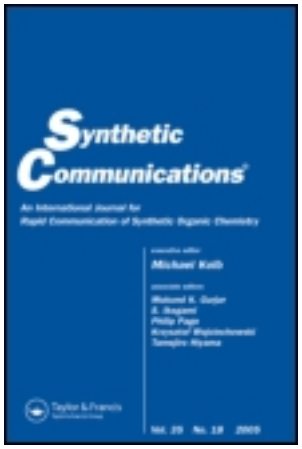

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Highly Anti-Selective One-Pot Multicomponent Synthesis of Mannich-Type N-Acylated β-Amino Acid Derivatives by Copper or Sodium Salt Catalysis

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HIGHLY *ANTI*-SELECTIVE ONE-POT MULTICOMPONENT SYNTHESIS OF MANNICH-TYPE N-ACYLATED β-AMINO ACID DERIVATIVES BY COPPER OR SODIUM SALT CATALYSIS

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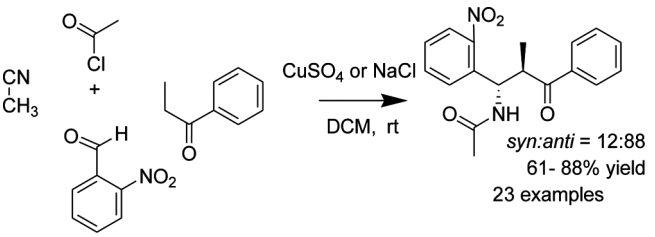
GRAPHICAL ABSTRACT



Abstract *A stereo-defined process has been developed for the synthesis of Mannich-type products using readily available copper sulfate or sodium chloride as catalyst. Good to excellent diastereoselectivity has been achieved for a broad array of substrates. The observed diastereoselectivity is explained on the basis of the steric interaction between the acyloxy group of the aldehyde carbon and the more hindered α-substituted enolate anion. This steric interaction helps the addition to take place through the less-hindered face to produce the* anti-*isomers predominantly.*

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Keywords Amido ketone; common salt; Mannich-type; multicomponent reaction; stereoselectivity

INTRODUCTION

The traditional chemical industry was hazardous and polluting. It generated stoichiometric amounts of waste, causing much pollution of both air and water. Today, the escalating costs of petrochemicals and increasing energy and raw material consumption are forcing a change. As a consequence, the industry demands from chemists the development of new reaction methodologies to obtain novel compounds

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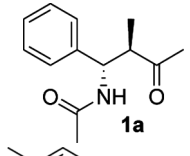
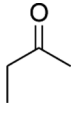
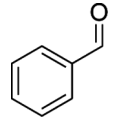
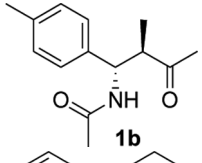
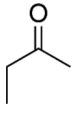
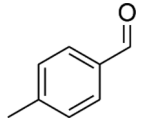
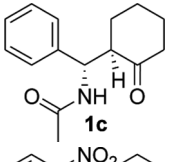
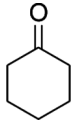
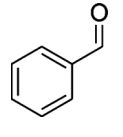
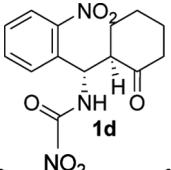
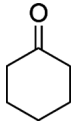
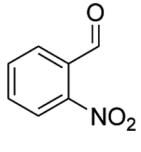
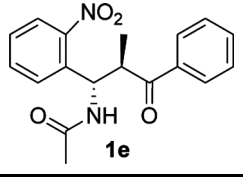
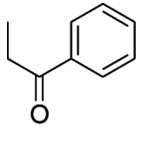
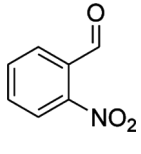
in a fast, clean, and efficient way.[1] In this scenario, multicomponent reactions (MCRs) offer an alternative to the traditional synthesis mainly because they are based on available starting materials, operationally simple, easily automatable, resource effective, atom economical, and ecologically benign.[1b,2] Mannich-type products, specifically β-amino carbonyl compounds, are useful chiral building blocks for the synthesis of β-amino acids, β-lactams, β-amino alcohols, and so forth.[3] These compounds are generally synthesized by chiral Lewis acids–assisted catalytic asymmetric reactions of imines derived from aldehydes and amines with enolate compounds. Several efficient Lewis acid–have been reported over the years,[4] and a recent attraction in this field is the development of the concept of bifunctional catalysis, wherein both partners of a bimolecular reaction are simultaneously activated, is very powerful for developing efficient asymmetric catalysts.[5] Even though these chiral Lewis acids have proven to be efficient for many reactions, a major drawback is that most Lewis acids are unstable in the presence of water, and some of them are even moisture sensitive. Also, multistep reactions demand high synthetic skill. As an efficient alternative to the synthesis of Mannich-type products, we and other groups have developed a one-pot multicomponent protocol based on the coupling of an aldehyde, an enolizable ketone, and a nitrile molecule in the presence of an acid chloride and an acid catalyst.[6] Several efficient catalysts have been reported by various research groups, including copper(II) tetrafluoroborate,[7a] $SnCl_4/SiO_2$,[7b] $Cu(OTf)_2$ and $Sc(OTf)_3$,[7c] $Mn(bpdo)_2Cl_2$/MCM-41,[7d] $CeCl_3 \cdot 7H_2O$,[7e] $ZrOCl_2 \cdot 8H_2O$,[7f] iron(III) chloride.[7g] (For a detailed list, see the supporting information.) Approaches with stereocontrol are limited. Until recently, the scope of this three-component process was limited to the synthesis of β-acetamido carbonyl compounds. Recent developments in this area, particularly from our laboratory,[6b] revealed that this process is highly useful for the one-step synthesis of highly functionalized organic intermediates.

Our continuing interest is in developing this methodology as a novel route to access highly functionalized structural scaffolds in a cost-effective and environmentally friendly manner, and more importantly, as a process that requires less operational skill and conditions. We considered the possibility of performing this reaction in very mild conditions for the incorporation of a large variety of substrates. For this, we decided to follow this reaction in the presence of salts such as NaCl and $CuSO_4 \cdot 5H_2O$.

RESULTS AND DISCUSSION

We initiated our studies with the synthesis of the β-amino carbonyl compound **1a** (Table 1). The sequential addition of benzaldehyde, ethyl methyl ketone and acetyl chloride in the presence of sodium chloride or copper sulphate in acetonitrile resulted in the rapid formation of **1a**. With a very low amount of the salt (50 mg), the reaction reached 70% conversion (with respect to the consumption of aldehyde and ketone) within 10 minutes with a diastereoselectivity 90%. An identical reaction with ammonium chloride afforded **1a** in 15–23% yield with moderate stereoselectivity (35:65). Here the nitrile source acted as both reagent and solvent. Many nitriles are expensive and their uses in quantities at solvent level are not affordable. To overcome this problem, we then examined the synthesis of **1a** in solvents like chloroform and dichloromethane with stoichiometric amounts of aldehyde, enolizable ketone, nitrile

Table 1. Copper or sodium salt catalyzed stereoselective three component reactions of aldehydes, α -substituted ketones, and acetonitrile[a]

		Copper sulphate as catalyst		Sodium chloride as catalyst		Components			
Entry	Product	% Yield[b]	*syn: anti*[c]	% Yield[b]	*syn: anti*[c]	A	B	C	D
1	 **1a**	64	9:91	57	13:87				
2	 **1b**	82	9:91	70	12:88				
3	 **1c**	64	9:91	60	14:86				
4	 **1d**	61	10:90	58	10:90				
5	 **1e**	69	12:88	61	13.87				

[a]All reactions were carried out at room temperature.
[b]Isolated yield, all products were identified by comparing their NMR and IR values with those for authentic samples.[6a,6b]
[c]Assigned based on comparison with literature value for the coupling constants of methine proton.[6a]

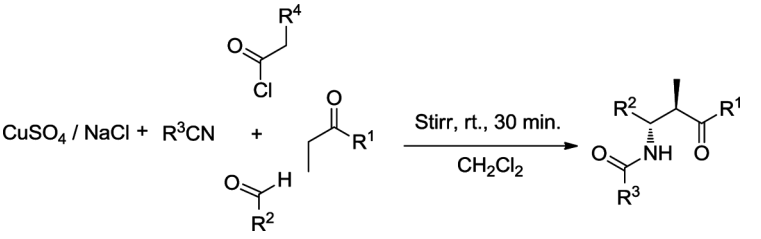
source and acid chloride, and successfully isolated the desired β-amino acid derivatives in comparable yield corresponding to that obtained from reactions carried out with an excess amount of nitriles.

The reaction can be readily followed by Fourier transform—infrared (FT-IR) spectroscopy by recording the disappearance of the aldehyde peak followed by the appearance of amide peak at 1650 cm^{-1}. The structure of the product was confirmed via ^{1}H NMR, ^{13}C NMR, FT-IR, and mass spectral studies. Stereochemistry was assigned by comparing the *J* values of the methine proton with reported data.[6a]

The substrate scope of the reaction was demonstrated with various aldehydes and ketones (Scheme 1, Tables 1–3). The reactions were generally conducted with 50 mg of sodium chloride or copper sulfate for 30 min. In general, variations in the substitution patterns on aldehyde and ketone units were well tolerated (Table 1). Aliphatic aldehydes including α,β-unsaturated aldehydes such as crotonaldehyde were not good substrates for the reaction. On the other hand, aromatic α,β-unsaturated aldehydes such as cinnamaldehyde afforded the corresponding product in moderate yield (Table 3, entry 8). We highlight here that the reactions carried out in the presence of other acid chlorides resulted in the formation of desired products in satisfactory yield (Table 2, entry 8). The only unmatched result was found in the reaction of cinnamoyl chloride, which fails to produce the desired product. The outcome of the reaction was observed to be a bit sensitive to the presence of polar substituent in substrates. Thus, our studies with electron-withdrawing groups present in substrates such as nitrobenzaldehyde gave lower yields but maintained the *anti*-diastereoselectivity. Interestingly, reactions of cyclohexanone were found to proceed in a controlled manner and, workup with solvent mixtures afforded analytically pure products (Table 1, entries 3 and 4).

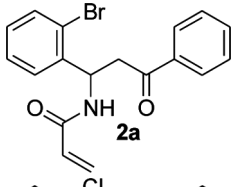
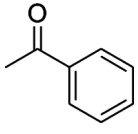
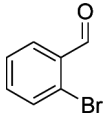
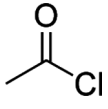
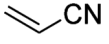
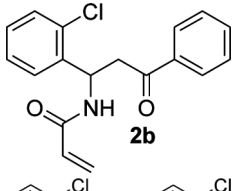
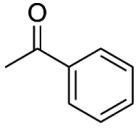
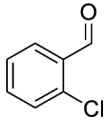
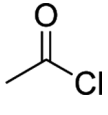
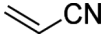
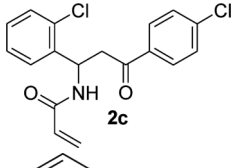
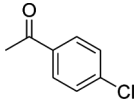
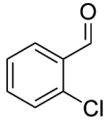
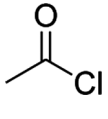
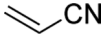
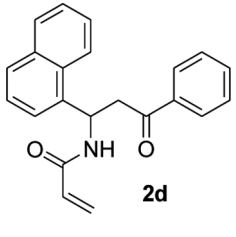
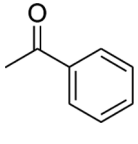
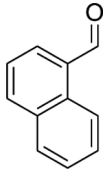
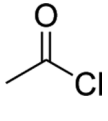
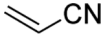
We subsequently investigated the reaction with various nitriles. Nitriles with terminal double bonds were highly compatible and afforded a broad verity of amino ketone derivatives (Table 2, entries 1–4). Use of other nitriles such as benzyl cyanide, benzonitrile, valeronitrile, and propionitrile resulted in the formation of the title compounds in moderate to good yields (Table 2, entries 5–10). Control reactions done in the absence of acid chloride and catalyst failed to produce the β-amino acid derivatives with all combination of substrates.

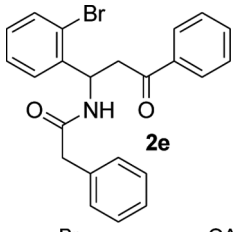
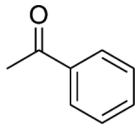
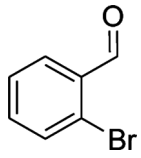
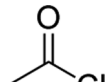
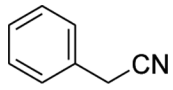
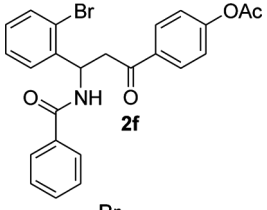
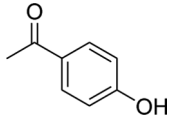
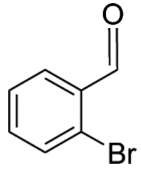
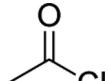
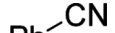
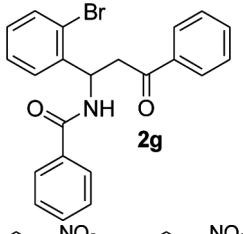
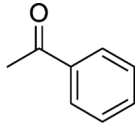
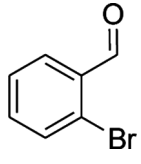
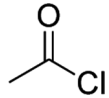
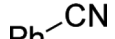
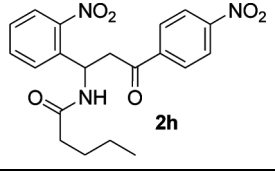
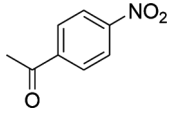
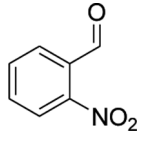
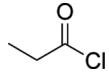
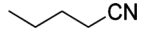
A possible catalytic cycle that illustrates formation of *anti*-selective Mannich-type product is given in Scheme 2. The reaction is initiated by the complexation of the carbonyl oxygen of the ketone to the metal atom of the catalyst to produce a more sterically hindered enolate anion **5** with a more nucleophilic α carbon. Subsequent reactions of this metal enolate with aldehyde and acid chloride resulted in carbon–carbon bond formation to produce a β-acyloxy ketone derivative **6**. The steric interaction between



Scheme 1. Sodium chloride catalyzed *anti*-selective formation of β-amino carbonyl compound scaffolds.

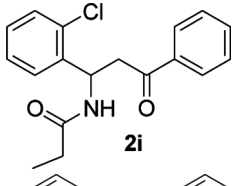
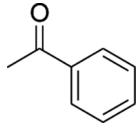
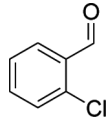
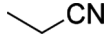
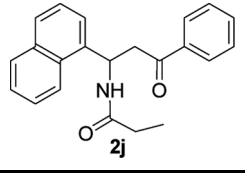
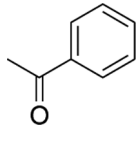
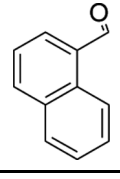
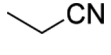
Table 2. Copper or sodium salt catalyzed three component reactions of aldehydes and α-unsubstituted ketones with various nitriles[a]

Entry	Product	Yielding using $CuSO4^{b}$ (%)	Yielding using NaCl as catalyst[b] (%)	Components			
				A	B	C	D
1	 **2a**	66	58				
2	 **2b**	71	65				
3	 **2c**	74	68				
4	 **2d**	68	60				

5	 **2e**	69	64				
6	 **2f**	71	60				
7	 **2g**	69	60				
8	 **2h**	60[c]	51[c]				

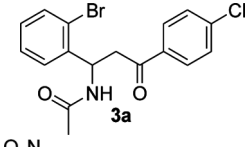
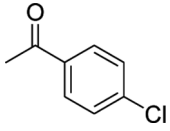
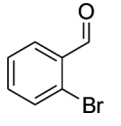
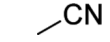
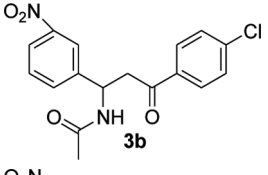
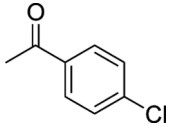
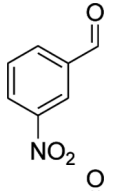
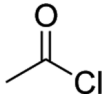
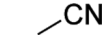
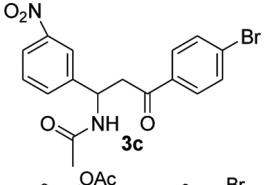
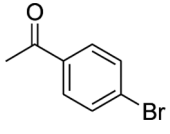
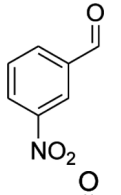
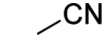
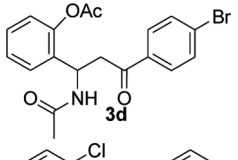
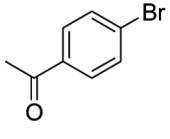
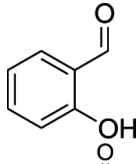
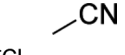
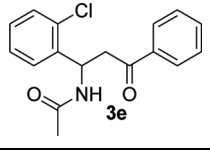
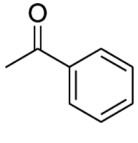
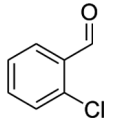
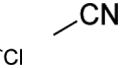
(*Continued*)

Table 2. Continued

Entry	Product	Yielding using $CuSO4^b$ (%)	Yielding using NaCl as catalyst[b] (%)	Components			
				A	B	C	D
9	 **2i**	88	71				
10	 **2j**	79	85				

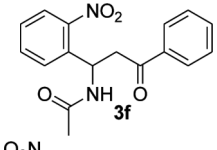
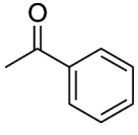
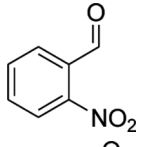
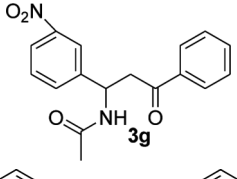
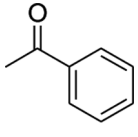
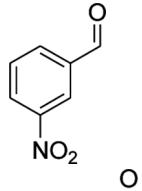
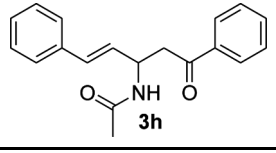
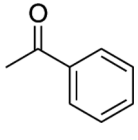
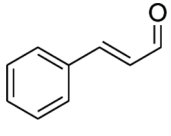
[a]All reactions were carried out at room temperature using dichloromethane as solvent.
[b]Isolated yield.
[c]Product was identified by comparing its NMR and IR values with those for authentic samples.[6b]

Table 3. Copper or sodium salt catalyzed three-component reactions of aldehydes, α -unsubstituted ketones, and acetonitrile[a]

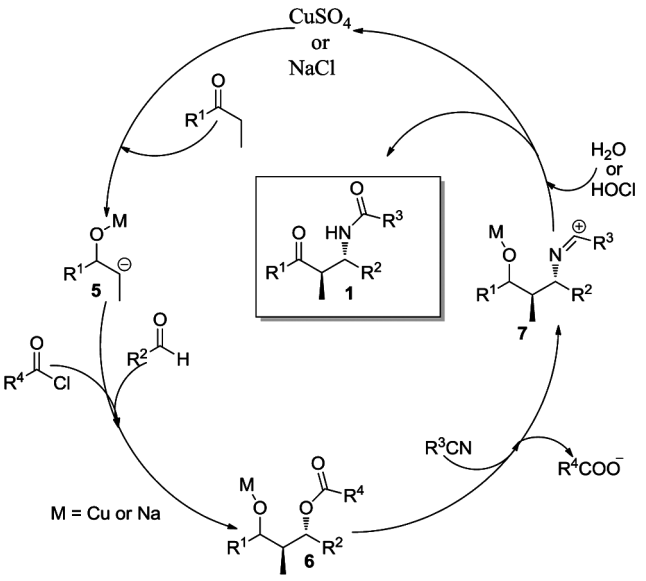
Entry	Product	Yielding using $CuSO4^{b}$ (%)	Yielding using NaCl as catalyst[b] (%)	Components			
				A	B	C	D
1	 **3a**	86	77				
2	 **3b**	74	69				
3	 **3c**	73	65				
4	 **3d**	79	65				
5	 **3e**	79	73				

(*Continued*)

Table 3. Continued

Entry	Product	Yielding using CuSO4[b] (%)	Yielding using NaCl as catalyst[b] (%)	Components			
				A	B	C	D
6	 **3f**	87	75				
7	 **3g**	81	68				
8	 **3h**	65	53				

[a]All reactions were carried out at room temperature.
[b]Isolated yield.
[c]Products were identified by comparing their NMR and IR values with those for authentic samples.[6]



Scheme 2. Proposed catalytic cycle for the *anti*-diastereoselective formation of β-amido carbonyl scaffolds using sodium chloride or copper sulfate as catalyst.

the acyloxy group present in the aldehyde carbon and the more hindered α -substituted enolate anion forces the addition to take place through the less hindered face to produce **6** in the *anti* form. The acyloxy group in **6** is then displaced by nucleophilic nitrogen of the nitrile to produce a stable cation intermediate **7**. Addition of water or other reactive species such as HOCl[8] formed during the reaction leads to the formation of the *anti*-diastereomer **1** and closes the catalytic cycle.[6b]

CONCLUSIONS

In conclusion, we have developed an efficient multicomponent process to access stereo-defined β-amino acid derivatives using readily available salts such as sodium chloride or copper sulfate as catalyst. The new protocol is highly convenient for the diastereoselective construction of scaffold diversity suitable for organic and pharmaceutical chemistry. The simplicity, environmental acceptability, and cost-effectiveness of this one-pot strategy makes it a practical alternative to the synthesis of Mannich-type N-substituted amino acid derivatives.

EXPERIMENTAL

Typical Experimental Procedure for the Stereoselective One-Pot, Three-Component Coupling Reactions of Aldehydes with α-Substituted Ketones and Acetonitrile with Sodium Chloride or Copper Sulfate as Catalyst (1a)

Powdered $CuSO_4 \cdot 5H_2O$ (0.050 g, 8 mol% by weight of benzaldehyde) was added to an acetonitrile (4 mL) solution of benzaldehyde (0.265 g, 2.5 mmol), ethyl

methyl ketone (0.180 g, 2.5 mmol), and acetyl chloride (1 mL) at room temperature. The resulting mixture was stirred for 10 min. The reaction mixture was then poured into distilled water and stirred well. The precipitate obtained was collected by filtration, washed with distilled water (3×20 mL), and dried under vacuum. The dried solid was then washed with diethyl ether (3×15 mL) and airdried to yield the pure β-amino acid derivative **1a**. ^{1}H NMR analysis was used to determine the diastereoselectivity of the reaction. The product was identified by comparing its NMR and IR values with those for an authentic sample.[6b] Reactions of cyclohexanone required solvent workup or chromatography. The crude product obtained from aqueous workup was purified by flash chromatography on silica gel (EtOAc/petroleum ether, 1:8) to yield analytically pure products. similar procedure was adopted for the purification of products obtained from other nitrile reactions.

Spectral Data

N-(1-(2-Bromophenyl)-3-oxo-3-phenylpropyl)acrylamide (2a). ^{1}H NMR, (400 MHz, DMSO-d_6): δ 8.00–7.97 (dd, $J = 5.6$ and 7.6 Hz, 2H), 7.66–7.58 (m, 2H), 7.54–7.48 (m, 3H), 7.40–7.38 (dd, $J = 1.2$ and 7.2 Hz, 1H), 7.22–7.20 (dd, $J = 2$ and 8 Hz, 1H), 5.70–5.64 (m, 1H), 3.75–3.72 (t, 2H), 3.53–3.46 (dd, J = 9.6 and 17.2 Hz, 1H), 2.59–2.56 (t, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 196.27, 168.25, 141.76, 136.29, 133.35, 132.61, 128.91, 128.71, 128.04, 127.80, 122.19, 48.79, 43.29, 40.91, 40.12; FT-IR (KBr) γ max 3298.64, 3065.30, 2962.13, 1682.59, 1649.80, 1595.81, 1549.52, 1438.64, 1406.82, 1384.64, 1356.68, 1231.33, 1019.19, 747.28, 689.42 cm^{-1}; MS m/z 358.1 (M^+), 261.1.

N-(1-(2-Chlorophenyl)-3-oxo-3-phenylpropyl)acrylamide (2c). ^{1}H NMR, (400 MHz, DMSO-d_6): δ 8.55–8.53 (d, $J = 7.20$ Hz, 1H), 7.98–7.96 (t, 2H), 7.66–7.62 (t, 1H), 7.54–7.49 (m, 3H), 7.44–7.41 (dd, 1H), 7.36–7.25 (m, 2H), 5.77 (s, 1H), 3.74–3.71 (t, 3H), 3.54–3.48 (t, 1H), 2.58–2.55 (t, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 196.40, 168.23, 140.13, 136.31, 133.32, 131.58, 129.31, 128.71, 128.68, 128.58, 128.02, 127.70, 127.29, 46.40, 43.17, 40.90, 40.12, 39.91, 39.71, 39.50, 39.29, 39.08, 38.87, 38.17; FT-IR (KBr) γ max 3292.86, 3086.51, 2970.80, 1682.59, 1647.88, 1596.77, 1552.42, 1442.49, 1404.49, 1384.64, 1356.68, 1287.25, 1231.33, 1196.61, 1119.26, 748.24, 690.39, 614.21 cm^{-1}; MS m/z 314.1 (M^+), 229.1.

N-(1-(2-Chlorophenyl)-3-(4-chlorophenyl)-3-oxopropyl)acrylamide (2d). ^{1}H NMR, (400 MHz, DMSO-d_6): δ 8.55–8.53 (d, $J = 7.2$ Hz, 1H), 8.00–7.98 (d, $J = 8.4$ Hz, 2H), 7.94–7.60 (d, 2H), 7.51–7.49 (dd, $J = 1.6$ and 8 Hz, 1H), 7.44–7.41 (dd, $J = 1.2$ and 8 Hz, 1H), 7.25–7.26 (m, 2H), 5.73–5.68 (m, 1H), 3.74–3.66 (dd, $J = 6$ and 12.8 Hz, 2H), 3.53–3.46 (dd, $J = 9.6$ and 17.6 Hz, 1H), 2.58-2.55 (t, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 195.54, 168.24, 139.98, 138.24, 134.99, 131.59, 129.98, 129.31, 128.79, 128.63, 127.31, 127.27, 46.37, 43.21, 40.88, 40.12; FT-IR (KBr) γ max 3285.14, 3088.44, 2973.70, 2911.99, 1685.48, 1648.84, 1590.02, 1552.42, 1440.56, 1401.03, 1357.64, 1281.47, 1230.36, 1094.40, 997.98, 813.81, 755.95 cm^{-1}; MS m/z 348.1 (M^+) 346.1, 350.1, 277.1.

N-(1-(Naphthalen-1-yl)-3-oxo-3-phenylpropyl)acrylamide (2f). ^{1}H NMR, (400 MHz, DMSO-d_6): δ 8.63–8-61 (d, $J = 7.6$ Hz, 1H), 8.09–8.07 (d, $J = 8$ Hz, 1H),

8.00–7.94 (m, 3H), 7.85–7.83 (d, $J = 8.4$ Hz, 1H), 7.66–7.46 (m, 7H), 6.25–6.23 (d, 6 Hz, 1H), 3.76–3.73 (t, 2H), 3.66–3.60 (dd, $J = 8$ and 17.6 Hz, 1H), 2.59–2.56 (t, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 197.17, 168.10, 137.97, 137.95, 136.47, 133.42, 133.40, 133.32, 133.31, 133.30, 128.72, 128.68, 128.08, 128.05, 127.53, 126.36, 125.68, 123.19, 122.88, 45.09, 43.64, 40.94, 40.12, 39.92, 39.71; FT-IR (KBr) γ max 3283.21, 3062.41, 2969.84, 2904.27, 1683.55, 1649.80, 1596.77, 1551.45, 1447.31, 1359.57, 1272.79, 999.91, 801.27, 777.17, 755.95, 688.46 cm^{-1}; MS m/z 331.2 (M + 1), 330.2 (M$^+$), 229.1.

N-(1-(2-Bromophenyl)-3-oxo-3-phenylpropyl)-2-phenylacetamide (2i). ^{1}H NMR, (400 MHz, DMSO-d_6): δ 8.64–8.62 (d, $J = 7.6$ Hz, 1H), 8.00–7.97 (dd, $J = 1.2$ and 9.6 Hz, 2H), 7.67–7.62 (m, 1H), 7.59–7.50 (m, 3H), 7.44–7.36 (m, 1H), 7.35–7.32 (m, 1H), 7.28–7.18 (m, 6H), 5.66–5.63 (m, 1H), 3.54–3.51 (d, 10 Hz, 2H), 3.41 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 196.43, 169.29, 141.93, 136.32, 136.14, 133.34, 132.60, 128.89, 128.70, 128.08, 128.05, 127.84, 127.64, 126.25, 122.18, 48.80, 42.14, 40.10; FT-IR (KBr) γ max 3297.68, 3061.44, 1680.66, 1655.59, 1547.59, 1447.31,1359.57, 1266.04, 1208.18, 1019.19, 752.10, 688.46 cm^{-1}; MS m/z 424.1 (M + 2), 422.1 (M$^+$), 229.1, 227.1.

N-(1-(2-Bromophenyl)-3-oxo-3-(4-acetoxyphenyl)propyl)benzamide (2j). ^{1}H NMR, (400 MHz, DMSO-d_6): δ 8.89–8.87 (d, $J = 6.8$ Hz, 1H), 8.08–8.06 (dd, $J = 2$ and 6.8 Hz, 2H), 7.83–7.81 (dd, $J = 1.2$ and 8.4 Hz, 2H), 7.63–7.61 (dd, $J = 1.2$ and 8.0 Hz, 1H), 7.56–7.51 (m, 2H), 7.47–7.43 (dd, $J = 6.4$ and 7.6 Hz, 2H), 7.39 (s, 1H), 7.29–7.27 (dd, $J = 2$ and 6.8 Hz, 2H), 7.23–7.21 (dd, $J = 1.6$ and 7.6 Hz, 1H), 5.88 (s, 1H), 3.81–3.74 (dd, $J = 10.4$ and 17.6 Hz, 1H), 3.27–3.26 (d, $J = 2.8$ Hz, 1H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 196.04, 169.52, 166.46, 154.92, 143.05, 134.94, 134.67, 133.34, 131.99, 130.48, 129.57, 128.94, 128.69, 128.42, 128.00, 122.86, 122.80, 49.92, 43.74, 40.84, 40.63, 40.42, 40.21, 21.58; FT-IR (KBr) γ max 3312.14, 1753.94, 1684.52, 1637.27, 1600.63, 1531.20, 1383.68, 1305.57, 1213.97, 1163.83, 1015.34, 991.23, 748.24, 696.17 cm^{-1}; MS m/z 466.1 (M$^+$), 261.1, 227.1.

N-(1-(2-Bromophenyl)-3-oxo-3-phenylpropyl)benzamide (2k). ^{1}H NMR, (400 MHz, DMSO-d_6): δ 8.94–8.87 (m, 1H), 8.09–7.90 (m, 2H), 7.82–7.80 (m, 2H), 7.73–7.59 (m, 2H), 7.57–7.49 (m, 4H), 7.45–7.37 (m, 2H), 7.35–7.25 (m, 1H), 7.21–7.17 (m, 1H), 5.90–5.73 (m, 1H), 3.80–3.72 (dd, $J = 10.8$ and 18.0 Hz, 1H), 3.26–3.25 (d, $J = 2.8$ Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 197.08, 166.44, 143.09, 137.05, 134.94, 134.03, 133.34, 131.98, 129.57, 129.41, 128.94, 128.75, 128. 69, 128.44, 128.00, 122.80, 49.92, 43.78; FT-IR (KBr) γ max 3327.57, 3055.66, 1686.44, 1634.38, 1578.45, 1529.27, 1354.75, 1230.36, 757.88, 693.28 cm^{-1}; MS m/z 410.1 (M$^+$), 409.1 (M-1), 229.1.

N-(1-(2-Chlorophenyl)-3-oxo-3-phenylpropyl)propionamide (2o). ^{1}H NMR, (400 MHz, DMSO-d_6): δ 8.30–8.28 (d, $J = 7.6$ Hz, 1H), 7.99–7.96 (dd, $J = 0.8$ and 8 Hz, 2H), 7.66–7.62 (m, 1H), 7.54–7.46 (m, 3H), 7.43–7.41 (dd, $J = 1.6$ and 8 Hz, 1H), 7.36–7.25 (m, 2H), 5.76 (s, 1H), 3.49–3.46 (d, $J = 9.6$ Hz, 1H), 3.29–3.28 (d, $J = 4$ Hz, 1H), 2.09–2.04 (dd, J = 7.6 and 15.2 Hz, 2H), 0.96–0.92 (t, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 196.59, 172.15, 140.58, 136.37, 133.30, 131.59, 129.31, 128.68, 128.49, 128.02, 127.58, 127.34, 46.16, 43.24,

40.12, 28.32, 9.80; FT-IR (KBr) γ max 3296.80, 3067.23, 2977.55, 2938.02, 1681.02, 1649.80, 1595.81, 1549.52, 1445.39, 1354.75, 1248.68, 1199.51, 754.03, 688.46 cm^{-1}; MS m/z 318.2 (M + 2), 317.2 (M + 1), 316.2 (M^+).

N-(1-(Naphthalen-1-yl)-3-oxo-3-phenylpropyl)propionamide (2p). ^1H NMR, (400 MHz, DMSO-d_6): δ 8.37–8.35 (d, $J = 7.6$ Hz, 1H), 8.10–8.08 (d, $J = 8.4$ Hz, 1H), 8.00–7.97 (m, 2H), 7.96–7.94 (m, 1H), 7.84–7.82 (d, $J = 8$ Hz, 1H), 7.66–7.62 (m, 1H), 7.59–7.46 (m, 6H); FT-IR (KBr) γ max 3281.29, 3060.48, 2978.52, 2938.02, 1685.48, 1645.95, 1595.81, 1545.67, 1447.31, 1358.60, 1271.82, 1245.79, 802.24, 776.20, 755.95, 688.46 cm^{-1}; MS m/z 265.1 (M + 2), 263.1, 229.1, 227.1, 219.2.

N-(1-Oxo-1,5-diphenylpent-4-en-3-yl)acetamide (3 m). ^1H NMR, (300 MHz, $CDCl_3$): δ 7.97–7.94 (d, $J = 7.5$ Hz, 2H), 7.62–7.57 (t, 1H), 7.50–7.45 (t, 2H), 7.34–7.21 (m, 5H), 6.61–6.54 (t, 2H), 6.39–6.31 (dd, $J = 6.9$ and 15.9 Hz,^1H), 3.57–3.50 (dd, $J = 3.9$ and 17.4 Hz, 1H), 3.39–3.32 (dd, $J = 5.1$ and 17.4 Hz, 1H), 2.01 (s, 3H); FT-IR (KBr) γ max 3286.11, 3059.51, 3027.69, 1686.44, 1644.98, 1541.81, 1447.31, 1371.14, 1290.14, 1225.54, 969.05, 757.88, 691.35 cm^{-1}; MS m/z 294.6 (M^+), 250.5, 235.2, 176.4, 154.3, 136.3, 105.3.

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