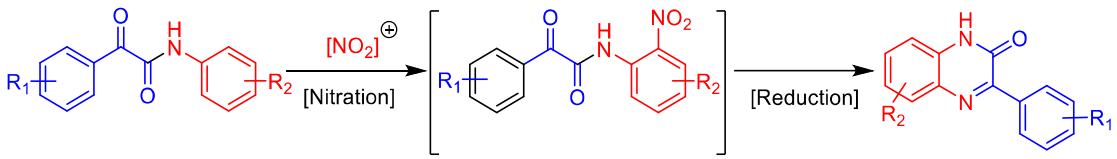
In the case of unsymmetrical *ortho*-phenylenediamines, different regioselective quinoxalinone products were observed (**Scheme 3.4**). For instance, the reaction of 4-methyl 1,2-phenylenediamine with *α*-ketoamide **1aa** or **1da** provides a mixture of **9d** and **9e** in 1:1

ratio while the quinoxalinone **9e** was obtained as the major product from 4-nitro-1,2-phenylenediamine.



Scheme 3.4 Regioselectivity in quinoxalinone synthesis. Reaction conditions: Substrate **(1aa, 1da**: 0.5 mmol), ortho-phenylenediamines (**7b, 7c**: 55 mg, 67 mg 1.1 equiv.) in methanol (3 mL) at 50°C. isolated yields presented.

Nevertheless, to avoid these regioselective issues, we envisioned an alternative two-step route for the regioselective preparation of quinoxalinones from *N*-aryl *α*-ketoamides via nitration followed by reduction as shown in **Scheme 3.5**.

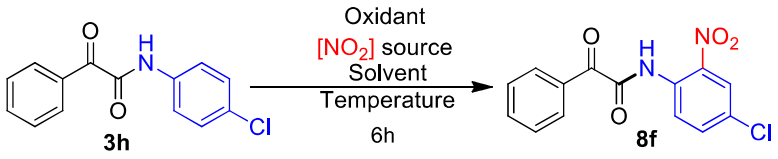


Scheme 3.5 Regioselective preparation of quinoxalinones from *N*-aryl *α*-ketoamides.

However, unlike *N*-acyl anilines, there is no existing protocol found in the literature for the nitration of *N*-aryl *α*-ketoamides. Hence, in the beginning, optimization of ortho-nitration of *N*-aryl *α*-ketoamides was investigated using *N*-(4-chlorophenyl)-2-oxo-2-

phenylacetamide (**3h**) as a model substrate under different nitration conditions (**Table 3.6**). In particular, we focused on the previous procedures that were reported for the nitration of simple *N*-acyl and *N*-sulfonyl anilines [16]. This includes, HNO_3/H_2SO_4 [16a], TBN or $TBN/Cu(NO_3)_2.3H_2O$ [16b,f,g,h], $HNO_3/Cu(NO_3)_2$ [16c], $NaNO_2/PhI(OAc)_2$ [16d], $NaNO_2/KHSO_5$ [16e], and $NaNO_2/K_2S_2O_8$ [16i]. However, none of these reagents gave the desired product in satisfactory yields.

Table 3.6 *ortho*-Nitration of *N*-(4-chlorophenyl)-2-oxo-2-phenylacetamide (**3h**) under different conditions.

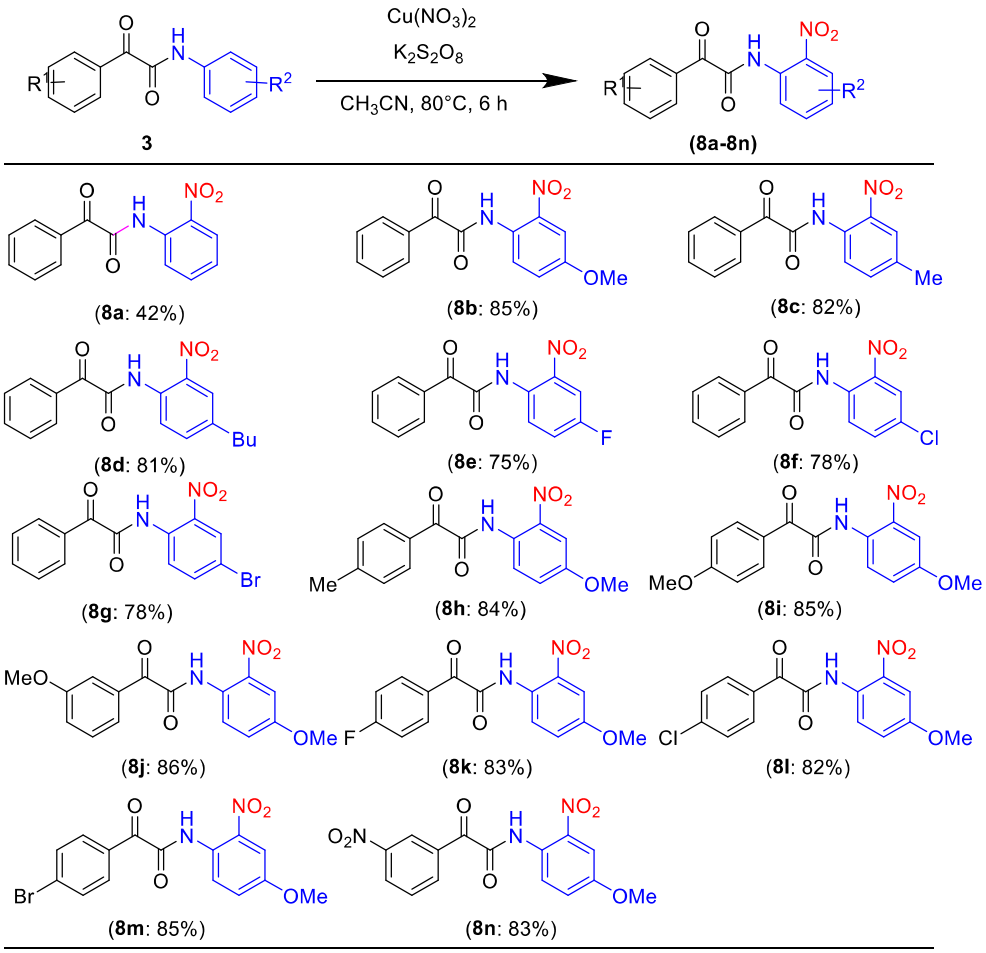


Entry	Solvent	Oxidant	[NO_2] Source	Temp (°C)	Yield (%)[b]
1	CH_3CN	$Cu(NO_3)_2$	TBN	80	<10
2	CH_3CN	$Cu(NO_3)_2$	HNO_3	100	45
3	CH_3CN	$PhI(OAc)_2$	$NaNO_2$	100	<5
4	CH_3CN	Oxone	$NaNO_2$	100	<5
5	CH_3CN	$K_2S_2O_8$	$NaNO_2$	100	<5
6	CH_3CN	$PhI(OAc)_2$	TBN	80	5
7	CH_3CN	$K_2S_2O_8$	$Bi(NO_3)_3$	100	60
8	CH_3CN	$K_2S_2O_8$	HNO_3	100	<30
9	CH_3CN	$K_2S_2O_8$	$Cu(NO_3)_2$	80	80
10	CH_3NO_2	$K_2S_2O_8$	$Cu(NO_3)_2$	80	50
11	Dioxane	$K_2S_2O_8$	$Cu(NO_3)_2$	80	0
12	DCE	$K_2S_2O_8$	$Cu(NO_3)_2$	80	40
13	MeOH	$K_2S_2O_8$	$Cu(NO_3)_2$	80	0
14	Toluene	$K_2S_2O_8$	$Cu(NO_3)_2$	80	<10
15	THF	$K_2S_2O_8$	$Cu(NO_3)_2$	80	0

Reaction conditions: Substrate (130 mg, 0.5 mmol), NO_2 source (1.0 equiv.), oxidant (1.0 equiv.) in solvent (3 mL). Isolated yields.

Hence, the nitration reaction was further optimized with different nitro source and oxidant combinations such as TBN/$PhI(OAc)_2$ (**Table 3.6, entry 6**), $Bi(NO_3)_3/K_2S_2O_8$ (**Table 3.6, entry 7**), $HNO_3/K_2S_2O_8$ (**Table 3.6, entry 8**), $Cu(NO_3)_2/K_2S_2O_8$ (**Table 3.6, entry 9**). To our delight, $Cu(NO_3)_2/K_2S_2O_8$ system in acetonitrile provided the desired nitration product **8f** in 78% yield in acetonitrile at 80 °C in 6 h.

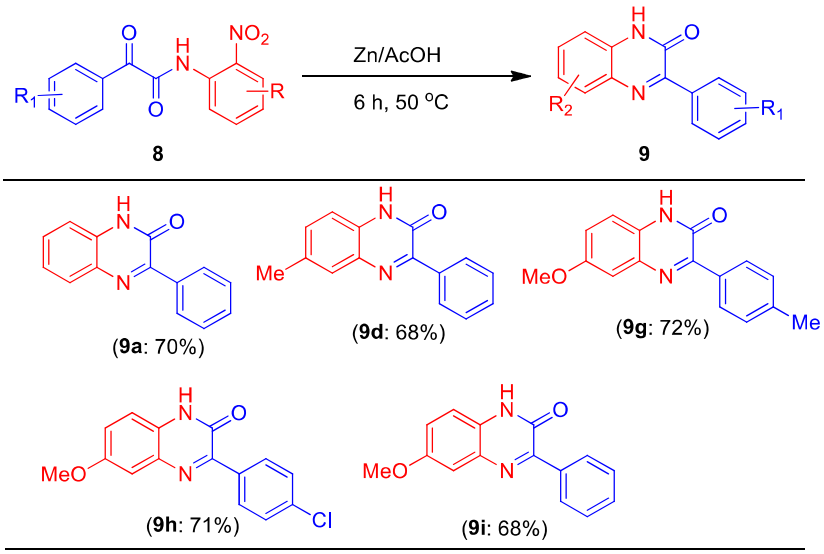
Table 3.7 *ortho*-Nitration of different α-ketoamides with copper(II) nitrate.



Reaction conditions: Substrate (0.5 mmol), copper nitrate trihydrate (120 mg, 1.0 equiv.), potassium persulfate (135 mg, 1.0 equiv.) in solvent (3 mL) at 80 °C. Isolated yields presented.

Having the optimized conditions in hand, we attempted the *ortho*-nitration of different *para*-substituted *α*-Ketoamides (**Table 3.7**). To our satisfaction, *N*-aryl *α*-ketoamides bearing electron-donating (methoxy, methyl and *n*-Butyl,) and electron-withdrawing groups (chloro, fluoro and bromo) at the *para*-position of *N*-aryl ring gave the *ortho*-nitrated products **8a-8g** in good yields (42-85%). On the other hand, *N*-aryl *α*-ketoamides bearing different acyl groups also underwent nitration and gave the desired nitro products 8h-8n in good to excellent yields (i.e. 82-86%).

Table 3.8. Synthesis of quinoxalinones from different *ortho-nitro-α*-ketoamides.



Reaction conditions: Substrate (0.5 mmol), zinc (4.0 equiv.) in MeOH:AcOH (3:1) at 50 °C. Isolated yields presented.

After establishing the first step, selected *ortho*-nitro *N*-aryl *α*-Ketoamides were subjected to the reduction under different reactions conditions such as Zn(2.0 eq)/NH_4Cl, Zn(2.0 eq)/HCl, Zn(2.0 eq)/AcOH and Zn(4.0 eq)/AcOH (**Table 3.8**). Among all, Zn(4.0 eq)/AcOH system gave the desired quinoxalinones in good yields.

3.3 Conclusion

In conclusion, an efficient and promising strategy for the synthesis of *N*-aryl *α*-ketoamides via transamidation of *N*-Ts and *N*-Boc *α*–ketoamides with aromatic amines was demonstrated in the presence of DBU. Moreover, transesterification of *α*–ketoamides with thiols and alcohols was also successfully achieved in excellent yields in the presence of DBU. Transamidation of *α*–ketoamides with ortho-phenylenediamine in methanol gave biologically relevant quinoxalinone molecules in excellent yields. Alternatively, *N*-aryl *α*–ketoamides were used as the substrates for the regioselective preparation of quinoxalinones in good yields *via ortho*-nitration with $Cu(NO_3)_2/K_2S_2O_8$ followed by reduction with Zn/AcOH.

3.4 Experimental Section

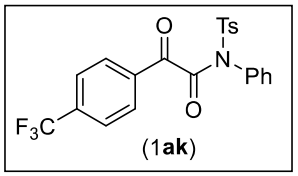
General procedure for the transamidation with aryl amines: To a stirred solution of aniline (0.55 mmol) and DBU (0.55 mmol) in DCM (3 mL) was added *N*-tosyl *N*-phenyl *α*-ketoamide [or] *N*-Boc *N*-phenyl *α*-ketoamide (0.5 mmol) at room temperature. The resulting mixture was allowed to stir for 30 min at room temperature. After completion, the reaction mixture was diluted with water (10 mL) and extracted with EtOAc (30 mL). The combined organic phases were dried over anhydrous Na_2SO_4 and concentrated under vacuum. The residue was purified by column chromatography on silica gel (gradient eluent of EtOAc in petroleum ether) to give the desired products.

General procedure for the nitration of aryl amines: *α*-Keto amide (1.0 mmol), copper nitrate (1.0 mmol, 120 mg) and potassium persulfate (1.0 mmol, 135 mg) were taken in a

pressure tube containing 3 mL of CH_3CN. The resulting mixture was stirred at 80 °C for 6h. On completion, suspension was filtered through celite and concentrated under vacuum. The crude product was purified by column chromatography (SiO_2:100-200 mesh; EtOAc:hexane 20:80).

3.5 Synthesis of 2-oxo-*N*-phenyl-*N*-tosyl-2-(4-(trifluoromethyl)phenyl)acetamide (1ak)

To a solution of 2-oxo-2-(4-(trifluoromethyl)phenyl)acetic acid (1 mmol) in CH_2Cl_2 (2 mL) were added oxalyl chloride (0.1 mL, 1.2 mmol, 1.2 equiv.) and DMF (two drops) at 0 °C. The mixture was stirred until gas evolution stopped. Then, the reaction mixture was concentrated under reduced pressure and was used directly in the next step. To a mixture of the *N*-phenyl sulfonamide (1 mmol), DMAP (0.5 mmol%) and Et_3N (0.155 mL, 2 mmol) in CH_2Cl_2 (10 mL) was added slowly the acyl chloride made above in CH_2Cl_2 (2 ml) at 0oC. The reaction mixture was stirred at room temperature for 2 h. Then the reaction mixture was washed with 5% HCl, brine and H_2O. The organic layer was dried over Na_2SO_4, filtered and evaporated under reduced pressure to give crude product, which was purified by column chromatography on silica gel to afford *N*-tosyl *α*-ketoamides **1ak**.



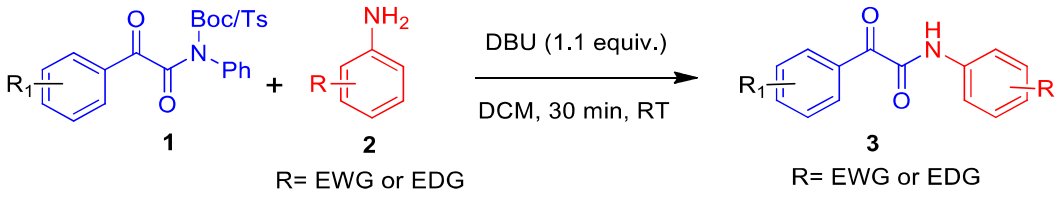
(1**ak**)

The title compound was obtained as a pale white solid, M.p. 145–148 °C. The residue was purified by column chromatography in silica gel eluting with hexane: EtOAc (80:20), R_f = 0.52, Yield 85% (379 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.09 (d, J = 8.1 Hz, 2H), 7.81 (d, J = 8.3

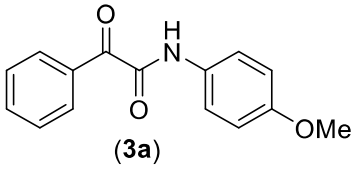
Hz, 2H), 7.70 (d, J = 8.2 Hz, 2H), 7.49–7.44 (m, 1H), 7.41 (t, J = 7.7 Hz, 2H), 7.35 (d, J = 8.3 Hz, 2H), 7.13 (d, J = 7.4 Hz, 2H), 2.48 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 186.3, 166.2, 146.1, 135.58 (q, J = 32.5 Hz), 135.4, 133.6, 133.1, 130.3, 129.8, 129.8, 129.5, 128.9, 125.99 (q, J = 3.75 Hz), 123.35 (q, J = 271.25 Hz), 21.7. HRMS: Calc. for $C_{22}H_{17}F_3NSO_4$ $[M+H]^+$: 448.0830, Obser.: 448.0825.

3.6 General procedure for the transamidation with aryl amines:

To a stirred solution of aniline (0.55 mmol) and DBU (0.55 mmol) in DCM (3 mL) was added *N*-tosyl *N*-phenyl *α*-ketoamide [or] *N*-Boc *N*-phenyl *α*-ketoamide (0.5 mmol) at room temperature. The resulting mixture was allowed to stir for 30 min at room temperature. After completion, the reaction mixture was diluted with water (10 mL) and extracted with EtOAc (30 mL). The combined organic phases were dried over anhydrous Na_2SO_4 and concentrated under vacuum. The residue was purified by column chromatography on silica gel (gradient eluent of EtOAc in petroleum ether) to give the desired products **3a-4i**.



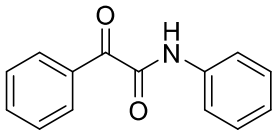
3.6.1. *N*-(4-Methoxyphenyl)-2-oxo-2-phenylacetamide (3a)



(**3a**)

The title compound was obtained as a yellow solid, M.P. 95-97 °C. The residue was purified by column chromatography in silica gel eluting with hexane/EtOAc (90:10), R_f = 0.55, Yield 95% (121 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.88 (s, 1H), 8.42–8.40 (m, 2H), 7.67–7.61(m, 3H), 7.52–7.49 (m, 2H), 6.94–6.91 (m, 2H), 3.82 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 187.5, 158.6, 157.0, 134.5, 133.2, 131.4, 129.7, 128.5, 121.4, 114.3, 55.5.

3.6.2. 2-Oxo-*N*-2-diphenylacetamide (3b)

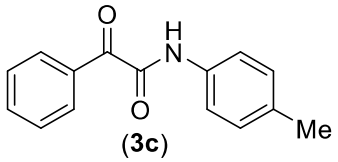


(**3b**)

The title compound was obtained as a pale yellow solid, M.P. 61-62 °C. The residue was purified by column chromatography in silica gel eluting with hexane/EtOAc (90:10), R_f = 0.65, Yield 88% (99 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.97 (s, 1H), 8.43–8.41 (m, 2H), 7.71 (d, J = 8.2 Hz, 2H), 7.66 (dd, J = 10.8, 4.1 Hz, 1H), 7.51 (t, J = 7.8 Hz, 2H), 7.40 (t, J = 7.9 Hz, 2H), 7.20 (t, J = 7.4 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 187.3, 158.8,

136.6, 134.6, 133.0, 131.4, 129.2, 128.5, 125.2, 119.9.

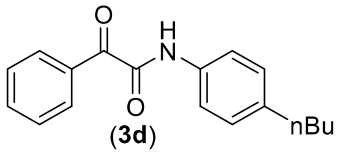
3.6.3. 2-Oxo-2-phenyl-*N*-(*p*-tolyl)acetamide (3c)



(**3c**)

The title compound was obtained as a yellow solid, M.P. 112-114 °C. The residue was purified by column chromatography in silica gel eluting with hexane/EtOAc (90:10), R_f = 0.64, Yield 90% (108 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.89 (s, 1H), 8.43–8.41 (m, 2H), 7.67–7.64 (m, 1H), 7.59 (d, J = 8.4 Hz, 2H), 7.49 (t, J = 7.8 Hz, 2H), 7.20 (d, J = 8.3 Hz, 2H), 2.33 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 187.5, 158.7, 135.0, 134.5, 134.0, 133.1, 131.4, 129.7, 128.5, 119.8, 20.9.

3.6.4. *N*-(4-Butylphenyl)-2-oxo-2-phenylacetamide (3d)

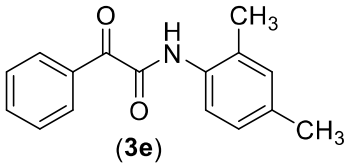


(**3d**)

The title compound was obtained as a yellow solid, M.P. 95-97 °C. The residue was purified by column chromatography in silica gel eluting with hexane/EtOAc (90:10), R_f = 0.55, Yield 88% (124 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.92 (s, 1H),

8.41 (d, J = 7.3 Hz, 2H), 7.68–7.59 (m, 3H), 7.51 (t, J = 7.8 Hz, 2H), 7.21 (d, J = 8.4 Hz, 2H), 2.63–2.59 (m, 2H), 1.64–1.56 (m, 2H), 1.39-1.32 (m, 2H), 0.93 (t, J = 7.4 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 187.5, 140.1, 134.5, 134.2, 133.1, 131.4, 129.0, 128.5, 119.8, 35.1, 33.58, 22.2, 13.9.

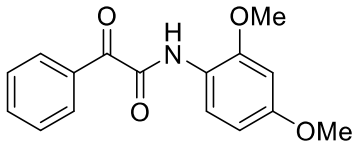
3.6.5. *N*-(2,4-Dimethylphenyl)-2-oxo-2-phenylacetamide (3e)



(**3e**)

The title compound was obtained as a yellow gum. The residue was purified by column chromatography in silica gel eluting with hexane/EtOAc (90:10), R_f = 0.66, Yield 88% (111 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.85 (s, 1H), 8.44 (dt, J = 8.5, 1.4 Hz, 2H), 7.94 (d, J = 8.1 Hz, 1H), 7.66 (t, J = 7.4 Hz, 1H), 7.54–7.48 (m, 2H), 7.09–7.06 (m, 2H), 2.33 (s, 3H), 2.33 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 187.6, 158.8, 135.4, 134.5, 133.1, 131.9, 131.4, I31.3, 128.8, 128.5, 127.4, 121.8, 20.9, 17.5.

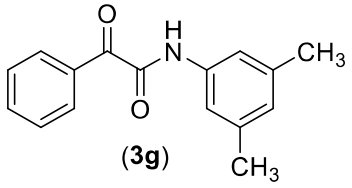
3.6.6. *N*-(2,4-Dimethoxyphenyl)-2-oxo-2-phenylacetamide (3f)



(**3f**)

The title compound was obtained as a white solid, M.P. 46-48 °C. The residue was purified by column chromatography in silica gel eluting with hexane/EtOAc (90:10), R_f = 0.66, Yield 92% (132 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 9.35 (s, 1H), 8.41–8.38 (m, 3H), 7.64 (t, J = 7.4 Hz, 1H), 7.51 (t, J = 7.8 Hz, 2H), 6.54–6.51 (m, 2H), 3.91 (s, 3H), 3.82 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 187.6, 158.5, 157.3, 150.1, 134.3, 133.3, 131.3, 128.4, 120.5, 120.0, 103.7, 98.7, 55.7, 55.5. HRMS: Calc. for $C_{16}H_{16}NO_4$ $[M+Na]^+$: 286.1075, Obser.: 286.1079.

3.6.7. *N*-(3,5-Dimethylphenyl)-2-oxo-2-phenylacetamide (3g)

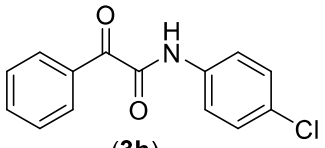


(**3g**)

The title compound was obtained as a yellow solid, M.P. 108-108.5 °C. The residue was purified by column chromatography in silica gel eluting with hexane/EtOAc (90:10), R_f = 0.65, Yield 89% (113 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.87 (s, 1H), 8.42 (dt, J = 8.5, 1.5 Hz, 2H), 7.68–7.62 (m, 1H), 7.53–7.48 (m, 2H), 7.34 (s, 2H), 6.85 (s, 1H), 2.34

(s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 187.4, 158.7, 138.9, 136.4, 134.5, 133.1, 131.4, 128.5, 127.0, 117.6, 21.3.

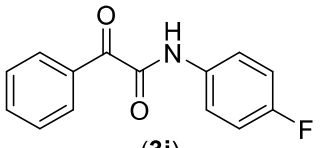
3.6.8. *N*-(4-Chlorophenyl)-2-oxo-2-phenylacetamide (3h)



(**3h**)

The title compound was obtained as a light yellow solid, M.P. 157–159 °C. The residue was purified by column chromatography in silica gel eluting with hexane/EtOAc (90:10), R_f = 0.63, Yield 86% (112 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ= 9.00 (s, 1H), 8.4–8.39 (m, 2H), 7.68–7.65 (m, 3H), 7.51 (t, *J* = 7.9 Hz, 2H), 7.37–7.34(m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 187.0, 158.8, 135.2, 134.7, 132.9, 131.5, 130.4, 129.3, 128.6, 121.1.

3.6.9. *N*-(4-Fluorophenyl)-2-oxo-2-phenylacetamide (3i)

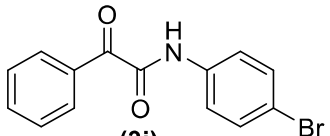


(**3i**)

The title compound was obtained as a light yellow solid, M.P. 114-115 °C. The residue was purified by column chromatography in silica gel eluting with hexane/EtOAc (90:10), R_f = 0.62, Yield 85% (103 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.96 (s, 1H), 8.42–8.40 (m, 2H), 7.69–7.65 (m, 3H), 7.53–7.50

(m, 2H), 7.12–7.07 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 187.2, 159.88 (d, J = 245.73 Hz), 158.7, 134.7, 132.83 (d, J = 40 Hz), 131.4, 128.5, 121.65 (d, J = 7.5 Hz), 116.0, 115.8.

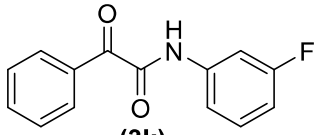
3.6.10. *N*-(4-Bromophenyl)-2-oxo-2-phenylacetamide (3j)



(3j)

The title compound was obtained as a light yellow solid, M.P. 162-162 °C. The residue was purified by column chromatography in silica gel eluting with hexane/EtOAc (90:10), R_f = 0.64, Yield 86% (131 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ= 8.98 (s, 1H), 8.40 (dd, J = 8.2, 1.0 Hz, 2H), 7.67 (dd, J = 10.6, 4.3 Hz, 1H), 7.62–7.60 (m, 2H), 7.53–7.50 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 186.9, 158.7, 135.7, 134.7, 132.9, 132.2, 131.4, 128.6, 121.4, 118.0.

3.6.11. *N*-(3-Fluorophenyl)-2-oxo-2-phenylacetamide (3k)

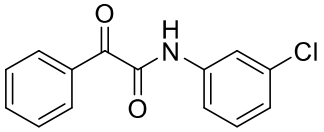


(3k)

The title compound was obtained as a light yellow solid, M.P. 97-98 °C. The residue was purified by column chromatography in silica gel eluting with

hexane/EtOAc (90:10), R_f = 0.59, Yield 80% (98 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 9.03 (s, 1H), 8.41 (dd, J = 5.5, 4.0 Hz, 2H), 7.70–7.65 (m, 2H), 7.51 (dd, J = 11.1, 4.6 Hz, 2H), 7.35–7.33 (m, 2H), 6.92–6.88 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 186.9, 163.9, 162.0, 158.8, 138.06 (d, J = 10.8 Hz), 134.7, 132.8, 131.8, 130.34 (d, J = 9.3 Hz), 128.6, 115.30 (d, J = 3.0 Hz), 112.1, 111.9, 107.5, 107.3.

3.6.12. *N*-(3-Chlorophenyl)-2-oxo-2-phenylacetamide (3l)

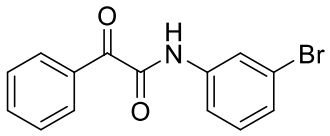


(**3l**)

The title compound was obtained as a light yellow solid, M.P. 115-117 °C. The residue was purified by column chromatography in silica gel eluting with hexane/EtOAc (90:10), R_f = 0.65, Yield 81% (105 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.99 (s, 1H), 8.41 (dd, J = 8.4, 1.3 Hz, 2H), 7.87 (t, J = 2.0 Hz, 1H), 7.69–7.65 (m, 1H), 7.54–7.49 (m, 3H), 7.32 (t, J = 8.1 Hz, 1H), 7.19–7.17 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 186.8, 158.7, 137.7, 134.9, 134.8,

132.8, 131.5, 130.2, 128.6, 125.3, 120.0, 117.8.

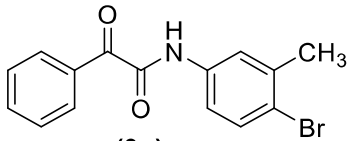
3.6.13. *N*-(3-Bromophenyl)-2-oxo-2-phenylacetamide (3m)



(**3m**)

The title compound was obtained as a light yellow solid, M.P. 103-105 °C. The residue was purified by column chromatography in silica gel eluting with hexane/EtOAc (90:10), R_f = 0.60, Yield 78% (118 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.99 (s, 1H), 8.42–8.40 (m, 2H), 8.00 (t, J = 1.9 Hz, 1H), 7.69–7.65 (m, 1H), 7.59–7.57 (M 1H), 7.53–7.50 (m, 2H), 7.34–7.32 (M, 1H), 7.27–7.24 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 186.8, 158.7, 137.8, 134.8, 132.8, 131.4, 130.4, 128.6, 128.2, 122.8, 122.8, 118.3.

3.6.14. *N*-(4-Bromo-3-methylphenyl)-2-oxo-2-phenylacetamide (3n):

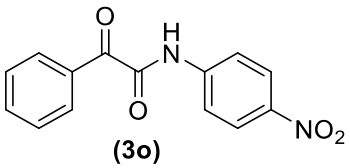


(**3n**)

The title compound was obtained as a yellow solid, M.P. 46-48 °C. The residue was purified by column chromatography in silica gel eluting with hexane/EtOAc (90:10), R_f = 0.59, Yield 79% (126 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.95 (s, 1H), 8.40 (d, J = 7.4 Hz, 2H), 7.68–7.61 (m, 2H), 7.54–

7.48 (m, 3H), 7.40 (dd, J = 8.6, 2.5 Hz, 1H), 2.41 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ = 187.0, 158.7, 138.9, 135.7, 134.7, 132.9, 132.8, 131.4, 128.5, 121.9, 120.6, 118.8, 23.0. HRMS: Calc. for $C_{15}H_{13}BrNO_2$ $[M+Na]^+$: 318.0130, Obser.: 318.0122.

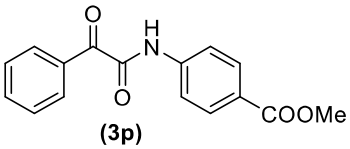
3.6.15. *N*-(4-Nitrophenyl)-2-oxo-2-phenylacetamide (3o)



(3o)

The title compound was obtained as a yellow solid, M.P. 170-172 °C. The residue was purified by column chromatography in silica gel eluting with hexane/EtOAc (80:20), R_f = 0.50, Yield 74% (100 mg). ^{1}H NMR (500 MHz, $CDCl_3$+DMSO-d_6) δ = 10.57 (s, 1H), 8.14–8.06 (m, 3H), 7.99–7.82 (m, 2H), 7.53 (s, 1H), 7.39 (d, J = 6.3 Hz, 2H), 7.24 (dd, J = 3.4, 1.6 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 187.2, 161.2, 143.3, 143.0, 134.2, 130.3, 128.2, 124.2, 119.6.

3.6.16. Methyl 4-(2-oxo-2-phenylacetamido)benzoate (3p)

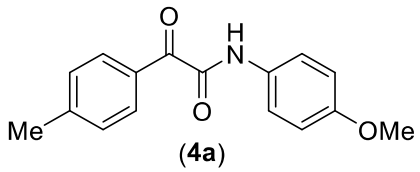


(3p)

The title compound was obtained as a yellow solid, M.P. 75-77 °C. The residue was purified by column

chromatography in silica gel eluting with hexane/EtOAc (90:10), R_f = 0.40, Yield 74% (105 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 9.15 (s, 1H), 8.44–8.38 (m, 2H), 8.08 (d, *J* = 8.5 Hz, 2H), 7.79 (d, *J* = 8.5 Hz, 2H), 7.67 (t, *J* = 7.2 Hz, 1H), 7.52 (t, *J* = 7.7 Hz, 2H), 3.92 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ =186.8, 166.3, 158.8, 140.6, 134.8, 132.7, 131.4, 130.9, 128.6, 126.6, 119.1, 52.1.

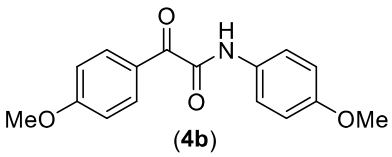
3.6.17. *N*-(4-Methoxyphenyl)-2-oxo-2-(p-tolyl)acetamide (4a)



(**4a**)

The title compound was obtained as a pale-yellow solid, M.P. 129-131 °C. The residue was purified by column chromatography in silica gel eluting with hexane/EtOAc (90:10), R_f = 0.59, Yield 92% (124 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.90 (s, 1H), 8.34 (d, *J* = 8.2 Hz, 2H), 7.65–7.58 (m, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 6.96–6.89 (m, 2H), 3.82 (s, 3H), 2.44 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 187.0, 158.9, 156.9, 145.8, 131.6, 130.6, 129.8, 129.2, 121.4, 114.3, 55.4, 21.8.

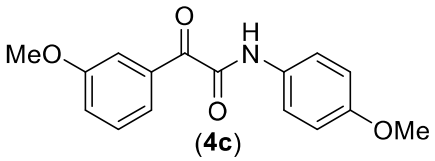
3.6.18. *N*,2-Bis(4-methoxyphenyl)-2-oxoacetamide (4b)



(**4b**)

The title compound was obtained as a yellow solid, M.P. 118-120 °C. The residue was purified by column chromatography in silica gel eluting with hexane/EtOAc (90:10), R_f = 0.63, Yield 91% (130 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.93 (s, 1H), 8.52–8.49 (m, 2H), 7.63–7.60 (m, 2H), 6.98–6.96 (m, 2H), 6.94–6.91 (m, 2H), 3.90 (s, 3H), 3.82 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 185.4, 164.8, 159.2, 156.9, 134.2, 129.9, 126.2, 121.4, 114.3, 113.9, 55.5, 55.4.

3.6.19. 2-(3-Methoxyphenyl)-*N*-(4-methoxyphenyl)-2-oxoacetamide (4c)

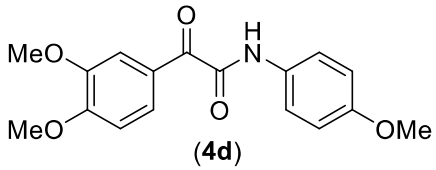


(**4c**)

The title compound was obtained as a yellow solid, M.P. 78-79 °C. The residue was purified by column chromatography in silica gel eluting with hexane/EtOAc (90:10), R_f = 0.58, Yield 89% (127 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.86 (s, 1H), 8.10–8.04 (m, 1H), 7.91 (dd, J = 2.5, 1.5 Hz, 1H), 7.66–7.57 (m, 2H), 7.41 (t, J = 8.0 Hz, 1H), 7.21–7.19 (m 1H), 6.96–6.90 (m, 2H), 3.88 (s, 3H), 3.82 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 187.2,

159.5, 158.6, 157.0, 134.3, 129.7, 129.5, 124.3, 121.6, 121.5, 115.0, 114.3, 55.4.

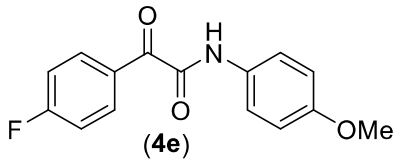
3.6.20. 2-(3,4-Dimethoxyphenyl)-*N*-(4-methoxyphenyl)-2-oxoacetamide (4d)



(**4d**)

The title compound was obtained as a yellow solid, M.P. 132-136 °C. The residue was purified by column chromatography in silica gel eluting with hexane/EtOAc (90:10), R_f = 0.59, Yield 88% (139 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.94 (s, 1H), 8.34 (dd, J = 8.6, 2.0 Hz, 1H), 7.95 (d, J = 1.9 Hz, 1H), 7.63–7.58 (m, 2H), 6.97–6.87 (m, 3H), 3.98 (s, 3H), 3.96 (s, 3H), 3.81 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 185.2, 159.3, 157.0, 154.8, 148.8, 129.8, 127.6, 126.2, 121.5, 114.3, 112.9, 110.2, 56.1, 56.0, 55.4.

3.6.21. 2-(4-Fluorophenyl)-*N*-(4-methoxyphenyl)-2-oxoacetamide (4e)

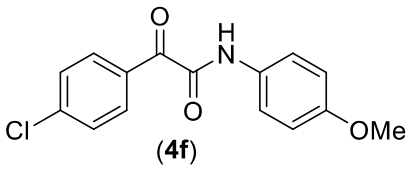


(**4e**)

The title compound was obtained as a yellow solid, M.P. 132-136 °C. The residue was purified by column chromatography in silica gel eluting with hexane/EtOAc (90:10), R_f = 0.61, Yield 85% (116

mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.90 (s, 1H), 8.55–8.50 (m, 2H), 7.64–7.58 (m, 2H), 7.20–7.14 (m, 2H), 6.95–6.90 (m, 2H), 3.82 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 185.7, 166.67 (d, J = 225 Hz), 158.5, 157.1, 135.3, 134.54 (d, J = 10.0 Hz), 129.6, 121.5, 115.83 (d, J = 22.5 Hz), 114.3, 55.5.

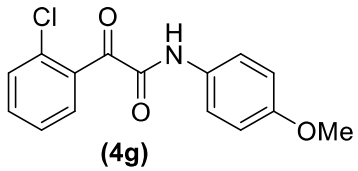
3.6.22. 2-(4-Chlorophenyl)-*N*-(4-methoxyphenyl)-2-oxoacetamide (4f)



(**4f**)

The title compound was obtained as a yellow solid, M.P. 110-111 °C. The residue was purified by column chromatography in silica gel eluting with hexane/EtOAc (90:10), R_f = 0.55, Yield 87% (126 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.88 (s, 1H), 8.47–8.36 (m, 2H), 7.64–7.57 (m, 2H), 7.50–7.44 (m, 2H), 6.98–6.90 (m, 2H), 3.82 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 186.2, 158.3, 157.1, 141.3, 132.9, 131.5, 129.6, 128.9, 121.5, 114.3, 55.4.

3.6.23. 2-(2-Chlorophenyl)-*N*-(4-methoxyphenyl)-2-oxoacetamide (4g)

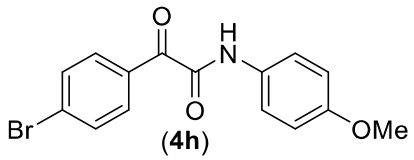


(**4g**)

The title compound was obtained as a yellow solid, M.P. 68-70 °C. The residue was purified by column chromatography in silica gel eluting with

hexane/EtOAc (90:10), R_f = 0.53, Yield 79% (114 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.75 (s, 1H), 7.75–7.70 (m, 1H), 7.64–7.60 (m, 2H), 7.51–7.45 (m, 2H), 7.40–7.37 (m 1H), 6.92 (d, J = 9.0 Hz, 2H), 3.81 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 190.3, 157.5, 157.1, 133.7, 133.1, 131.2, 130.4, 129.6, 126.5, 121.3, 114.4, 55.4. HRMS: Calc. for $C_{15}H_{13}ClNO_3$ $[M+Na]^+$: 290.0584, Obser.: 290.0581.

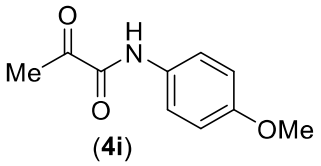
3.6.24. 2-(4-Bromophenyl)-*N*-(4-methoxyphenyl)-2-oxoacetamide (4h)



(**4h**)

The title compound was obtained as a yellow solid, M.P. 114-117 °C. The residue was purified by column chromatography in silica gel eluting with hexane/EtOAc (90:10), R_f = 0.55, Yield 89% (148 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.87 (s, 1H), 8.37–8.30 (m, 2H), 7.69–7.64 (m, 2H), 7.63–7.56 (m, 2H), 6.96–6.90 (m, 2H), 3.82 (s, 3H). ^{13}C NMR (125 = MHz, $CDCl_3$) δ = 186.4, 158.2, 157.1, 132.9, 131.9, 130.3, 129.6, 121.5, 114.4, 55.5.

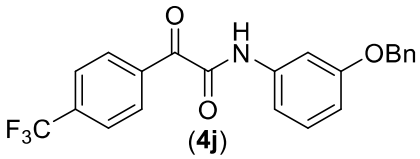
3.6.25. 2-(4-Bromophenyl)-*N*-(4-methoxyphenyl)-2-oxoacetamide (4i)



(**4i**)

The title compound was obtained as a yellowish brown solid, M.P. 118-119°C. The residue was purified by column chromatography in silica gel eluting with hexane/EtOAc (90:20), R_f = 0.32, Yield 90% (87 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.65 (s, 1H), 7.56 (d, J = 9.0 Hz, 2H), 6.90 (d, J = 9.0 Hz, 2H), 3.80 (s, 3H), 2.56 (s, 3H).^{13}C NMR (125 = MHz, $CDCl_3$) δ = 197.5, 157.2, 157.0, 129.4, 121.2, 114.3, 55.4, 24.0.

3.6.26. 2-(4-Bromophenyl)-*N*-(4-methoxyphenyl)-2-oxoacetamide (4j)



(**4j**)

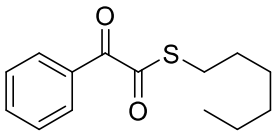
The title compound was obtained as a yellow solid, M.P. 157-160 °C. The residue was purified by column chromatography in silica gel eluting with hexane/EtOAc (90:20), R_f = 0.60, Yield 86% (172 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.97 (s, 1H), 8.51 (d, J = 8.2 Hz, 2H), 7.76 (d, J = 8.3 Hz, 2H), 7.55 (t, J = 2.2 Hz, 1H), 7.46 (d, J = 7.1 Hz, 2H), 7.41 (dd, J = 10.0, 4.7 Hz, 2H), 7.37–7.33 (m, 1H), 7.29 (t, J = 8.1 Hz, 1H), 7.19 (dd, J = 8.0, 1.2 Hz,

1H), 6.84 (dd, J = 8.0, 2.1 Hz, 1H), 5.10 (s, 2H).^{13}C NMR (125 = MHz, $CDCl_3$) δ = 186.4, 159.4, 158.0, 137.4, 136.5, 135.6, 135..4 (q, J =32.5 Hz), 131.7, 129.9, 128.5, 128.0, 127.4, 125.5 (q, J =3.75 Hz), 123.4 (q, J =271.25 Hz), 112.4, 112.2, 106.5, 70.0.

3.7. General procedure for the esterification of *N*-protected *α*-ketoamide with alcohols and thiols:

To a stirred solution of alcohol/phenol/thiol/thiophenol (0.55 mmol) and DBU (0.55 mmol, 65 µL) in DCM (3 mL) was added *N*-tosyl *N*-phenyl *α*-ketoamide (0.5 mmol, 189 mg) at room temperature. The resulting mixture was allowed to stir for 15 min at room temperature. After completion, the reaction mixture was diluted with water (10 mL) and extracted with EtOAc (30 mL). The combined organic phases were dried over anhydrous Na_2SO_4 and concentrated under vacuum. The residue was purified by column chromatography on silica gel (gradient eluent of EtOAc in petroleum ether) to give the desired products **6a-6h.**

3.7.1. *S*-Hexyl 2-oxo-2-phenylethanethioate (6a)

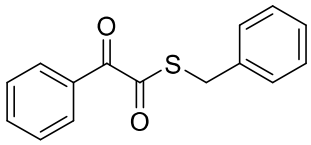


(**6a**)

The title compound was obtained as a yellow oil. The residue was purified by column chromatography in silica gel eluting with

hexane/EtOAc (100:00), R_f = 0.7, Yield 89% (112mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.3–8.05 (m, 2H), 7.72–7.58 (m, 1H), 7.50 (t, J = 7.9 Hz, 2H), 3.15–2.97 (m, 2H), 1.75–1.63 (m, 2H), 1.50–1.37 (m, 2H), 1.36–1.27 (m, 4H), 0.90 (dd, J = 9.1, 4.7 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 193.0, 186.4, 134.7, 131.6, 130.7, 128.7, 31.2, 29.0, 28.8, 28.5, 22.4, 13.9.

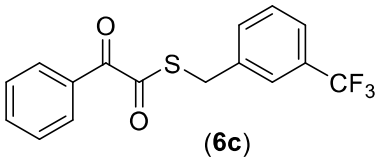
3.7.2. *S*-Benzyl 2-oxo-2-phenylethanethioate (6b)



(**6b**)

The title compound was obtained as a yellow oil. The residue was purified by column chromatography in silica gel eluting with hexane/EtOAc (100:00), R_f = 0.53, Yield 90% (115 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.18–8.10 (m, 2H), 7.68–7.65 (m, 1H), 7.50 (dd, J = 11.7, 4.0 Hz, 2H), 7.40–7.30 (m, 5H), 4.28 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 192.0, 185.9, 136.4, 134.8, 131.6, 130.7, 128.9, 128.8, 128.7, 127.6, 33.2.

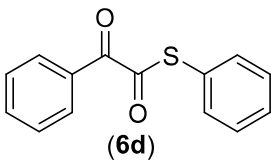
3.7.3. *S*-(3-(trifluoromethyl)benzyl) 2-oxo-2-phenylethanethioate(6c)



(**6c**)

The title compound was obtained as a yellow glue. The residue was purified by column chromatography in silica gel eluting with hexane/EtOAc (100:00), R_f = 0.25, Yield 84% (136 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.14 (dd, J = 8.3, 1.1 Hz, 2H), 7.66 (dd, J = 14.6, 7.1 Hz, 2H), 7.58–7.44 (m, 5H), 4.30 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 191.61, 185.44, 137.72, 135.04, 132.36, 131.46, 131.10 (q, J =32.5 Hz), 130.81, 129.23, 128.8, 125.73 (q, J =3.75 Hz), 124.45 (q, J =3.75 Hz) 123.91 (q, J =271.25 Hz), 32.7. HRMS: Calc. for $C_{16}H_{11}F_3NaSO_2$ $[M+H]^+$: 347.0330, Obser.: 347.0296.

3.7.4. *S*-Phenyl 2-oxo-2-phenylethanethioate (6d)

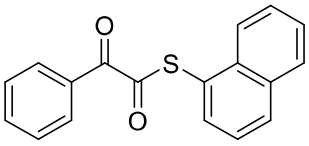


(**6d**)

The title compound was obtained as a yellow liquid. The residue was purified by column chromatography in silica gel eluting with

hexane/EtOAc (100:00), R_f = 0.60, Yield 92% (108 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.18–8.15 (m, 2H), 7.6–7.64 (m, 1H), 7.56–7.44 (m, 6H).^{13}C NMR (125 MHz, $CDCl_3$) δ = 190.96, 185.91, 135.03, 134.65, 131.43, 130.80, 129.94, 129.45, 128.85, 126.32.

3.7.5. *S*-(Naphthalen-1-yl) 2-oxo-2-phenylethanethioate (6e)

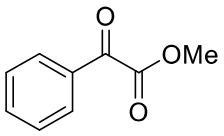


(**6e**)

The title compound was obtained as a yellow liquid. The residue was purified by column chromatography in silica gel eluting with hexane/EtOAc (100:00), R_f = 0.34, Yield 91% (133 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.21 (dd, J = 7.8, 0.8 Hz, 1H), 8.17 (dd, J = 7.5, 0.7 Hz, 2H), 8.02 (d, J = 8.2 Hz, 1H), 7.97–7.90 (m, 1H), 7.79 (d, J = 7.1 Hz, 1H), 7.69–7.63 (m, 1H), 7.63–7.54 (m, 3H), 7.49 (t, J = 7.9 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 190.6, 185.9, 135.2, 135.0, 134.2, 131.4, 131.3, 130.8, 128.8, 128.7, 127.4, 126.6, 125.6, 124.9, 123.71. HRMS: Calc. for $C_{18}H_{12}NaSNO_2$

$[M+H]^+$: 315.0456, Obser.: 315.0427.

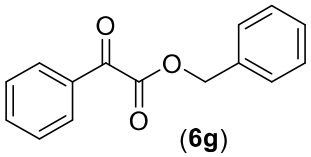
3.7.6. Methyl 2-oxo-2-phenylacetate (6f)



(**6f**)

The title compound was obtained as a colorless oil. The residue was purified by column chromatography in silica gel eluting with hexane/EtOAc (95:05), R_f = 0.6, Yield 86% (70 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.04–7.97 (m, 2H), 7.65 (td, J = 7.7, 0.9 Hz, 1H), 7.50 (t, J = 7.7 Hz, 2H), 3.97 (s, 3H).^{13}C NMR (125 MHz, $CDCl_3$) δ = 186.0, 163.9, 134.9, 132.3, 130.0, 128.8, 52.7.

3.7.7. Benzyl 2-oxo-2-phenylacetate (6g)

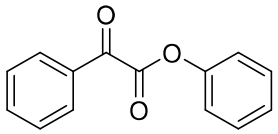


(**6g**)

The title compound was obtained as a colorless oil. The residue was purified by column chromatography in silica gel eluting with hexane/EtOAc (90:10), R_f = 0.55, Yield 82% (99 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.0–7.93 (m, 2H), 7.65 (ddd, J = 5.1, 2.5, 1.2 Hz, 1H), 7.52–7.43 (m, 4H), 7.42–7.35 (m, 3H),

5.42 (s, 2H).^{13}C NMR (125 MHz, $CDCl_3$) δ = 186.0, 163.6, 134.9, 134.5, 132.4, 130.0, 128.8, 128.8, 128.7, 128.6, 67.7.

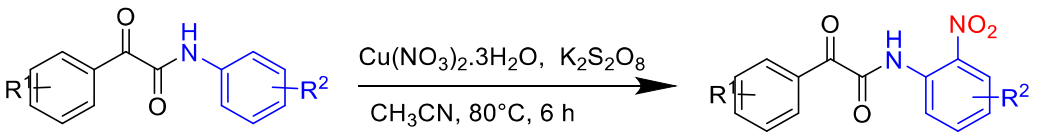
3.7.8. Phenyl 2-oxo-2-phenylacetate (6h)



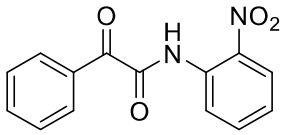
(**6h**)

The title compound was obtained as a colorless oil. The residue was purified by column chromatography in silica gel eluting with hexane/EtOAc (99:01), R_f = 0.6, Yield 80% (91 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.13 (dt, J = 8.5, 1.5 Hz, 2H), 7.75–7.67 (m, 1H), 7.60–7.54 (m, 2H), 7.5–7.43 (m, 2H), 7.35–7.30 (m, 1H), 7.30–7.26 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 185.2, 161.7, 149.8, 135.2, 132.2, 130.1, 129.7, 129.0, 126.7, 121.2.

3.8. General procedure for the nitration of aryl amines: α-Keto amide (1.0 mmol), copper nitrate (1.0 mmol, 120 mg) and potassium persulfate (1.0 mmol, 135 mg) were taken in a pressure tube containing 3 mL of CH_3CN. The resulting mixture was stirred at 80 °C for 6 h. On completion, suspension was filtered through celite and concentrated under vacuum. The crude product was purified by column chromatography (SiO_2:100-200 mesh; EtOAc:hexane 20:80).



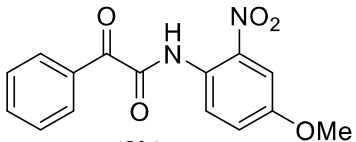
3.8.1. *N*-(2-Nitrophenyl)-2-oxo-2-phenylacetamide (8a)



(**8a**)

The title compound was obtained as a yellow solid, M.P. 95-97 °C. The residue was purified by column chromatography in silica gel eluting with hexane/EtOAc (80:20), R_f = 0.57, Yield 42% (57 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 11.88 (s, 1H), 8.90 (dd, J = 8.5, 1.1 Hz, 1H), 8.46–8.36 (m, 2H), 8.30 (dd, J = 8.4, 1.5 Hz, 1H), 7.77–7.71 (m, 1H), 7.71–7.65 (m, 1H), 7.57–7.50 (m, 2H), 7.32-7.29 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 186.0, 159.8, 137.2, 135.8, 134.8, 133.3, 132.7, 131.4, 128.6, 126.1, 124.4, 121.9.

3.8.2. *N*-(4-Methoxy-2-nitrophenyl)-2-oxo-2-phenylacetamide (8b):

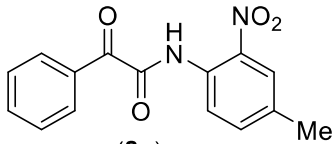


(**8b**)

The title compound was obtained as a yellow solid, M.P. 95-97 °C. The residue was purified by column chromatography in silica

gel eluting with hexane/EtOAc (90:10), R_f = 0.25, Yield 85% (128 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 11.62 (s, 1H), 8.79 (d, J = 9.3 Hz, 1H), 8.44–8.36 (m, 2H), 7.76 (d, J = 3.0 Hz, 1H), 7.71–7.65 (m, 1H), 7.5–7.49 (m, 2H), 7.30 (dd, J = 9.3, 3.0 Hz, 1H), 3.90 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 186.3, 159.6, 155.8, 137.99 (s), 134.7, 132.8, 131.3, 128.6, 126.8, 123.4, 122.9, 109.3, 55.9. HRMS: Calc. for $C_{15}H_{13}N_2O_5$ $[M+H]^+$: 301.0824, Obser. 301.0800.

3.8.3. *N*-(4-Methyl-2-nitrophenyl)-2-oxo-2-phenylacetamide (8c)

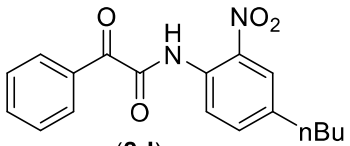


(**8c**)

The title compound was obtained as a yellow solid, M.P. 95-97 °C. The residue was purified by column chromatography in silica gel eluting with hexane/EtOAc (90:10), R_f = 0.38, Yield 82 % (117 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 11.77 (s, 1H), 8.76 (d, J = 8.6 Hz, 1H), 8.40 (dd, J = 8.2, 0.9 Hz, 2H), 8.10 (d, J = 1.1 Hz, 1H), 7.68 (t, J = 7.4 Hz,

1H), 7.53 (dd, *J* = 13.3, 5.8 Hz, 3H), 2.44 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 186.2, 159.7, 137.0, 136.6, 134.9, 134.7, 132.7, 131.3, 130.8, 128.6, 126.0, 121.8, 20.7. HRMS: Calc. for $C_{15}H_{12}N_2O_4$ $[M+H]^+$: 285.0875, Obser.: 285.0848.

3.8.4. *N*-(4-Butyl-2-nitrophenyl)-2-oxo-2-phenylacetamide (8d)

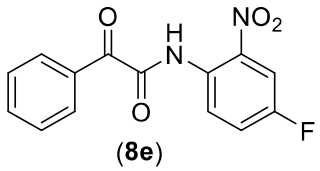


(**8d**)

The title compound was obtained as a yellow solid, M.P. 95-97 °C. The residue was purified by column chromatography in silica gel eluting with hexane/EtOAc (90:10), R_f = 0.28, Yield 81% (132 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 11.76 (s, 1H), 8.81–8.72 (m, 1H), 8.40 (d, *J* = 7.5 Hz, 2H), 8.09 (s, 1H), 7.67 (s, 1H), 7.53 (dd, *J* = 13.6, 7.5 Hz, 3H), 2.69 (t, *J* = 7.0 Hz, 2H), 1.68–1.59 (m, 2H), 1.38 (dq, *J* = 14.1, 7.1 Hz, 2H), 0.95 (td, *J* = 7.3, 2.3 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 186.1, 159.7, 139.9, 137.1, 135.9, 134.7, 132.7, 131.3, 130.9, 128.6, 125.3,

121.8, 34.6, 33.0, 22.1, 13.8. HRMS: Calc. for $C_{18}H_{19}N_2O_4$ $[M+H]^+$: 327.1345, Obser.: 327.1327.

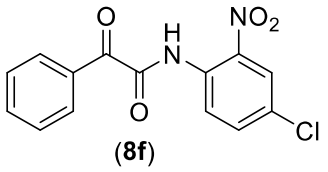
3.8.5. *N*-(4-Fluoro-2-nitrophenyl)-2-oxo-2-phenylacetamide (8e)



(**8e**)

The title compound was obtained as a yellow solid, M.P. 95-97 °C. The residue was purified by column chromatography in silica gel eluting with hexane/EtOAc (90:10), R_f = 0.32, Yield 75% (108 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 11.77 (s, 1H), 8.94 (dd, J = 9.3, 5.1 Hz, 1H), 8.40 (d, J = 7.6 Hz, 2H), 8.02 (dd, J = 8.4, 3.0 Hz, 1H), 7.69 (t, J = 7.4 Hz, 1H), 7.56–7.45 (m, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 185.8, 159.6, 158.7, 156.7, 137.51(d, J = 8.7 Hz), 134.9, 132.6, 131.4, 129.92 (d, J = 3.2 Hz), 128.7, 123.71 (d, J = 7.5 Hz), 123.29 (d, J = 22.5 Hz), 112.98 (d, J = 27.5 Hz). HRMS: Calc. for $C_{14}H_{10}FN_2O_4$ $[M+H]^+$: 389.0625, Obser.: 389.0597.

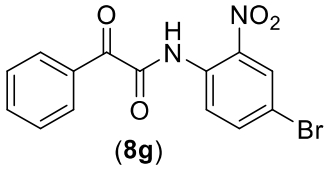
3.8.6. *N*-(4-Chloro-2-nitrophenyl)-2-oxo-2-phenylacetamide (8f)



(**8f**)

The title compound was obtained as a yellow solid, M.P. 95-97 °C. The residue was purified by column chromatography in silica gel eluting with hexane/EtOAc (90:10), R_f = 0.35, Yield 78% (119 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 11.85 (s, 1H), 8.91 (d, J = 9.0 Hz, 1H), 8.40 (d, J = 7.3 Hz, 2H), 8.30 (d, J = 2.4 Hz, 1H), 7.74–7.66 (m, 2H), 7.54 (t, J = 7.8 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 185.6, 159.6, 137.3, 135.8, 134.9, 132.5, 132.0, 131.4, 129.7, 128.7, 125.8, 123.0. HRMS: Calc. for $C_{14}H_9ClN_2NaO_4$ $[M+Na]^+$: 327.0149, Obser.: 327.0123.

3.8.7. *N*-(4-Bromo-2-nitrophenyl)-2-oxo-2-phenylacetamide (8g)

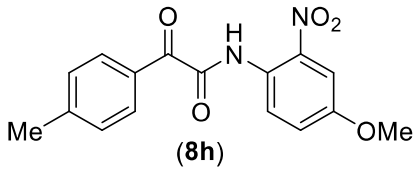


(**8g**)

The title compound was obtained as a yellow solid, M.P. 95-97 °C. The residue was purified by column chromatography in silica gel eluting with hexane/EtOAc (90:10), R_f = 0.35, Yield 78% (136 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 11.82 (s, 1H), 8.83 (d, J =

9.0 Hz, 1H), 8.51–8.31 (m, 3H), 7.88–7.77 (m, 1H), 7.73–7.63 (m, 1H), 7.53 (dd, J = 8.1, 7.5 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 185.6, 159.6, 138.6, 137.4, 134.9, 132.5, 132.4, 131.4, 128.7, 128.6, 123.2, 116.6. HRMS: Calc. for $C_{14}H_9BrN_2NaO_4$ $[M+Na]^+$: 370.9637, Obser.: 370.9607.

3.8.8. *N*-(4-Methoxy-2-nitrophenyl)-2-oxo-2-(p-tolyl)acetamide (8h)

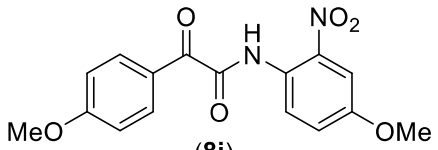


(**8h**)

The title compound was obtained as a yellow solid, M.P. 95-97 °C. The residue was purified by column chromatography in silica gel eluting with hexane/EtOAc (90:10), R_f = 0.30, Yield 84% (131 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 11.62 (s, 1H), 8.79 (d, J = 9.3 Hz, 1H), 8.32 (d, J = 8.2 Hz, 2H), 7.75 (d, J = 3.0 Hz, 1H), 7.35–7.27 (m, 3H), 3.89 (s, 3H), 2.45 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 185.7, 159.8, 155.7, 146.1, 137.9, 131.5, 130.3, 129.3, 126.9, 123.3, 122.9, 109.2, 55.9, 21.9. HRMS: Calc. for

$C_{16}H_{15}N_2O_5$ $[M+H]^+$: 315.0981, Obser.: 315.0956..

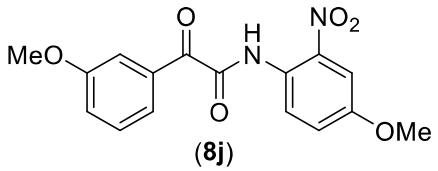
3.8.9. *N*-(4-Methoxy-2-nitrophenyl)-2-(4-methoxyphenyl)-2-oxoacetamide (8i)



(**8i**)

The title compound was obtained as a yellow solid, M.P. 95-97 °C. The residue was purified by column chromatography in silica gel eluting with hexane/EtOAc (90:10), R_f = 0.30, Yield 85% (140 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 11.64 (s, 1H), 8.78 (d, J = 9.3 Hz, 1H), 8.50–8.46 (m, 2H), 7.75 (d, J = 3.0 Hz, 1H), 7.29 (dd, J = 9.3, 3.0 Hz, 1H), 7.00–6.96 (m, 2H), 3.91 (s, 3H), 3.89 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 184.1, 164.9, 160.2, 155.7, 137.9, 134.1, 126.9, 125.8, 123.4, 122.9, 114.0, 109.2, 55.9, 55.6. HRMS: Calc. for $C_{16}H_{15}N_2O_6$ $[M+H]^+$: 331.0930, Obser.: 331.0903.

3.8.10. *N*-(4-Methoxy-2-nitrophenyl)-2-(3-methoxyphenyl)-2-oxoacetamide (8j)

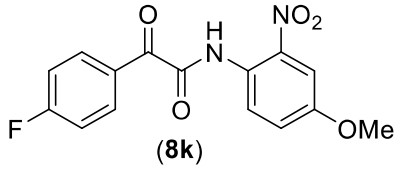


(**8j**)

The title compound was obtained as a yellow solid, M.P. 95-97 °C. The residue was

purified by column chromatography in silica gel eluting with hexane/EtOAc (90:10), R_f = 0.32, Yield 86% (142 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 11.62 (s, 1H), 8.78 (d, J = 9.3 Hz, 1H), 8.06 (dd, J = 7.7, 0.7 Hz, 1H), 7.88 (d, J = 1.5 Hz, 1H), 7.76 (d, J = 3.0 Hz, 1H), 7.43 (t, J = 8.0 Hz, 1H), 7.29 (dd, J = 9.3, 3.0 Hz, 1H), 7.24–7.20 (m, 1H), 3.89 (s, 3H), 3.88 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 186.0, 159.6, 159.5, 155.8, 137.9, 133.9, 129.6, 126.8, 124.3, 123.4, 122.9, 121.8, 114.8, 109.3, 55.9, 55.4. HRMS: Calc. for $C_{16}H_{15}N_2O_6$ $[M+H]^+$: 331.930, Obser.: 331.0906.

3.8.11. 2-(4-Fluorophenyl)-*N*-(4-methoxy-2-nitrophenyl)-2-oxoacetamide (8k)

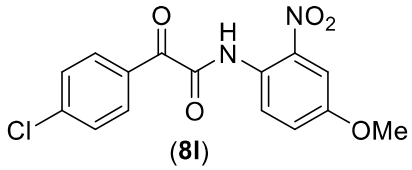


(**8k**)

The title compound was obtained as a yellow solid, M.P. 95-97 °C. The residue was purified by column chromatography in silica gel eluting with hexane/EtOAc (90:10), R_f = 0.40, Yield 83% (132 mg). ^{1}H NMR (500

MHz, $CDCl_3$) δ = 11.66 (s, 1H), 8.77 (d, J = 9.2 Hz, 1H), 8.51 (dd, J = 8.5, 5.7 Hz, 2H), 7.76 (d, J = 2.7 Hz, 1H), 7.30 (dd, J = 9.2, 2.8 Hz, 1H), 7.19 (t, J = 8.6 Hz, 2H), 3.90 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 184.4, 167.8, 165.7, 159.4, 155.9, 138.0, 134.5, 134.4, 129.3, 126.6, 123.3, 122.9, 121.4, 116.0, 115.8, 114.3, 109.3, 55.9. HRMS: Calc. for $C_{15}H_{11}FN_2NaO_5$ $[M+Na]^+$: 341.0550, Obser.: 341.0526.

3.8.12. 2-(4-Chlorophenyl)-*N*-(4-methoxy-2-nitrophenyl)-2-oxoacetamide (8l)

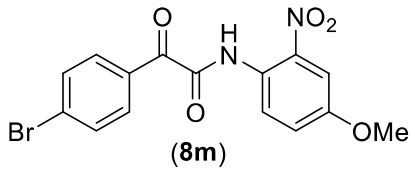


(**8l**)

The title compound was obtained as a yellow solid, M.P. 95-97 °C. The residue was purified by column chromatography in silica gel eluting with hexane/EtOAc (90:10), R_f = 0.38, Yield 82% (137 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 11.65 (s, 1H), 8.81–8.72 (m, 1H), 8.40 (dd, J = 6.9, 1.6 Hz, 2H), 7.76 (dd, J = 2.9, 1.2 Hz, 1H), 7.50 (dd, J = 6.9, 1.6 Hz, 2H), 7.31–7.28 (m, 1H), 3.90 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ = 184.9, 159.2, 155.9, 141.6, 138.0, 132.8, 131.1, 129.0, 126.6, 123.3, 122.9, 109.3, 55.9. HRMS: Calc. for $C_{15}H_{12}ClN_2O_5$ $[M+H]^+$: 335.0435, Obser.: 335.0406.

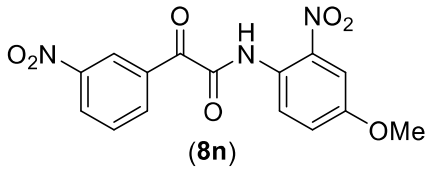
3.8.13. 2-(4-Bromophenyl)-*N*-(4-methoxy-2-nitrophenyl)-2-oxoacetamide (8m)



(**8m**)

The title compound was obtained as a yellow solid, M.P. 95-97 °C. The residue was purified by column chromatography in silica gel eluting with hexane/EtOAc (90:10), R_f = 0.34, Yield 85% (161 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 11.65 (s, 1H), 8.76 (d, J = 9.3 Hz, 1H), 8.31 (d, J = 8.7 Hz, 2H), 7.76 (d, J = 3.0 Hz, 1H), 7.67 (d, J = 8.7 Hz, 2H), 7.30 (dd, J = 9.2, 3.0 Hz, 1H), 3.90 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 185.2, 159.2, 155.9, 137.9, 132.8, 132.0, 131.5, 130.5, 126.6, 123.3, 122.9, 109.3, 55.9. HRMS: Calc. for $C_{15}H_{12}BrN_2O_5$ $[M+H]^+$: 378.9930, Obser.: 378.9900.

3.8.14. *N*-(4-Methoxy-2-nitrophenyl)-2-(3-nitrophenyl)-2-oxoacetamide (8n)



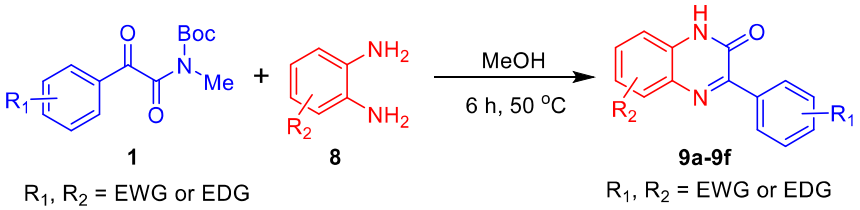
(**8n**)

The title compound was obtained as a yellow solid, M.P. 95-97 °C. The residue was purified by column chromatography in silica gel eluting with hexane/EtOAc (90:10), R_f = 0.50, Yield 83% (143 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 11.71 (s, 1H), 9.37–9.26 (m, 1H), 8.83–8.68 (m, 2H), 8.53-8.51 (m, 1H), 7.84–7.69 (m, 2H), 7.31 (dd, J = 9.2, 3.0 Hz, 1H), 3.91 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 184.2, 158.4, 156.1, 148.2, 138.0, 136.7, 134.0, 129.8, 128.7, 126.4, 126.2, 123.4, 122.9, 109.5, 56.0. HRMS: Calc. for $C_{15}H_{12}N_3O_7$ $[M+H]^+$: 346.0675, Obser.: 346.0645.

3.9. General procedure for the synthesis of quinoxalinones:

METHOD A: A solution of substituted phenylenediamine (1.0 mmol) was stirred at 50 °C in methanol (3 mL), to which a solution of *N*-Boc α-ketoamide (1 mmol in 2 mL of methanol) was added dropwise. The resulting reaction mixture was allowed to stir for 6 hrs at 50 °C. After completion, the solvent was evaporated purified by column chromatography

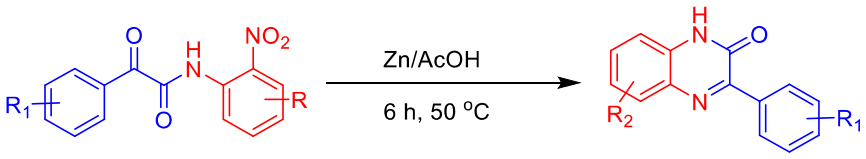
on silica gel (gradient eluent of EtOAc in petroleum ether) to give the desired products **9a-9f**.



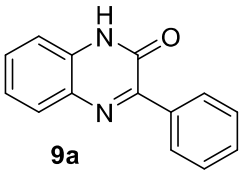
1 **8** **9a-9f**

R_1, R_2 = EWG or EDG R_1, R_2 = EWG or EDG

METHOD B: To a solution of substituted *ortho*-nitro α-ketoamide (0.5 mmol) in methanol (3 mL) were added Zn (4.0 equiv.) and AcOH (1.0 mL). The resulting mixture was stirred at 50 °C for 6 hrs. After completion, the reaction mixture was cooled to room temperature and filtered in celite. The filtrate was evaporated purified by column chromatography on silica gel (gradient eluent of EtOAc in petroleum ether) to give the desired products **9**.



3.9.1. 3-Phenylquinoxalin-2(1H)-one (9a)

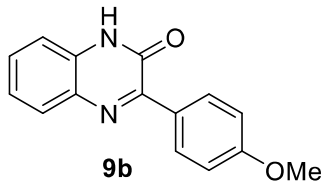


9a

The title compound was obtained as a straw yellow solid, M.P. >250 °C. The residue was purified by column chromatography in silica gel eluting with hexane/EtOAc (80:20), R_f = 0.43,

Yield 88% (98 mg). ^{1}H NMR (500 MHz, DMSO-d_6) δ = 8.31–8.29 (m, 2H), 7.84 (dd, J = 8.0, 0.9 Hz, 1H), 7.57–7.48 (m, 4H), 7.36–7.32 (m, 2H). ^{13}C NMR (125 MHz, DMSO-d_6) δ = 154.6, 154.1, 135.6, 132.0, 132.0, 130.3, 130.2, 129.2, 128.7, 127.8, 123.4, 115.1.

3.9.2. 3-(4-Methoxyphenyl)quinoxalin-2(1H)-one (9b)

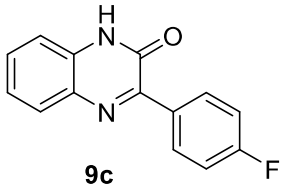


9b

The title compound was obtained as a straw yellow solid, M.P. >250 °C. The residue was purified by column chromatography in silica gel eluting with hexane/EtOAc (80:20), R_f = 0.46, Yield 89% (112 mg). ^{1}H NMR (500 MHz, DMSO-d_6) δ = 12.52 (s, 1H), 8.43–8.37 (m, 2H), 7.81 (d, J = 7.7 Hz, 1H), 7.53–7.49 (m, 1H), 7.33–7.30 (m, 2H), 7.06–7.04 (m, 2H), 3.84 (s, 3H). ^{13}C NMR (125 MHz, DMSO-d_6) δ =

161.0, 154.7, 153.1, 132.0, 131.7, 131.0, 129.7, 128.4, 128.1, 123.3, 115.0, 113.3, 55.3.

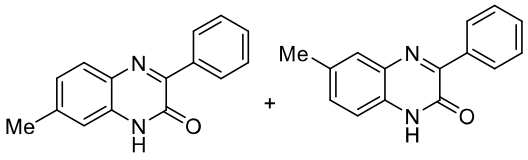
3.9.3. 3-(4-Fluorophenyl)quinoxalin-2(1H)-one (9c)



9c

The title compound was obtained as a pale white solid, M.P. 273 °C. The residue was purified by column chromatography in silica gel eluting with hexane:EtOAc (90:10), R_f = 0.47, Yield 85% (102 mg). ^{1}H NMR (500 MHz, DMSO-d_6) δ = 12.59 (s, 1H), 8.41 (dd, J = 9.0, 5.8 Hz, 2H), 7.83 (d, J = 7.5 Hz, 1H), 7.56–7.51 (m, 1H), 7.34–7.30 (m, 4H). ^{13}C NMR (125 MHz, DMSO-d_6) δ = 164.3, 162.3, 154.5, 152.8, 132.0–131.9 (m), 131.6 (d, J = 8.6 Hz), 130.3, 128.7, 123.4, 116.0, 115.8, 115.1, 114.9, 114.7.

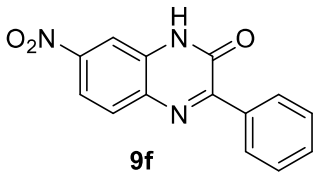
3.9.4. 6-Methyl-3-phenylquinoxalin-2(1H)-one+7-Methyl-3-phenylquinoxalin-2(1H)-one



9d **9e**

The title compounds were obtained as a straw yellow solid (inseparable mixture of isomers ~1:1 ratio). The residue was purified by column chromatography in silica gel eluting with hexane:EtOAc (90:10), R_f = 0.40, Yield 87% (103 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 12.27 (s, 1H), 8.45–8.37 (m, 2H), 7.85–7.73 (m, 1H), 7.56–7.49 (m, 3H), 7.38–7.27 (m, 1H), 7.20–7.12 (m, 1H), 2.48 (d, J = 4.3 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 156., 156.3, 154.1, 153.1, 141.4, 135.7, 134.2, 133.2, 131.8, 131.5, 131.1, 130.3, 130.2, 129.4, 129.3, 129.1, 129.0, 128.9, 128.1, 125.9, 115.1, 115.1, 21.8, 21.0.

3.9.5. 7-Nitro-3-phenylquinoxalin-2(1H)-one (9f)

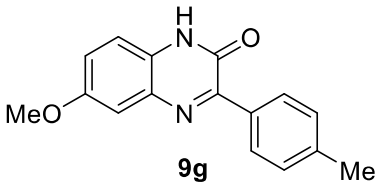


9f

The title compound was obtained as a straw yellow sticky liquid. The residue was purified by column chromatography in silica gel eluting

with hexane:EtOAc (90:10), R_f = 0.39, Yield 83% (111 mg). ^{1}H NMR (500 MHz, DMSO-d_6) δ = 8.33–8.31(m, 2H), 8.07 (ddd, J = 26.1, 18.7, 5.5 Hz, 3H), 7.54 (dt, J = 26.2, 7.2 Hz, 3H). ^{13}C NMR (125 MHz, DMSO-d_6) δ = 157.6, 154.4, 147.0, 135.5, 135.0, 132.4, 131.2, 130.0, 129.7, 128.0, 117.6, 110.6.

3.9.6. 6-Methyl-3-phenylquinoxalin-2(1H)-one (9d)

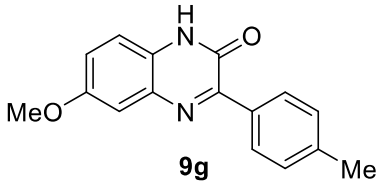


9g

The title compound was obtained as a straw yellow solid, M.P. >250 °C. The residue was purified by column chromatography in silica gel eluting with hexane/EtOAc (80:20), R_f = 0.46, Yield 89% (118 mg). ^{1}H NMR (500 MHz, DMSO-d_6) δ = 12.00 (s, 1H), 8.46–8.36 (m, 2H), 7.75 (s, 1H), 7.58–7.49 (m, 3H), 7.35 (d, J = 8.2 Hz, 1H), 7.24 (s, 1H), 2.48 (s, 3H). ^{13}C NMR

(125 MHz, DMSO-d_6) δ = 156.2, 154.2, 135.7, 134.2, 133.2, 131.8, 130.4, 129.4, 129.1, 128.9, 128.1, 126.9, 119.8, 115.0, 21.0.

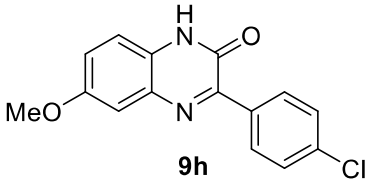
3.9.7. 6-Methoxy-3-(p-tolyl)quinoxalin-2(1H)-one (9g)



9g

The title compound was obtained as a light-yellow solid, M.P. 248-250 °C. The residue was purified by column chromatography in silica gel eluting with hexane/EtOAc (80:20), R_f = 0.46, Yield 72% (96 mg). ^{1}H NMR (500 MHz, DMSO-d_6) δ = 12.46 (s, 2H), 8.28 (d, J = 8.1 Hz, 1H), 7.83 (d, J = 8.1 Hz, 1H), 7.64 (dd, J = 28.6, 5.2 Hz, 1H), 7.35–.25 (m, 4H), 3.83 (s, 3H), 2.37 (s, 3H). ^{13}C NMR (125 MHz, DMSO-d_6) δ = 155.5, 154.3, 140.1, 130.5, 129.3, 129.2, 129.1, 128.5, 127.9, 126.2, 119.6, 115.9, 110.0, 55.6, 21.1.

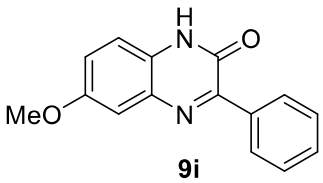
3.9.8. 3-(4-Chlorophenyl)-6-methoxyquinoxalin-2(1H)-one (9h)



9h

The title compound was obtained as a straw yellow solid, M.P. 190-192 °C. The residue was purified by column chromatography in silica gel eluting with hexane/EtOAc (80:20), R_f = 0.39, Yield 71% (102 mg). ^{1}H NMR (500 MHz, DMSO-d_6) δ = 12.57 (s, 2H), 8.42–8.39 (m, 1H), 7.95–7.92 (m, 1H), 7.70 – 7.44 (m, 3H), 7.27 (ddd, J = 22.4, 11.7, 2.7 Hz, 2H), 3.84 (s, 3H).^{13}C NMR (125 MHz, DMSO-d_6) δ = 155.5, 154.1, 135.0, 134.4, 132.6, 131.1, 130.9, 128.7, 127.9, 126.3, 120.1, 116.0, 110.0, 55.6. HRMS: Calc. for $C_{15}H_{12}ClN_2O_2$ $[M+H]^+$: 287.0587, Obser.: 287.0580.

3.9.9. 6-Methoxy-3-phenylquinoxalin-2(1H)-one (9i)



9i

The title compound was obtained as a straw yellow solid, M.P. >250 °C. The residue was purified by column

chromatography in silica gel eluting with hexane/EtOAc (80:20), R_f = 0.46, Yield 68% (86 mg). ^{1}H NMR (500 MHz, DMSO-d_6) δ = 12.50 (s, 1H), 8.32 (dd, J = 7.8, 1.6 Hz, 2H), 7.54–7.46 (m, 3H), 7.36 (d, J = 2.6 Hz, 1H), 7.28 (d, J = 8.9 Hz, 1H), 7.21 (dd, J = 8.9, 2.7 Hz, 1H), 3.84 (s, 3H). ^{13}C NMR (125 MHz, DMSO-d_6) δ = 155.9, 154.6, 136.1, 133.1, 130.6, 129.6, 128.3, 126.7, 120.3, 116.4, 110.5, 56.0.

3.10 Spectral Data for Few Products:

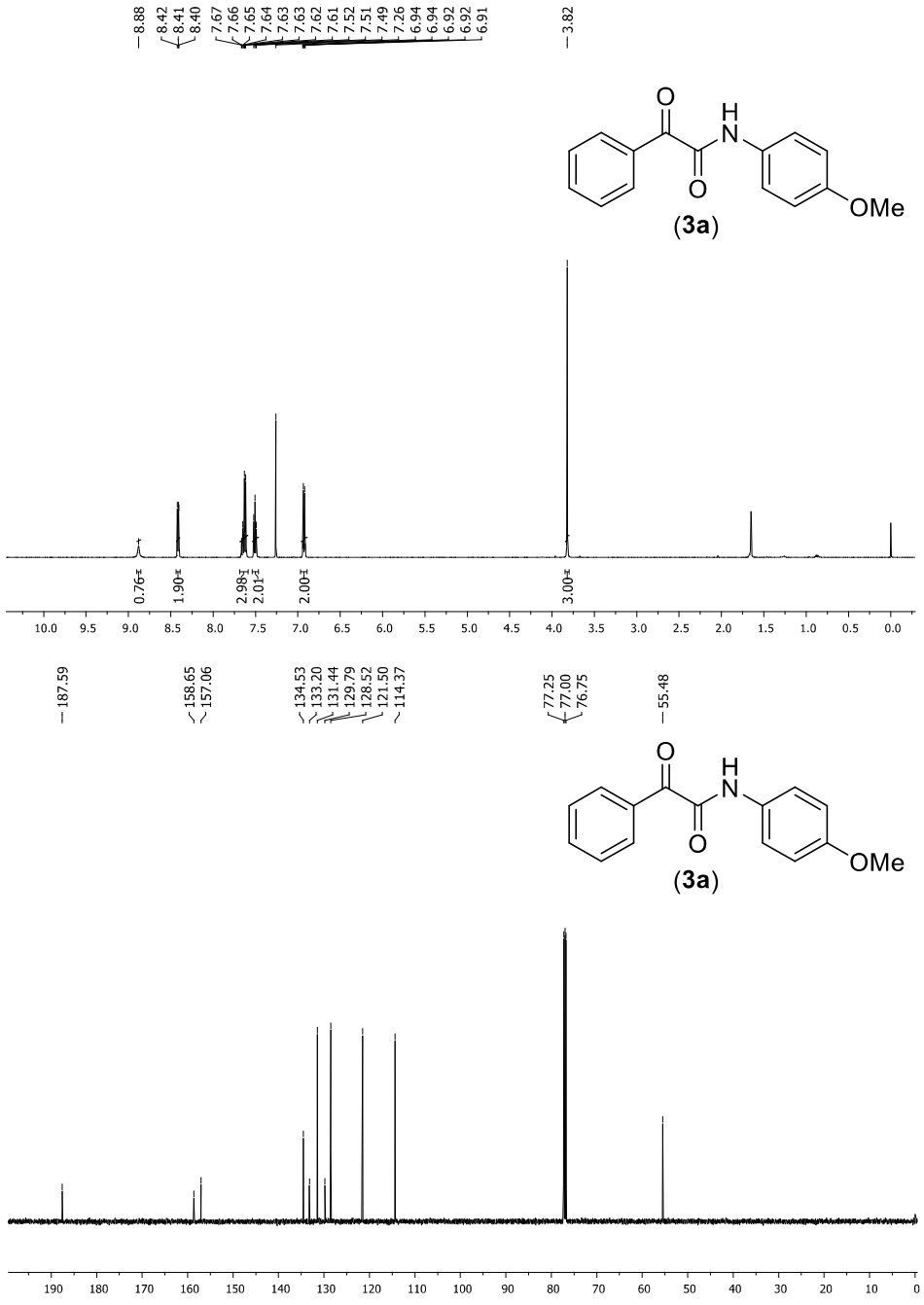


Figure 3.2 ^{1}H NMR and ^{13}C NMR of product **3a** in **$CDCl_3$.**

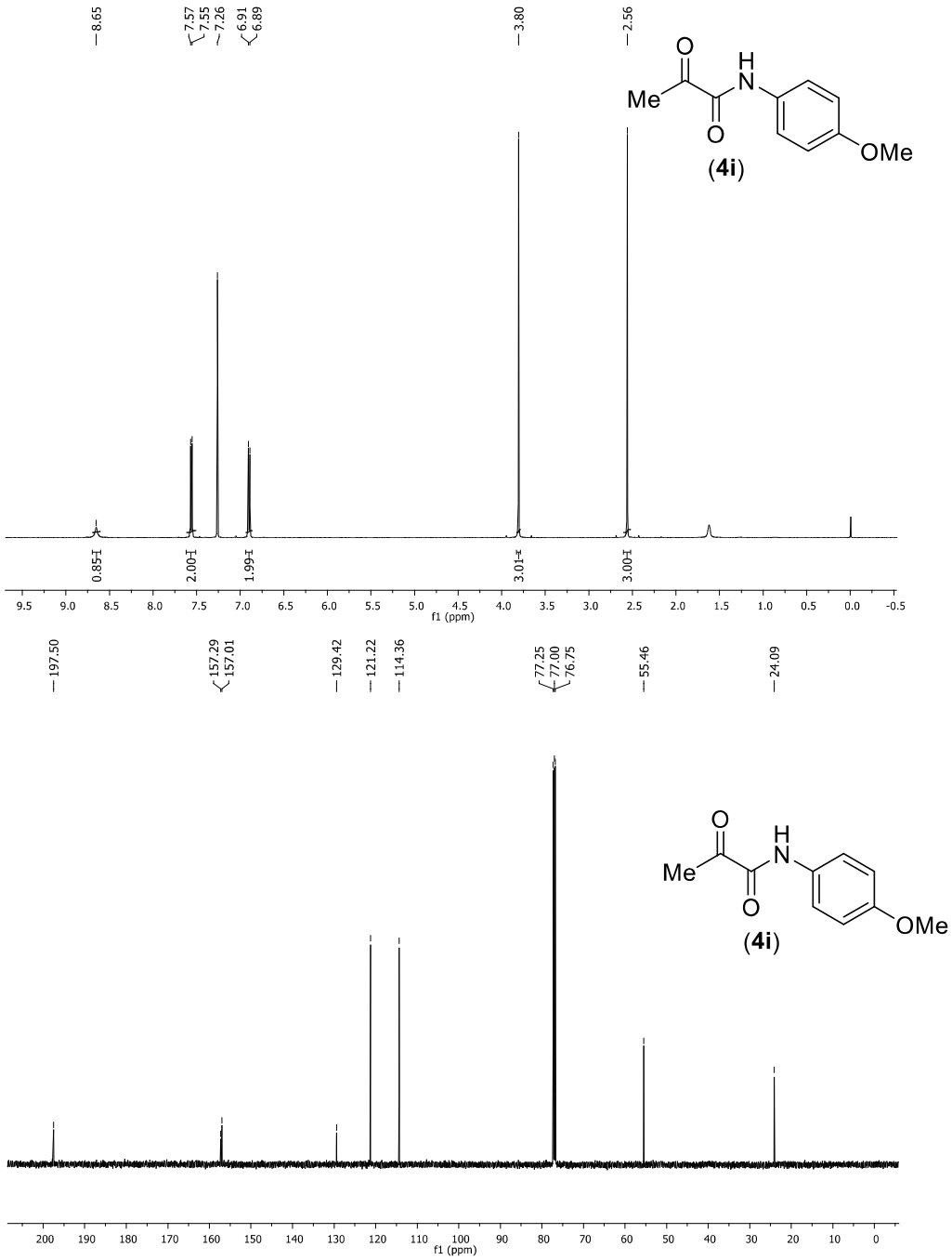


Figure 3.3 ^{1}H and ^{13}C NMR of product **4i** in **$CDCl_3$.**

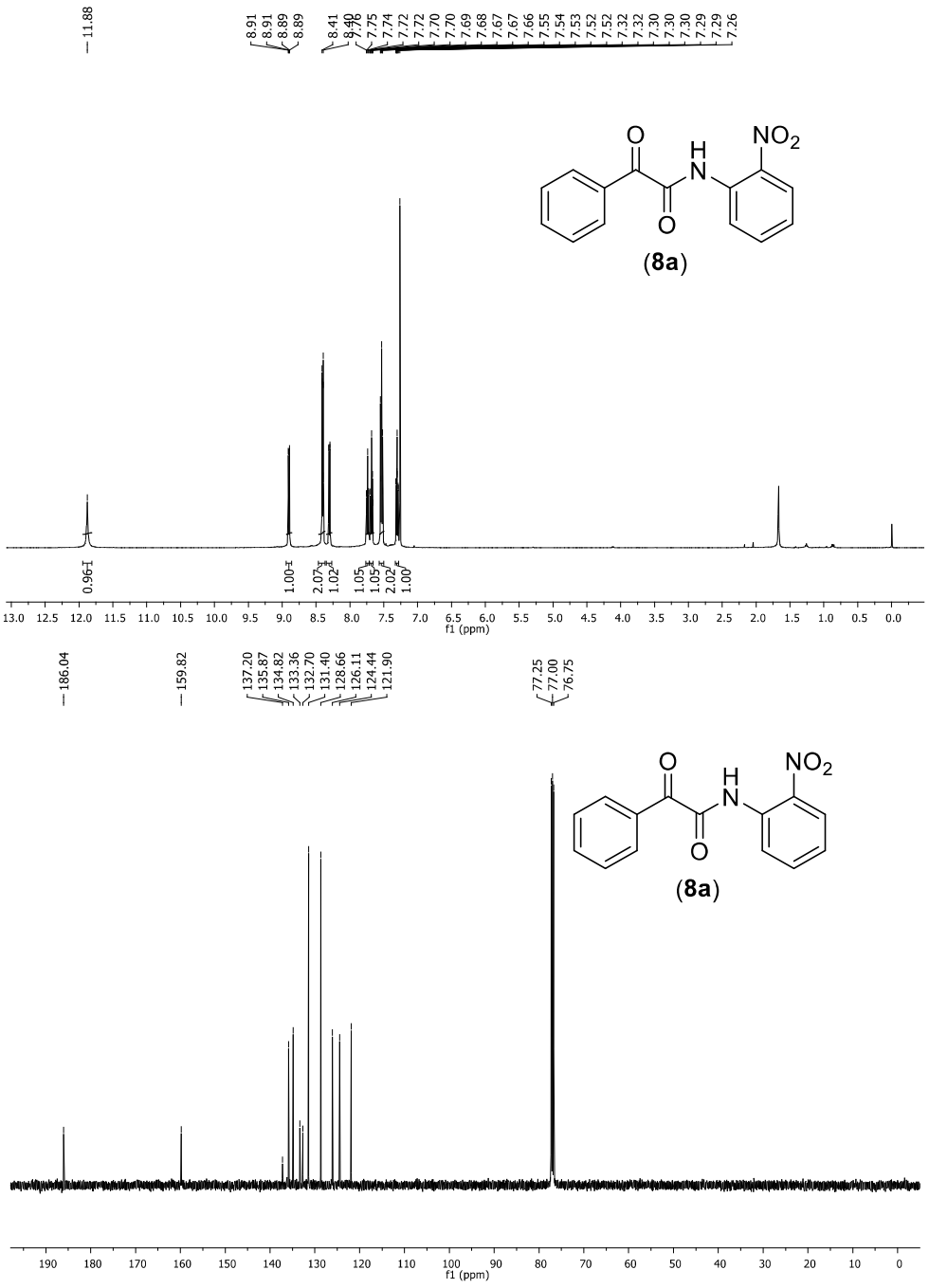


Figure 3.4 ^{1}H and ^{13}C NMR of product **8a** in **$CDCl_3$.**

3.11 References

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