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α-Carbonylimine to α-Carbonylamide: An Efficient Oxidative Amidation Approach

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Our interest in generating amide bonds by employing the activated C=N system has led to the development of an efficient oxidative amidation reaction between 2-oxoaldehyde and weak nucleophilic amines (anilines, benzamides and sulfonamides). Mechanistic studies support the involvement of α-carbonylimine (–CO–C=N–) based compounds or intermediates as a central feature of the reaction, in which an adjacent CO moiety enhances the electrophilicity of the C=N system, which favors attack of the oxidant (TBHP or SeO_2), thereby resulting in the generation of the desired products in good yields. The direct oxidative coupling of 2-oxoaldehydes and weak nucleophilic amines has been accomplished through either $MgSO_4$–TBHP–pyridine/CuBr, or SeO_2·pyridine promoted methods. In the current study, SeO_2·pyridine emerged as a versatile reagent with which to promote initial α-carbonylimine formation between 2-oxoaldehyde and weak nucleophilic amine, and subsequent oxidation to the corresponding α-carbonylamide. The reported methodology constitutes one of the few reports of the synthesis of α-ketoamides from anilines, perhaps the second report for the generation of α-ketoimides, and the first report of the generation of 2-oxoamides with sulfonamides.

Introduction

In the past few years, a number of novel routes for the generation of valuable α-ketoamides have been established.[1,2] Our group has contributed towards the generation of α-ketoamides through the use of the iminium ion as a reactive intermediate.[1c] The potential of our method lies in the direct amidation procedure between 2-oxoaldehydes and secondary amines via the iminium intermediate under mild reaction conditions. Although this highly challenging process was achieved by using dimethyl sulfoxide (DMSO) promoted oxidative amidation reaction, it failed to produce the desired products with anilines (Scheme 1). This limitation was attributed to 1) weak nucleophilicity of anilines, 2) low reactivity of the imine compared with the iminium ion under neutral conditions, and/or 3) failure of the reaction to produce the imine in DMSO. However, for the success of reactions with secondary amines, we presume that the α-carbonyl moiety further activates the iminium ion electrophilicity and facilitates nucleophilic attack. Herein, the C1-oxygen atom of the α-ketoamide was derived from DMSO, which acted as nucleophile/solvent. In this context, we initiated a program to test imines with different nucleophilic oxidants to generate new chemistry and perhaps establish a general oxidative coupling protocol that overcomes the limitation towards the use of weak nucleophilic amines.

Beyond the synthesis of α-ketoamides with anilines, the group of Wu recently reported the generation of α-ketoimides through I_2-catalyzed oxidative cross-coupling reaction between acetophenones/2-oxoaldehydes and benzamidine hydrochlorides.[3] Although these reactions generated valuable compounds in high yields, they failed to generate the desired results with benzamides. Moreover, there are very few reports of the direct utilization of the acyl C–H moiety of aldehydes under oxidative conditions with weak nucleophilic amines.[4] In view of this, a method is required that facilitates reaction with a complete set of weak nucleophilic amines. In our current work, we have successfully accomplished TBHP·pyridine, TBHP-CuBr, $MgSO_4$–TBHP–pyridine, and SeO_2·pyridine promoted oxidative amidation methods to achieve novel transformations of α-carbonylimines into α-carbonylamides. The reaction conditions works well with both α-carbonylimine (CI) as substrate (Scheme 1 a) and with CI generated in situ (Scheme 1 b and c).

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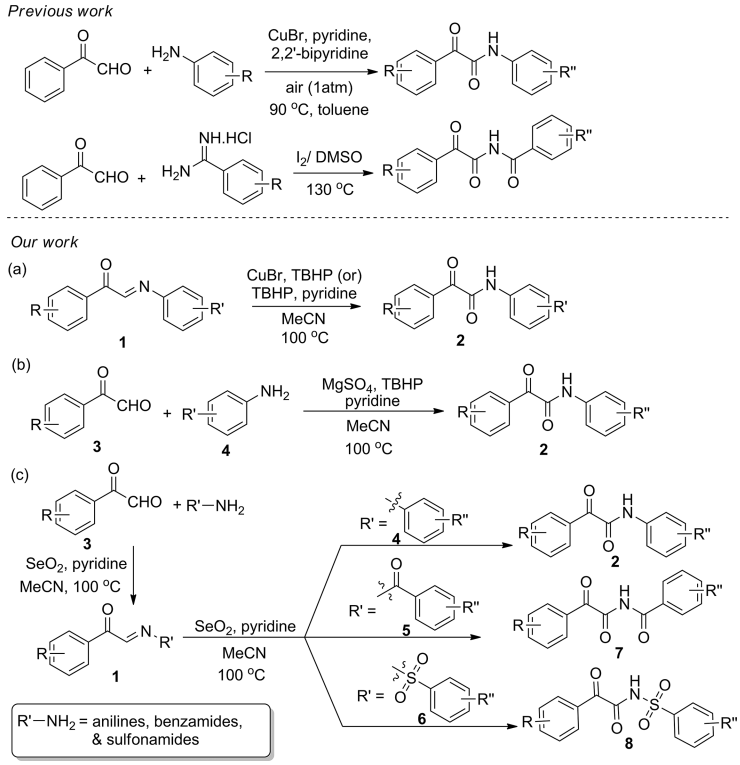
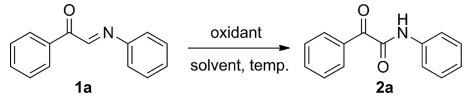


Scheme 1. Oxidative amidation reactions between 2-oxoaldehydes and weak nucleophilic amines.

Results and Discussion

We started our investigation with imine **1a** as a model substrate for testing against oxidants with nucleophilic propensity (Table 1, entries 4 and 8–10). It was observed that the desired product **2a** was obtained in 40 and 20% yields when **1a** was treated with TBHP and SeO_2, respectively, at 100 °C in acetonitrile (MeCN). Reactions with other oxidants either failed or produced the required product in trace amounts (entries 9 and 8). To improve the yield, we initiated a program to test the reaction of **1a** with TBHP in the presence of different concentrations of pyridine (entries 5–7). Upon optimization, the combination of **1a** (0.5 mmol) and TBHP (1.25 mmol) with pyridine (1 mmol) in MeCN at 100 °C was found to be the best reaction conditions for this transformation; these conditions furnished the desired product **2a** in 92% yield (entry 7). Although TBHP·pyridine furnished the desired product in good yields, we were keen to see whether the use of TBHP-metal salts could provide a milder option. To this end, a test reaction was performed between **1a** (0.5 mmol) and TBHP (1.25 mmol) in the presence of 20 mol-% copper salts (entries 11–17); it was found that the best results were obtained when CuBr was used as catalyst (90% yield, entry 13). Further optimization of the reaction was performed with different amounts of CuBr, wherein the reaction with 10 mol% CuBr gave yields that were comparable with those achieved with TBHP·pyridine (entry 12). Furthermore, performing the reaction between **1a** (0.5 mmol) and SeO_2 (0.5 mmol) with pyridine (1 mmol) in MeCN at 100 °C produced **2a** in 95% yield (entry 18).

Table 1. Optimization studies for the synthesis of α-carbonylamides from α-carbonylimines.



Entry	Oxidant [mmol]	Base [mM] or metal [mol-%]	Solvent	Temp. [°C]	Time [h]	Yield [%][a]
1	TBHP (0.5)	–	MeCN	80	4	20
2	TBHP (0.5)	–	MeCN	100	4	30
3	TBHP (1)	–	MeCN	100	4	40
4	TBHP (1)	–	MeCN	120	4	40
5	TBHP (1.25)	pyridine (0.5)	MeCN	100	4	60
6	TBHP (1.25)	pyridine (0.75)	MeCN	100	4	80
7[b]	TBHP (1.25)	pyridine (1)	MeCN	100	2	92
8	MnO_2 (0.5)	–	MeCN	100	4	0
9	IBX (0.5)	–	MeCN	100	4	0
10	SeO_2 (0.5)	–	MeCN	100	4	20
11	TBHP (1.25)	CuCl (20)	MeCN	100	4	50
12[c]	TBHP (1.25)	CuBr (10)	MeCN	100	1	90
13	TBHP (1.25)	CuBr (20)	MeCN	100	1	90
14	TBHP (1.25)	CuCN (20)	MeCN	100	4	40
15	TBHP (1.25)	$CuCl_2$ (20)	MeCN	100	4	0
16	TBHP (1.25)	$CuBr_2$ (20)	MeCN	100	4	0
17	TBHP (1.25)	CuI (20)	MeCN	100	4	40
18[d]	SeO_2 (0.5)	pyridine (1)	MeCN	100	1	95
19	SeO_2 (0.5)	pyridine (1)	toulene	100	4	0
20	SeO_2 (0.5)	pyridine (1)	THF	100	4	0
21	SeO_2 (0.5)	pyridine (1)	MeOH	100	4	0
22	SeO_2 (0.5)	pyridine (1)	DMF	100	4	0
23	SeO_2 (0.5)	pyridine (1)	DMSO	100	4	0
24	SeO_2 (0.5)	pyridine (1)	1,4-dioxane	100	4	0

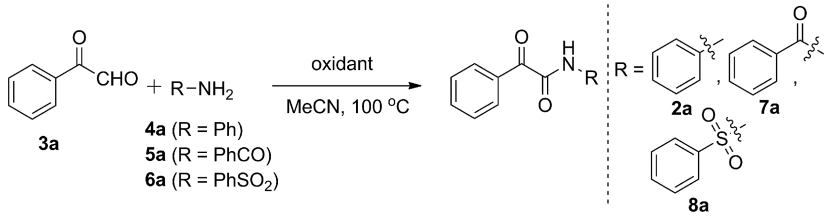
[a] Isolated yield. [b] Reaction conditions: α-carbonylimine (0.5 mmol), TBHP (1.25 mmol), pyridine (1 mmol), MeCN (3 mL). [c] α-Carbonylimine (0.5 mmol), TBHP (1.25 mmol), CuBr (10 mol%), MeCN (3 mL). [d] α-Carbonylimine (0.5 mmol), SeO_2 (0.5 mmol), pyridine (1 mmol), MeCN (3 mL).

With the optimized conditions in hand, reactions with a range of substituted imines were investigated. To our satisfaction, the results indicated that, irrespective of the nature of the substitution being used, the reactions afforded the desired products in good yields (90–95%; Table 3, entries **2a**–**d**). Although this transformation is unique, we wished to establish this method as a novel oxidative amidation protocol between 2-oxoaldehyde and sets of weak nucleophilic amines that have thus far presented a particular challenge. To this end, a reaction was initially planned between aniline **4a** and phenylglyoxal (**3a**) in MeCN at 100 °C with a range of oxidants (Table 2, entries 1–4). Initial screening results revealed that the desired product was obtained in 20% yield with SeO_2 (entry 4). Other oxidants including TBHP failed to produce **2a** (entries 1–4). However, when the reaction between **3a** and **4a** was carried out in the presence of 5 equiv. $MgSO_4$, the use of TBHP·pyridine (1.25:0.5) afforded the desired product with aniline in good yield (40%; entry 5). Further optimization established that the best result in this case was achieved when 0.5 mmol **3a** was treated with 0.5 mmol **4a** in the presence of 2.5 mmol $MgSO_4$ (80%; entry 7). However, when the same method was applied to benzamides and sulfonamides, the desired product was not produced.

We then focused on the use of SeO_2 to improve the yields and establish a general protocol for amidation. Based reported precedents, we tested the model reaction in the presence of a range of pyridine concentrations (entries 8–11).[5] It was observed that reaction with 2 equiv. pyridine produced the desired product **2a** in good yields (94%; entry 11) at 100 °C. The same reaction was subsequently examined in the presence of different bases to establish the role of pyridine. The results clearly revealed the dual function of pyridine. One role is perhaps as base and the second role is related to its tendency to enhance the nucleophilicity of SeO_2 through the formation of a pyridine-SeO_2 complex.[5] Looking in detail at the unprecedented results obtained between aniline **4a** and phenylglyoxal **3a**, we were keen to test the reaction of phenylglyoxal **3a** against benzamide **5a** and phenylsulfonamide **6a** (entries 18 and 19). Surprisingly, we found that this method gave good yields of the desired products in each case.

With these results in hand, sets of reactions between 2-oxoaldehydes **3** and weak nucleophilic amines **4**–**6** were carried out (as per optimization procedures), to overview the generality and substrate scope of these reactions. For this purpose, in each category, we conducted the reaction with electron-rich and electron-deficient substrates. In one set of experiments, the reaction was performed between 2-oxoaldehydes **3** and anilines **4** (Table 3, entries **2a**–**l**). In each case, we observed complete conversion of reactants into product **2**, irrespective of the nature of the substrate being used. Another set of reactions was performed between **3** and benzamides **5**. These reactions also proved to be excit-

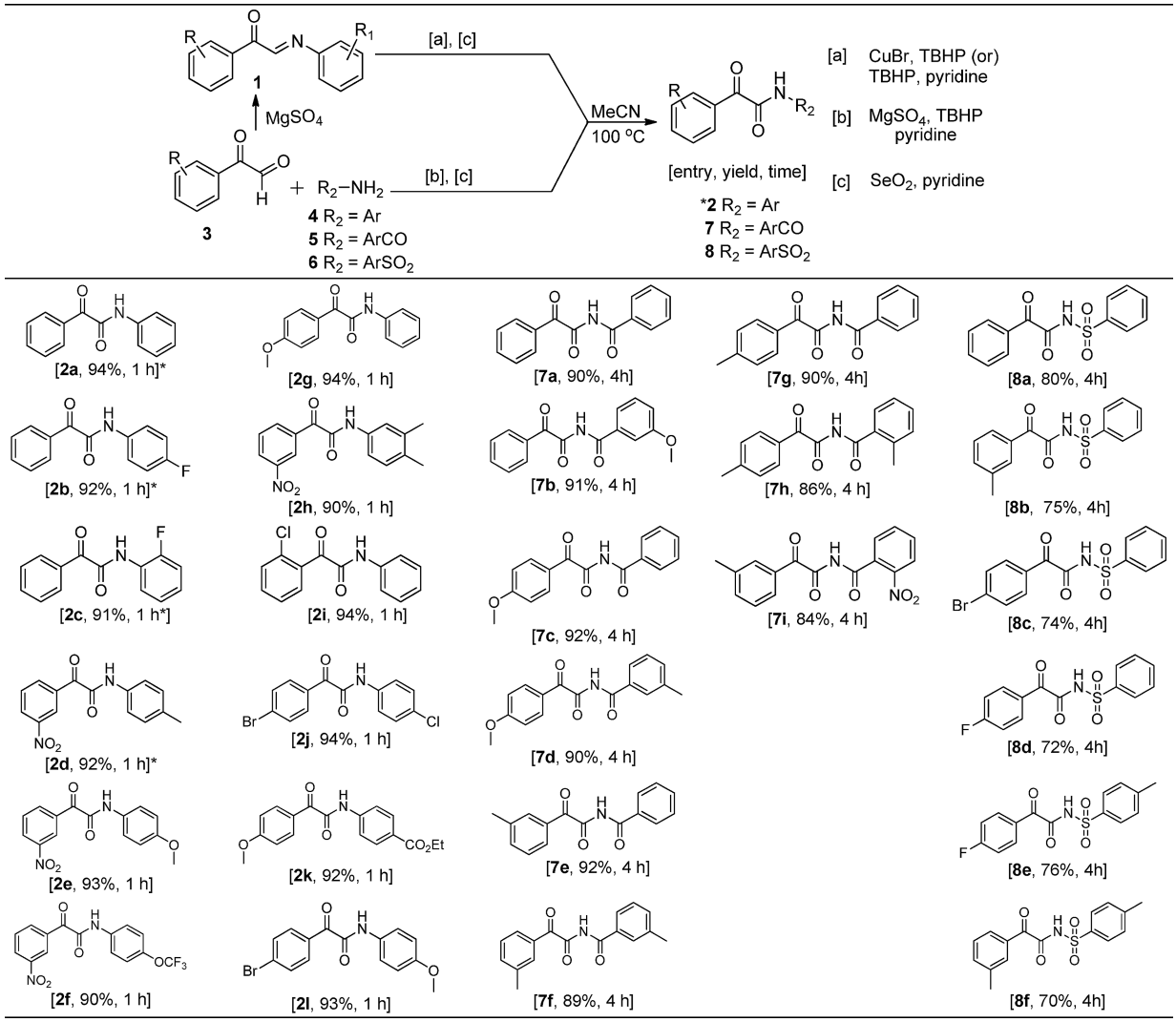
Table 2. Optimization studies for coupling of 2-oxoaldehydes and weak nucleophilic amines.



Entry	Oxidant additive [mmol]	Base [mmol]	Time [h]	Yield [%][a]
1	TBHP (0.5)	–	4	0
2	MnO_2 (0.5)	–	4	0
3	IBX (0.5)	–	4	0
4	SeO_2 (0.5)	–	4	20
5	TBHP (1.25) + $MgSO_4$ (2.5)	pyridine (0.5)	4	40
6	TBHP (1.25) + $MgSO_4$ (2.5)	pyridine (0.75)	4	60
7[b]	TBHP (1.25) + $MgSO_4$ (2.5)	pyridine (1)	4	80
8	SeO_2 (0.5)	pyridine (0.25)	1	25
9	SeO_2 (0.5)	pyridine (0.5)	1	50
10	SeO_2 (0.5)	pyridine (0.75)	1	80
11[c]	SeO_2 (0.5)	pyridine (1)	1	94
12	SeO_2 (0.25)	pyridine (1)	4	50
13	SeO_2 (0.25)	TEA (1)	4	60
14	SeO_2 (0.25)	NaOH (1)	4	0
15	SeO_2 (0.25)	KOH (1)	4	0
16	SeO_2 (0.25)	Na_2CO_3 (1)	4	0
17	SeO_2 (0.25)	K_2CO_3 (1)	4	0
18[d]	SeO_2 (0.25)	pyridine (1)	4	90
19[e]	SeO_2 (0.25)	pyridine (1)	2	80

[a] Isolated yield. [b] Reaction conditions: phenylglyoxal (0.5 mmol), aniline (0.5 mmol), TBHP (1.25 mmol), $MgSO_4$ (2.5 mmol), pyridine (1 mmol). [c] Reaction conditions: phenylglyoxal (0.5 mmol), aniline (0.5 mmol), SeO_2 (0.5 mmol), pyridine (1 mmol). [d] Reaction conditions: phenylglyoxal (0.5 mmol), benzamide (0.5 mmol), SeO_2 (0.5 mmol), pyridine (1 mmol). [e] Reaction conditions: phenylglyoxal (0.5 mmol), phenylsulfonamide (0.5 mmol), SeO_2 (0.5 mmol), pyridine (1 mmol).

Table 3. Oxidative amidation reactions of 2-oxoaldehyde with weak nucleophilic amines.[a]



[a] Reaction conditions (a): **1** (0.5 mmol) TBHP (1.25 mmol), CuBr (10 mol-%) or pyridine (1 mmol), MeCN (3 mL), 2 h, 100 °C. Reaction conditions (b): **3** (0.5 mmol), **4** (0.5 mmol), $MgSO_4$ (2.5 mmol), TBHP (1.25 mmol), pyridine (1 mmol), MeCN (3 mL), 3 h, 100 °C. Reaction conditions (c): **3** (0.5 mmol), **4** or **5** or **6** (0.5 mmol), SeO_2 (0.5 mmol), pyridine (1 mmol), MeCN (3 mL), 1–4 h, 100 °C. * Methods (a) and (b) produced the desired product in comparable yields.

ing, because they generated excellent yields of the desired products **7** in all cases (entries **7a**–**i**). To validate the substrate scope of our method between 2-oxoaldehydes **3** and sulfonamides **6**, we conducted a further set of reactions (Table 3, entries **8a**–**f**). In each case, we could isolate the desired product in good yield (70–94%). These results demonstrate clearly the generality of the method towards sulfonamides.

To shed light on the possible mechanism for the direct coupling between 2-oxoaldehyde and weak nucleophilic amine, a number of control experiments were conducted (Figure 1). In experiment (a), we established that no reaction took place under the optimized conditions when benzaldehyde was treated with aniline. Similarly, when imine substrate **11** was treated with SeO_2·pyridine complex as per the optimized procedure, all starting materials were recovered unchanged [experiment (b)]. These two observations clearly support our prediction that the α-carbonyl group further activates iminium ion electrophilicity and facilitates attack of oxidants and thereby leads to generation of the amide bond. To support our conclusion, LC-ESI-MS experiments were used to analyze the reaction between **3b** and **4a** after different time intervals; see experiment (c), page 3 in the Supporting Information. As depicted in Table 3, it is clear that the reaction is only feasible through α-carbonylimine under heating conditions. Given that the reaction works well with α-carbonylimine (CI) as substrate, we can confidently predict a mechanism that involves generation of CI as intermediate during the course of the reaction. Based on these elements, we propose a mechanism that can be summarized under two headings: 1) where TBHP acts as oxidant and 2) where SeO_2 acts as the oxidizing source (Figure 2). The TBHP-promoted oxidative coupling mechanism can be subcategorized further into two parts: a pyr-

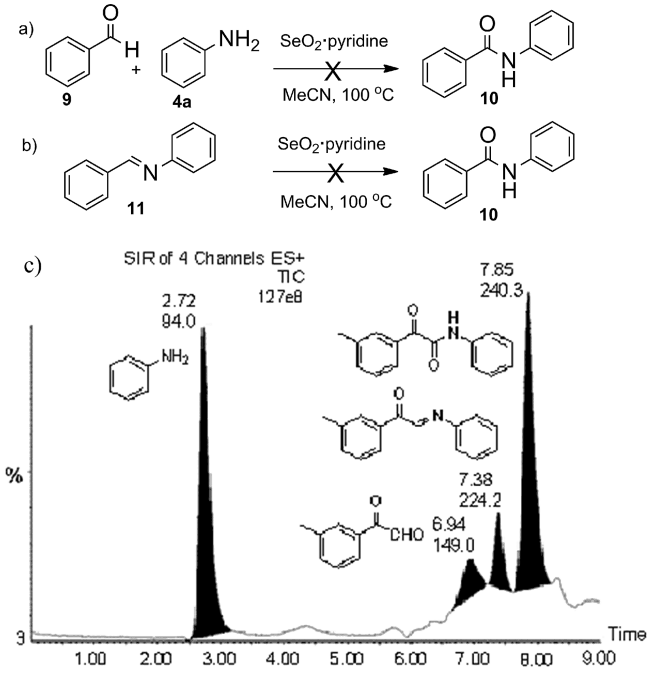


Figure 1. Mechanistic scenario.

idine-promoted ionic mechanism (Figure 2b) and a copper-catalyzed free-radical mechanism (Figure 2a). In the former mechanism, we presume that, after abstracting a proton from TBHP, pyridine genarates a *tert*-butyloxy anion that attacks the C=N system of CI leading to **12**. Finally, the latter produces the desired product through elimination of *tert*-butanol. In contrast to the anionic mechanism, the copper-catalyzed reaction proceeds through a free-radical mechanism.[6] As expected, copper(I) is oxidized to copper(II) by TBHP, generating a *tert*-butyloxy radical. Copper(II) and the *tert*-butyloxy radical, on reacting with TBHP, generate $Cu^{II}Br(OOtBu)$ and the *tert*-butylperoxy radical, respectively. The *tert*-butyloxy radical along with $Cu^{II}Br(OOtBu)$ attack the C=N system of CI, thereby generating **13**, which ultimately generates the desired product through *tert*-butanol elimination.

SeO_2 in the SeO_2-promoted reaction has dual role. Its preliminary role involves generation of α-carbonylimine, which is then oxidized to α-carbonylamide. Initially amine **4** reacts with 2-oxoaldehyde **3** in the presence of SeO_2 to form an intermediate **14**, which ultimately generates α-carbonylimine **1** through loss of selenous acid. As previously reported,[5] pyridine enhances the nucleophilicity of SeO_2 through formation of a pyridine-SeO_2 complex (Py_2SeO_2), which, in our case, led to the formation of the desired product in good yields by oxidizing the C=N system of CI. The work with SeO_2·pyridine was further extended by promoting the direct oxidative coupling of amines with aryl methyl ketones **16**. For this, a set of test reactions were performed in one pot with aryl methyl ketones **16** as source of 2-oxoaldehyde. In these reactions, SeO_2 primarily promoted the oxidation to the aryl methyl ketones, followed by formation of α-carbonylimines and finally its further oxidation to the

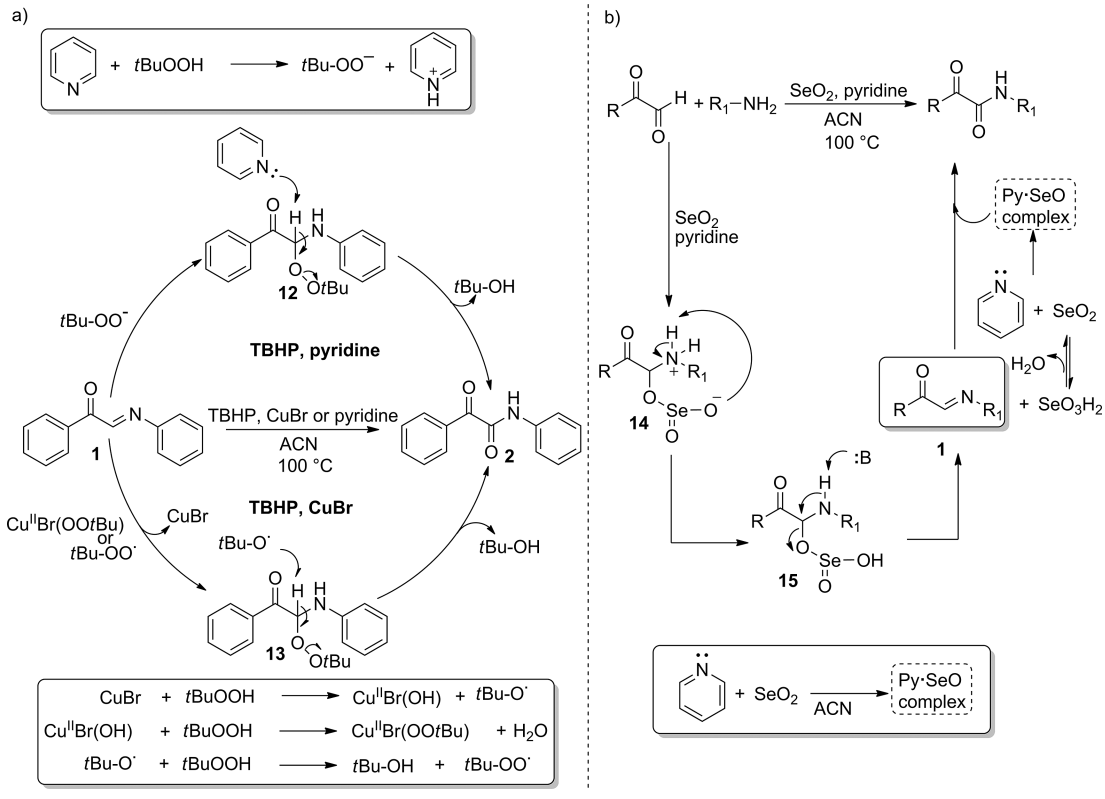
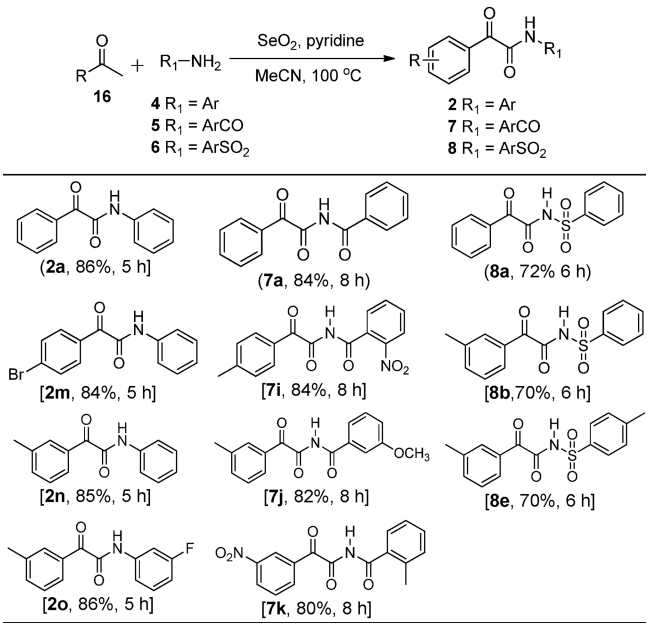


Figure 2. Control experiments.

respective products. In all the reactions tested, we observed comparable yields of the desired product (Table 4).

Table 4. Oxidative coupling reaction between aryl methyl ketones with weak nucleophilic amines.[a]



[a] Reaction conditions: **16** (0.5 mmol), **4** or **5** or **6** (0.5 mmol), SeO_2 (1.0 mmol), pyridine (1.0 mmol), MeCN (3 mL), 4–7 h, 100 °C.

Conclusions

We have applied the concept of 2-oxoimine-promoted reactions to establish a general oxidative amidation method between 2-oxoaldehydes and weak nucleophilic amines (anilines, benzamides and sulfonamides). Notably, this preliminary work demonstrates the first example of oxidative amidation reactions of benzamides and sulfonamides with 2-oxoaldehyde. A major part of this work highlights the potential of SeO_2·pyridine to promote α-carbonylimine formation with weak nucleophilic amines, that later undergo oxidation to α-carbonylamide. Further applications of this reagent in terms of a direct coupling protocol between acetophenones and weak nucleophilic amines was revealed.

Experimental Section

General: All chemicals were obtained from Sigma–Aldrich and used as received. ^1H and ^{13}C NMR spectra were recorded with Bruker-Avance DPX FT-NMR 500 and 400 MHz instruments. Chemical data for protons are reported in parts per million (ppm) downfield from tetramethylsilane and are referenced to the residual proton in the NMR solvents ($CDCl_3$: 7.26 ppm). ^{13}C NMR spectra ($CDCl_3$: 77.0 ppm) were recorded at 125 or 100 MHz: chemical data for carbon atoms are reported in parts per million (ppm, δ scale) downfield from tetramethylsilane and are referenced to the carbon resonance of the solvent. Mass spectra of compounds were recorded with VARIAN GC–MS-MS instrument, ESI-MS and HRMS spectra were recorded with Agilent 1100 LC-Q-TOF and HRMS-6540-UHD instruments. IR spectra were recorded with a Perkin–Elmer IR spectrophotometer.

General Procedure for the Conversion of α-Carbonylimine into α-Carbonylamide. Method (a): A mixture of α-carbonylimine **1** (0.5 mmol), TBHP (1.25 mmol), and either pyridine (1.0 mmol) or CuBr (10 mol-%) in acetonitrile (3 mL) was stirred at 100 °C for 2 h.

Method (c): A mixture of α-carbonylimine **1** (0.5 mmol), selenium dioxide (0.5 mmol) and pyridine (1 mmol) in acetonitrile (3 mL) was stirred at 100 °C for 1 h. After completion of the reaction, the crude mixture was cooled to room temperature, filtered, and purified by column chromatography [silica gel (100–200#); ethyl acetate/hexane, 0.1:10]. The desired product **2** (90–95% yield) was obtained as a yellow solid.

General Procedure for the Synthesis of α-Carbonylamides, α-Carbonylimides, and α-Carbonylsulfonamides from Arylglyoxals and Weak Nucleophilic Amines. Method (b): A mixture of arylglyoxal **3** (0.5 mmol), arylamine **4** (0.5 mmol), $MgSO_4$ (2.5 mmol), TBHP (1.25 mmol), and pyridine (1 mmol) in acetonitrile (3 mL) was stirred at 100 °C for 3 h.

Method (c): A mixture of arylglyoxal monohydrate (0.5 mmol), arylamine or arylamide or arylsulfonamide (0.5 mmol), selenium dioxide (0.5 mmol), and pyridine (1 mmol) in acetonitrile (3 mL) was stirred at 100 °C for 1–4 h. After completion of the reaction, the crude mixture was cooled to room temperature, filtered, and purified by column chromatography [silica gel (100–200#); ethyl acetate/hexane].

General Procedure for the Synthesis of α-Carbonylamides, α-Carbonylimides, and α-Carbonylsulfonamides from Aryl Methyl Ketones and Weak Nucleophilic Amines: A mixture of SeO_2 (0.5 mmol), acetonitrile (3 mL) and a catalytic amount of H_2O was heated until a clear solution was formed. Aryl methyl ketone (0.5 mmol) was added and heating was continued for 3 h. Arylamine or arylamide or arylsulfonamide (0.5 mmol) and a SeO_2·pyridine cocktail (0.5:1 mmol) were added, and the mixture was heated to 100 °C. Upon completion of the reaction, the crude mixture was cooled to room temperature, filtered, and purified by column chromatography [silica gel (100–200#); ethyl acetate/hexane].

2-Oxo-*N*,2-diphenylacetamide (2a):[1d] Yield 106 mg (94%); yellow solid. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.96 (br. s, 1 H), 8.42 (d, J = 8.0 Hz, 2 H), 7.70 (d, J = 8.0 Hz, 2 H), 7.66 (t, J = 7.5 Hz, 1 H), 7.51 (t, J = 7.6 Hz, 2 H), 7.40 (t, J = 7.6 Hz, 2 H), 7.20 (t, J = 7.3 Hz, 1 H) ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3360, 2919, 1667, 1596 cm^{-1}. LC-MS (ESI): m/z calcd. for $C_{14}H_{10}NO_2$ $[M - H]^-$ 224.0; found 224.0. HRMS (TOF): m/z calcd. for $C_{14}H_{10}NO_2$ $[M - H]^-$ 224.0712; found 224.0715.

***N*-(4-Fluorophenyl)-2-oxo-2-phenylacetamide (2b):**[1d] Yield 112 mg (92%); yellow solid. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.95 (br. s, 1 H), 8.44–8.39 (m, 2 H), 7.70–7.64 (m, 3 H), 7.54–7.49 (m, 2 H), 7.12–7.06 (t, J = 8.0 Hz, 2 H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 187.30, 159.95 (d, J = 245.1 Hz), 158.79, 134.80, 133.05, 132.7, 131.53, 128.66, 121.71 (d, J = 8.0 Hz), 116.05 (d, J = 22.7 Hz) ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3440, 3337, 1671, 1545, 1509 cm^{-1}. LC-MS (ESI): m/z calcd. for $C_{14}H_9FNO_2$ $[M - H]^-$ 242.0; found 241.9. HRMS (TOF): m/z calcd. for $C_{14}H_{11}FNO_2$ $[M + H]^+$ 244.0774; found 244.0774.

***N*-(2-Fluorophenyl)-2-oxo-2-phenylacetamide (2c):** Yield 110.5 mg (91%); yellow solid. ^1H NMR (400 MHz, $CDCl_3$): δ = 9.21 (br. s, 1 H), 8.47–8.38 (m, 3 H), 7.66 (t, J = 7.4 Hz, 1 H), 7.51 (t, J =

7.8 Hz, 2 H), 7.17 (tt, *J* = 5.8, 3.6 Hz, 3 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 186.67, 158.94, 152.95 (d, *J* = 245.5 Hz), 134.70, 132.98, 131.46, 128.61, 125.54 (d, *J* = 7.6 Hz), 125.28 (d, *J* = 10.3 Hz), 124.68 (d, *J* = 3.8 Hz), 121.43, 115.19 (d, *J* = 19.0 Hz) ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3385, 1671, 1620, 1595, 1528 cm^{-1}. LC-MS (ESI): *m*/*z* calcd. for $C_{14}H_9FNO_2$ [M – H]$^-$ 242.0; found 242.0. HRMS (TOF): *m*/*z* calcd. for $C_{14}H_{11}FNO_2$ [M + H]$^+$ 244.0774; found 244.0774.

2-(3-Nitrophenyl)-2-oxo-*N*-(*p*-tolyl)acetamide (2d): Yield 130.5 mg (92%); yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.28 (s, 1 H), 8.91 (br. s, 1 H), 8.83–8.78 (m, 1 H), 8.50 (ddd, *J* = 8.2, 2.3, 1.1 Hz, 1 H), 7.73 (t, *J* = 8.0 Hz, 1 H), 7.59 (d, *J* = 8.4 Hz, 2 H), 7.22 (d, *J* = 8.2 Hz, 2 H), 2.37 (s, 3 H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 185.44, 157.68, 148.27, 137.04, 135.62, 134.36, 133.65, 129.86, 129.79, 128.56, 126.40, 120.01, 21.02 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3572, 3563, 3458, 2075, 1658, 1650, 1643, 1633 cm^{-1}. LC-MS (ESI): *m*/*z* calcd. for $C_{15}H_{11}N_2O_4$ [M – H]$^-$ 283.0; found 283.0. HRMS: *m*/*z* calcd. for $C_{15}H_{13}N_2O_4$ [M + H]$^+$ 285.0875; found 285.0856.

***N*-(4-Methoxyphenyl)-2-(3-nitrophenyl)-2-oxoacetamide (2e):** Yield 139.5 mg (93%); yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.29 (s, 1 H), 8.89 (br. s, 1 H), 8.81 (d, *J* = 7.8 Hz, 1 H), 8.50 (dd, *J* = 8.2, 1.0 Hz, 1 H), 7.73 (t, *J* = 8.0 Hz, 1 H), 7.63 (t, *J* = 8.7 Hz, 2 H), 6.95 (d, *J* = 8.7 Hz, 2 H), 3.84 (s, 3 H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 185.51, 157.56, 157.39, 148.26, 137.03, 134.41, 129.79, 129.32, 128.55, 126.39, 121.63, 114.49, 55.53 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3834, 3746, 3669, 3646, 3355, 2919, 2850, 2060, 1673, 1650, 1512 cm^{-1}. LC-MS (ESI): *m*/*z* calcd. for $C_{15}H_{11}N_2O_5$ [M – H]$^-$ 299.0; found 298.9. HRMS: *m*/*z* calcd. for $C_{15}H_{13}N_2O_5$ [M + H]$^+$ 301.0824; found 301.0834.

2-(3-Nitrophenyl)-2-oxo-*N*-[4-(trifluoromethoxy)phenyl]acetamide (2f): Yield 159.0 mg (90%); yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.29 (s, 1 H), 9.02 (br. s, 1 H), 8.80 (d, *J* = 7.8 Hz, 1 H), 8.54–8.48 (m, 1 H), 7.79–7.73 (m, 3 H), 7.28 (d, *J* = 8.7 Hz, 2 H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 184.99, 157.78, 148.26, 146.29, 137.03, 134.80, 134.05, 129.93, 128.80, 126.43, 122.06, 121.30 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3851, 3441, 3339, 3116, 3084, 2954, 2923, 2853, 2079, 1685, 1531, 1260 cm^{-1}. LC-MS (ESI): *m*/*z* calcd. for $C_{15}H_8F_3N_2O_5$ [M – H]$^-$ 353.0; found 353.0. HRMS: *m*/*z* calcd. for $C_{15}H_{10}F_3N_2O_5$ [M + H]$^+$ 355.0542; found 355.0547.

2-(4-Methoxyphenyl)-2-oxo-*N*-phenylacetamide (2g):[11] Yield 120.0 mg (94%); yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.01 (br. s, 1 H), 8.50 (d, *J* = 9.0 Hz, 2 H), 7.69 (d, *J* = 7.6 Hz, 2 H), 7.39 (t, *J* = 7.9 Hz, 2 H), 7.19 (t, *J* = 7.4 Hz, 1 H), 6.97 (d, *J* = 9.0 Hz, 2 H), 3.90 (s, 3 H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 185.24, 164.95, 159.52, 136.79, 134.30, 129.22, 126.11, 125.19, 119.92, 113.96, 55.63 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3440, 3354, 2922, 2454, 2078, 1689, 1601, 1642 cm^{-1}. LC-MS (ESI): *m*/*z* calcd. for $C_{15}H_{12}NO_3$ [M + H]$^+$ 254.0; found 253.9. HRMS: *m*/*z* calcd. for $C_{15}H_{14}NO_3$ [M + H]$^+$ 256.0974; found 256.0974.

***N*-(3,4-Dimethylphenyl)-2-(3-nitrophenyl)-2-oxoacetamide (2h):** Yield 134.0 mg (90%); yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.28 (s, 1 H), 8.87 (br. s, 1 H), 8.81 (d, *J* = 7.8 Hz, 1 H), 8.53–8.46 (m, 1 H), 7.73 (t, *J* = 8.0 Hz, 1 H), 7.50 (s, 1 H), 7.43 (dd, *J* = 8.1, 1.9 Hz, 1 H), 7.17 (d, *J* = 8.1 Hz, 1 H), 2.30 (s, 3 H), 2.27 (s, 3 H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 185.48, 157.65, 148.23, 137.76, 137.06, 134.38, 134.35, 133.89, 130.30, 129.78, 128.54, 126.38, 121.21, 117.49, 19.97, 19.37 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3643, 3351, 3073, 2919, 2851, 1677, 1526 cm^{-1}. LC-MS (ESI) *m*/*z* calcd. for $C_{16}H_{13}N_2O_4$ [M – H]$^-$ 297.0; found 296.9. HRMS (TOF): *m*/*z* calcd. for $C_{16}H_{15}N_2O_4$ [M + H]$^+$ 299.1032; found 299.1038.

2-(2-Chlorophenyl)-2-oxo-*N*-phenylacetamide (2i):[7] Yield 122.0 mg (94%); yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.84 (br. s, 1 H), 7.76–7.65 (m, 3 H), 7.51–7.43 (m, 2 H), 7.41–7.33 (m, 3 H), 7.18 (t, *J* = 7.4 Hz, 1 H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 190.20, 157.94, 136.49, 133.64, 133.27, 133.19, 131.32, 130.51, 129.29, 126.63, 125.47, 119.89 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3900, 3735, 3364, 2922, 1682, 1599, 1536, 1495 cm^{-1}. LC-MS (ESI): *m*/*z* calcd. for $C_{14}H_{11}ClNO_2$ [M + H]$^+$ 260.0; found 260.1.

2-(4-Bromophenyl)-*N*-(4-chlorophenyl)-2-oxoacetamide (2j): Yield 158.0 mg (94%); yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.00 (br. s, 1 H), 8.34 (d, *J* = 8.4 Hz, 2 H), 7.68 (dd, *J* = 8.2, 5.6 Hz, 4 H), 7.39 (d, *J* = 8.7 Hz, 2 H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 185.97, 158.42, 135.04, 133.00, 132.06, 131.64, 130.70, 130.58, 129.37, 121.16 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3848, 3744, 3441, 3328, 2918, 2850, 1674, 1587, 1535, 1491 cm^{-1}. LC-MS (ESI): *m*/*z* calcd. for $C_{14}H_8BrClNO_2$ [M – H]$^-$ 335.9; found 337.9. HRMS (TOF): *m*/*z* calcd. for $C_{14}H_8BrClNO_2$ [M – H]$^-$ 335.9427; found 335.9419.

Ethyl 4-[2-(4-methoxyphenyl)-2-oxoacetamido]benzoate (2k): Yield 149.0 mg (92%); yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.20 (br. s, 1 H), 8.50 (d, *J* = 7.6 Hz, 2 H), 8.08 (d, *J* = 7.5 Hz, 2 H), 7.78 (d, *J* = 7.6 Hz, 2 H), 6.99 (d, *J* = 7.7 Hz, 2 H), 4.38 (q, *J* = 7.1 Hz, 2 H), 3.91 (s, 3 H), 1.40 (t, *J* = 7.1 Hz, 3 H) ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3744, 3340, 2985, 2923, 2849, 2586, 2043, 1925, 1720, 1691, 1642, 1602, 1587, 1531, 1512, 1271, 1161, 1026 cm^{-1}. LC-MS (ESI): *m*/*z* calcd. for $C_{14}H_8BrClNO_2$ [M – H]$^-$ 326.1; found 326.1.

2-(4-Bromophenyl)-*N*-(4-methoxyphenyl)-2-oxoacetamide (2l): Yield 155.0 mg (93%); yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.81 (br. s, 1 H), 8.25 (d, *J* = 8.4 Hz, 2 H), 7.55 (dd, *J* = 16.1, 8.6 Hz, 4 H), 6.85 (d, *J* = 8.8 Hz, 2 H), 3.75 (s, 3 H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 186.51, 158.31, 157.16, 132.98, 131.95, 130.39, 129.62, 121.55, 114.40, 55.52 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3349, 3241, 3138, 3086, 2920, 2850, 1657, 1582, 1512, 1033 cm^{-1}. LC-MS (ESI) *m*/*z* calcd. for $C_{15}H_{11}BrNO_3$ [M – H]$^-$ 331.9; found 332.0. HRMS (TOF): *m*/*z* calcd. for $C_{15}H_{11}BrNO_3$ [M – H]$^-$ 331.9922; found 331.9927.

2-(4-Bromophenyl)-2-oxo-*N*-phenylacetamide (2m):[8] Yield 127 mg (84%); yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.88 (br. s, 1 H), 8.25 (d, *J* = 8.4 Hz, 2 H), 7.60 (dd, *J* = 12.6, 8.4 Hz, 4 H), 7.33 (t, *J* = 7.7 Hz, 2 H), 7.13 (t, *J* = 7.4 Hz, 1 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 186.33, 158.53, 136.47, 132.98, 131.99, 131.84, 130.48, 129.28, 125.47, 119.98 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3850, 3646, 3442, 3333, 2918, 2850, 1682, 1659, 1580, 1537, 1496 cm^{-1}. LC-MS (ESI): *m*/*z* calcd. for $C_{14}H_{11}BrNO_2$ [M + H]$^+$ 303.9; found 304.0. HRMS (TOF): *m*/*z* calcd. for $C_{14}H_9BrNO_2$ [M – H]$^-$ 301.9817; found 302.0571.

2-Oxo-*N*-phenyl-2-(*m*-tolyl)acetamide (2n): Yield 101.5.0 mg (85%); yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.94 (br. s, 1 H), 8.22 (d, *J* = 6.9 Hz, 2 H), 7.70 (d, *J* = 8.0 Hz, 2 H), 7.47 (d, *J* = 7.3 Hz, 1 H), 7.40 (t, *J* = 7.6 Hz, 3 H), 7.20 (t, *J* = 7.3 Hz, 1 H), 2.44 (s, 3 H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 187.66, 159.03, 138.43, 136.68, 135.55, 133.06, 131.84, 129.26, 128.75, 128.51, 125.32, 119.95, 21.40 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3443, 3341, 3056, 2918, 2850, 1686, 1660, 1593, 1535, 1498, 1443 cm^{-1}. LC-MS (ESI): *m*/*z* calcd. for $C_{15}H_{12}NO_2$ [M – H]$^-$ 238.1; found 237.9. HRMS (TOF): *m*/*z* calcd. for $C_{15}H_{12}NO_2$ [M – H]$^-$ 238.0868; found 238.0861.

***N*-(3-Fluorophenyl)-2-oxo-2-(*m*-tolyl)acetamide (2o):** Yield 110.5 mg (86%); yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.07 (br. s, 1 H), 8.25–8.19 (m, 2 H), 7.71 (dd, *J* = 11.1, 1.5 Hz, 1 H), 7.49 (d, *J* = 7.5 Hz, 1 H), 7.42 (t, *J* = 7.6 Hz, 1 H), 7.35 (dd, *J* = 5.5, 4.4 Hz, 2 H), 6.96–6.89 (m, 1 H), 2.45 (s, 3 H) ppm. ^{13}C NMR (126 MHz,

$CDCl_3$): δ = 185.52, 161.32 (d, *J* = 245.6 Hz), 157.31, 136.80, 136.45 (d, *J* = 10.8 Hz), 134.00, 131.16, 130.13, 128.67 (d, *J* = 9.3 Hz), 127.08, 126.85, 113.65 (d, *J* = 3.0 Hz),110.37 (d, *J* = 21.4 Hz), 105.74 (d, *J* = 26.5 Hz), 19.67 ppm. LC-MS (ESI): *m*/*z* calcd. for $C_{15}H_{12}NO_2$ [M – H]$^-$ 256.1; found 256.3.

***N*-(2-Oxo-2-phenylacetyl)benzamide (7a):**[3a] Yield 114.0 mg (90%); white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.02 (br. s, 1 H), 8.12 (d, *J* = 7.5 Hz, 2 H), 7.94 (d, *J* = 8.0 Hz, 2 H), 7.64 (dd, *J* = 11.6, 7.4 Hz, 2 H), 7.52 (dd, *J* = 16.3, 8.1 Hz, 4 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 186.63, 165.35, 134.72, 134.02, 132.36, 130.98, 130.13, 129.14, 128.95, 128.15 ppm. IR ($CHCl_3$): ṽ = 3285, 2921, 2851, 1719, 1687, 1467, 1451, 1212 cm^{-1}. LC-MS (ESI) *m*/*z* calcd. for $C_{15}H_{10}NO_3$ [M – H]$^-$ 252.1; found 252.0. HRMS (TOF): *m*/*z* calcd. for $C_{15}H_{10}NO_3$ [M – H]$^-$ 252.0661; found 252.0665.

3-Methoxy-*N*-(2-oxo-2-phenylacetyl)benzamide (7b):[3a] Yield 129.0 mg (91%); white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.12 (br. s, 1 H), 8.10 (d, *J* = 7.4 Hz, 2 H), 7.66 (t, *J* = 7.0 Hz, 1 H), 7.58–7.46 (m, 4 H), 7.39 (t, *J* = 7.9 Hz, 1 H), 7.16 (d, *J* = 8.2 Hz, 1 H), 3.79 (s, 3 H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 186.75, 165.39, 160.12, 134.75, 132.31, 132.03, 130.16, 129.98, 129.02, 121.02, 120.13, 112.64, 55.54 ppm. IR ($CHCl_3$): ṽ = 3278, 2922, 2851, 1718, 1686, 1471, 1451, 1272, 1211 cm^{-1}. LC-MS (ESI): *m*/*z* calcd. for $C_{16}H_{12}NO_4$ [M – H]$^-$ 282.1; found 282.1. HRMS (TOF): *m*/*z* calcd. for $C_{16}H_{12}NO_4$ [M – H]$^-$ 282.0766; found 282.0762.

***N*-[2-(4-Methoxyphenyl)-2-oxoacetyl]benzamide (7c):**[3a] Yield 130.0 mg (92%); white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.91 (br. s, 1 H), 8.26 (d, *J* = 8.9 Hz, 2 H), 7.99–7.85 (m, 2 H), 7.71–7.60 (m, 1 H), 7.52 (dd, *J* = 10.6, 4.8 Hz, 2 H), 7.06–6.95 (m, 2 H), 3.91 (s, 3 H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 184.51, 165.13, 165.00, 133.79, 133.31, 131.69, 129.12, 128.01, 125.30, 114.35, 55.67 ppm. IR ($CHCl_3$): ṽ = 3743, 3281, 2934, 2844, 1717, 1681, 1599, 1463, 1451, 1265, 1218 cm^{-1}. LC-MS (ESI): *m*/*z* calcd. for $C_{16}H_{12}NO_4$ [M – H]$^-$ 282.1; found 282.1. HRMS (TOF): *m*/*z* calcd. for $C_{16}H_{12}NO_4$ [M – H]$^-$ 282.0766; found 282.0758.

***N*-[2-(4-Methoxyphenyl)-2-oxoacetyl]-3-methylbenzamide (7d):** Yield 133.5 mg (90%); white solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 10.00 (br. s, 1 H), 8.22 (s, 2 H), 7.77–7.67 (m, 2 H), 7.49–7.36 (m, 2 H), 7.00 (d, *J* = 7.3 Hz, 2 H), 3.90 (s, 3 H), 2.42 (s, 3 H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 184.68, 165.24, 165.07, 139.16, 134.64, 133.21, 131.54, 128.99, 128.70, 125.30, 125.07, 114.36, 55.70, 21.37 ppm. IR ($CHCl_3$): ṽ = 3744, 3292, 2921, 2850, 1716, 1680, 1599, 1464, 1266, 1216, 1165 cm^{-1}. LC-MS (ESI): *m*/*z* calcd. for $C_{17}H_{14}NO_4$ [M – H]$^-$ 296.1; found 296.1. HRMS (TOF): *m*/*z* calcd. for $C_{17}H_{14}NO_4$ [M – H]$^-$ 296.0923; found 296.0929.

***N*-[2-Oxo-2-(*m*-tolyl)acetyl]benzamide (7e):**[3b] Yield 123.0 mg (92%); white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.79 (br. s, 1 H), 7.85 (d, *J* = 7.4 Hz, 4 H), 7.56 (t, *J* = 7.2 Hz, 1 H), 7.43 (dd, *J* = 17.4, 9.4 Hz, 3 H), 7.34 (t, *J* = 7.5 Hz, 1 H), 2.36 (s, 3 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 186.80, 165.24, 138.88, 135.60, 133.95, 132.36, 130.48, 129.13, 128.83, 128.11, 127.46, 21.30 ppm. IR ($CHCl_3$): ṽ = 3292, 2921, 2851, 1718, 1682, 1465, 1242, 1157 cm^{-1}. LC-MS (ESI): *m*/*z* calcd. for $C_{16}H_{12}NO_3$ [M – H]$^-$ 266.1; found 266.1. HRMS (TOF): *m*/*z* calcd. for $C_{16}H_{12}NO_3$ [M – H]$^-$ 266.0817; found 266.0812.

3-Methyl-*N*-[2-oxo-2-(*m*-tolyl)acetyl]benzamide (7f): Yield 125.0 mg (89%); white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.16 (br. s, 1 H), 7.87–7.74 (m, 2 H), 7.71–7.63 (m, 2 H), 7.39–7.25 (m, 4 H), 2.32 (s, 3 H), 2.27 (s, 3 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 187.14, 165.80, 139.10, 138.90, 135.49, 134.81, 132.42, 130.69, 130.19, 128.96, 128.84, 127.19, 125.33, 21.31, 21.25 ppm. IR ($CHCl_3$): ṽ = 3786, 3284, 2922, 2852, 1717, 1681, 1466, 1243, 1156 cm^{-1}. LC-MS (ESI): *m*/*z* calcd. for $C_{17}H_{14}NO_3$ [M – H]$^-$ 280.1; found 280.1. HRMS (TOF): *m*/*z* calcd. for $C_{17}H_{14}NO_3$ [M – H]$^-$ 280.0974; found 280.0979.

***N*-[2-Oxo-2-(*p*-tolyl)acetyl]benzamide (7g):**[3a] Yield 120.0 mg (90%); white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.88 (br. s, 1 H), 7.98 (d, *J* = 7.7 Hz, 2 H), 7.85 (d, *J* = 7.6 Hz, 2 H), 7.56 (t, *J* = 7.4 Hz, 1 H), 7.44 (t, *J* = 7.6 Hz, 2 H), 7.26 (d, *J* = 7.9 Hz, 2 H), 2.37 (s, 3 H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 186.21, 165.26, 146.18, 133.98, 131.16, 130.42, 129.83, 129.75, 129.15, 128.13, 22.00 ppm. IR ($CHCl_3$): ṽ = 3851, 3744, 3387, 2920, 2851, 1717, 1681, 1606, 1465, 1248, 1176 cm^{-1}. LC-MS (ESI): *m*/*z* calcd. for $C_{16}H_{12}NO_3$ [M – H]$^-$ 266.1; found 266.0. HRMS (TOF): *m*/*z* calcd. for $C_{16}H_{12}NO_3$ [M – H]$^-$ 266.0817; found 266.0813.

2-Methyl-*N*-[2-oxo-2-(*p*-tolyl)acetyl]benzamide (7h): Yield 121.0 mg (86%); white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.44 (br. s, 1 H), 8.03 (d, *J* = 7.7 Hz, 2 H), 7.48 (d, *J* = 7.8 Hz, 1 H), 7.36 (t, *J* = 7.4 Hz, 1 H), 7.23 (t, *J* = 9.6 Hz, 4 H), 2.42 (s, 3 H), 2.37 (s, 3 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 185.79, 167.32, 146.28, 138.32, 132.47, 132.08, 131.91, 130.79, 129.83, 129.65, 127.41, 126.14, 21.96, 20.29 ppm. IR ($CHCl_3$): ṽ = 3851, 3747, 3671, 3242, 2922, 2852, 1715, 1680, 1606, 1453, 1285, 1176 cm^{-1}. LC-MS (ESI): *m*/*z* calcd. for $C_{17}H_{14}NO_3$ [M – H]$^-$ 280.1; found 280.1. HRMS (TOF): *m*/*z* calcd. for $C_{17}H_{14}NO_3$ [M – H]$^-$ 280.0974; found 280.0967.

2-Nitro-*N*-[2-oxo-2-(*p*-tolyl)acetyl]benzamide (7i): Yield 131.0 mg (84%); light-yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.83 (br. s, 1 H), 8.29 (d, *J* = 8.2 Hz, 1 H), 8.11 (d, *J* = 8.1 Hz, 2 H), 7.79 (t, *J* = 7.4 Hz, 1 H), 7.69 (t, *J* = 7.5 Hz, 1 H), 7.49 (d, *J* = 7.3 Hz, 1 H), 7.25 (d, *J* = 7.6 Hz, 2 H), 2.41 (s, 3 H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 184.21, 166.85, 146.91, 145.32, 134.59, 132.00, 131.46, 130.87, 129.58, 129.43, 127.89, 124.37, 22.01 ppm. IR ($CHCl_3$): ṽ = 3403, 3290, 2921, 2851, 1731, 1699, 1674, 1605, 1531, 1466, 1348 cm^{-1}. LC-MS (ESI): *m*/*z* calcd. for $C_{16}H_{11}N_2O_5$ [M – H]$^-$ 311.1; found 311.1. HRMS (TOF): *m*/*z* calcd. for $C_{16}H_{11}N_2O_5$ [M – H]$^-$ 311.0668; found 311.0672.

3-Methoxy-*N*-[2-oxo-2-(*m*-tolyl)acetyl]benzamide (7j): Yield 122.0 mg (82%); white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.13 (br. s, 1 H), 7.94–7.84 (m, 2 H), 7.48 (dt, *J* = 7.5, 6.7 Hz, 3 H), 7.40 (dd, *J* = 16.1, 7.9 Hz, 2 H), 7.15 (dd, *J* = 8.2, 1.8 Hz, 1 H), 3.80 (s, 3 H), 2.42 (s, 3 H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 187.32, 171.59, 166.26, 159.87, 138.84, 135.92, 133.74, 132.25, 130.73, 129.81, 128.78, 127.76, 119.39, 118.92, 112.64, 55.50, 21.29 ppm. LC-MS (ESI): *m*/*z* calcd. for $C_{17}H_{14}NO_4$ [M – H]$^-$ 296.1; found 296.1.

2-Methyl-*N*-[2-(3-nitrophenyl)-2-oxoacetyl]benzamide (7k): Yield 125.0 mg (80%); light-yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.51 (br. s, 1 H), 8.94 (s, 1 H), 8.52 (d, *J* = 6.9 Hz, 2 H), 7.76 (t, *J* = 8.0 Hz, 1 H), 7.61 (d, *J* = 7.6 Hz, 1 H), 7.47 (t, *J* = 7.4 Hz, 1 H), 7.33 (t, *J* = 7.7 Hz, 2 H), 2.49 (s, 3 H) ppm. LC-MS (ESI): *m*/*z* calcd. for $C_{16}H_{11}N_2O_5$ [M – H]$^-$ 311.1; found 311.1.

2-Oxo-2-phenyl-*N*-(phenylsulfonyl)acetamide (8a): Yield 115.5 mg (80%); white solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.26 (d, *J* = 7.5 Hz, 2 H), 8.16 (d, *J* = 7.5 Hz, 2 H), 7.74–7.61 (m, 2 H), 7.61–7.53 (m, 2 H), 7.50–7.41 (m, 2 H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 183.98, 158.09, 137.89, 135.46, 134.50, 131.78, 131.47, 129.18, 128.81, 128.60 ppm. IR ($CHCl_3$): ṽ = 3443, 3241, 3096, 3070, 2921, 2851, 1734, 1676, 1447, 1405, 1352, 1268, 1187, 1171, 544 cm^{-1}. LC-MS (ESI): *m*/*z* calcd. for $C_{14}H_{10}NO_4S$ [M – H]$^-$ 288.0; found 288.0. HRMS (TOF): *m*/*z* calcd. for $C_{14}H_{10}NO_4S$ [M – H]$^-$ 288.0331; found 288.0336.

2-Oxo-*N*-(phenylsulfonyl)-2-(*m*-tolyl)acetamide (8b): Yield 113.5 mg (75%); white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.53 (s, 1 H), 8.08 (d, J = 7.7 Hz, 2 H), 7.99 (d, J = 6.7 Hz, 2 H), 7.61 (t, J = 7.4 Hz, 1 H), 7.51 (t, J = 7.6 Hz, 2 H), 7.39 (d, J = 7.5 Hz, 1 H), 7.27 (t, J = 7.8 Hz, 1 H), 2.31 (s, 3 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 184.12, 158.15, 138.73, 137.98, 136.31, 134.44, 131.77, 131.74, 129.16, 128.73, 128.68, 128.57, 21.24 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3440, 3259, 2921, 2851, 1718, 1676, 1602, 1449, 1174, 544 cm^{-1}. LC-MS (ESI): *m*/*z* calcd. for $C_{15}H_{12}NO_4S$ [M – H]$^-$ 302.0; found 302.1. HRMS (TOF): *m*/*z* calcd. for $C_{15}H_{12}NO_4S$ [M – H]$^-$ 302.0487; found 302.0516.

2-(4-Bromophenyl)-2-oxo-*N*-(phenylsulfonyl)acetamide (8c): Yield 135.5 mg (74%); white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.59 (s, 1 H), 8.21–8.10 (m, 4 H), 7.70 (t, J = 7.3 Hz, 1 H), 7.60 (dd, J = 15.1, 7.9 Hz, 4 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 182.96, 157.77, 137.82, 134.57, 132.83, 132.25, 131.50, 130.53, 129.20, 128.60 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3857, 3440, 3239, 2922, 2065, 1732, 1682, 1643, 1633, 1585 cm^{-1}. LC-MS (ESI): *m*/*z* calcd. for $C_{14}H_9BrNO_4S$ [M – H]$^-$ 365.9; found 367.9. HRMS (TOF): *m*/*z* calcd. for $C_{14}H_9BrNO_4S$ [M – H]$^-$ 365.9436; found 365.9440.

2-(4-Fluorophenyl)-2-oxo-*N*-(phenylsulfonyl)acetamide (8d): Yield 110.5 mg (72%); white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.36 (dd, J = 7.8, 5.9 Hz, 2 H), 8.15 (d, J = 7.8 Hz, 2 H), 7.69 (t, J = 7.4 Hz, 1 H), 7.59 (t, J = 7.6 Hz, 2 H), 7.14 (t, J = 8.4 Hz, 2 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 190.2, 181.1, 135.4, 134.8, 134.6, 130.0, 128.3, 127.4, 125.1, 124.9, 110.3, 37.6 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3439, 3276, 2921, 2921, 2851, 1736, 1668, 1597, 1404, 1270 cm^{-1}. LC-MS (ESI): *m*/*z* calcd. for $C_{14}H_9FNO_4S$ [M – H]$^-$ 306.0; found 306.0. HRMS (TOF): *m*/*z* calcd. for $C_{14}H_9FNO_4S$ [M – H]$^-$ 306.0236; found 306.0237.

2-(4-Fluorophenyl)-2-oxo-*N*-tosylacetamide (8e): Yield 122 mg (76%); white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.42–8.32 (m, 2 H), 8.03 (d, J = 7.9 Hz, 2 H), 7.38 (d, J = 7.9 Hz, 2 H), 7.14 (t, J = 8.4 Hz, 2 H), 2.45 (s, 3 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 182.17, 167.19 (d, J = 259.9 Hz), 157.92, 145.83, 134.85, 134.61 (d, J = 9.9 Hz), 129.79, 128.66, 116.20 (d, J = 22.0 Hz), 21.74 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3435, 3245, 2921, 2851, 2346, 1733, 1674, 1596, 1270, 1171 cm^{-1}. LC-MS (ESI): *m*/*z* calcd. for $C_{15}H_{11}FNO_4S$ [M – H]$^-$ 320.0; found 320.0. HRMS (TOF): *m*/*z* calcd. for $C_{15}H_{11}FNO_4S$ [M + H]$^+$ 322.0549; found 322.0572.

2-Oxo-2-(*m*-tolyl)-*N*-tosylacetamide (8f): Yield 111.0 mg (70%); white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.03 (t, J = 7.5 Hz, 4 H), 7.45 (d, J = 7.4 Hz, 1 H), 7.35 (dd, J = 11.7, 8.0 Hz, 3 H), 2.44 (s, 3 H), 2.38 (s, 3 H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 184.27, 158.31, 145.72, 138.70, 136.28, 134.94, 131.79, 131.74, 129.79, 128.72, 128.68, 128.64, 21.77, 21.29 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3444, 3241, 3096, 3070, 2921, 2851, 1734, 1676, 1447, 1405, 1352, 1268, 1187, 1171 cm^{-1}. LC-MS (ESI): *m*/*z* calcd. for $C_{16}H_{14}NO_4S$ [M – H]$^-$ 316.0; found 316.0. HRMS (TOF): *m*/*z* calcd. for $C_{16}H_{14}NO_4S$ [M – H]$^-$ 316.0644; found 316.0648.

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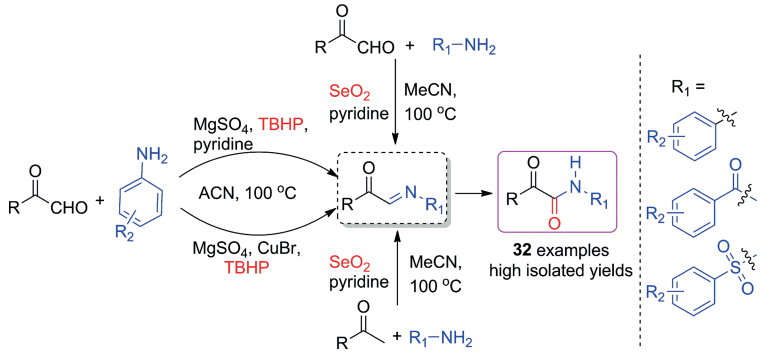

An efficient oxidative amidation reaction between 2-oxoaldehyde and weak nucleophilic amines (anilines, benzamides, and sulfonamides) is reported. Mechanistic studies show that α-carbonylimine (–CO–C=N–) based compounds are a central feature of the reaction. It was found that an adjacent CO moiety enhances the electrophilicity of the C=N system, which favors attack of oxidant (TBHP or SeO_2).

Keywords: Synthetic methods / Oxidation / Amines / Amides / Sulfonamides

