Research Article

Synthesis of β -Amino Carbonyl Compounds via the Iodine-Alumina Catalyzed Three-Component Coupling Reaction under Microwave Irradiation

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Received 3 September 2010; Accepted 13 December 2010

Academic Editor: Bill Baker

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Iodine-alumina was employed as a catalyst in the coupling reactions of aldehydes, enolizable ketones, or 1,3-dicarbonyls with methyl carbamate or aromatic amines under microwave irradiation to afford β -amino carbonyl compounds in good-to-excellent yields. The key features of this environmentally friendly methodology are its operational simplicity, mild reaction conditions, and less reaction time.

1. Introduction

In recent years, the use of multicomponent reactions has gained considerable attention in organic synthesis. In particular, the Mannich reaction has been widely used for the synthesis of β -amino carbonyl compounds. Owing to their importance as valuable building blocks for the preparation of 1,3-amino alcohols [1, 2], β -amino acids [3], as well as for the synthesis of various bioactive molecules such as the antibiotic nikkomycins and neopolyoxines [4, 5], several methods have been reported in the literature for the synthesis of β -amino carbonyl compounds using catalysts such as HClO_4 - SiO_2 [6], silica supported sulfuric acid [7], bromodimethylsulfonium bromide (BDMS) [8], TMSCl [9], p -TSA [10], Sml_3 [11], Amberlyst-15 [12], and AuCl_3 - PPh_3 [13]. These methods however, have certain drawbacks such as moisture sensitivity of the catalyst [9, 10], longer reaction time [6–8], and the use of expensive metal salt as catalyst [11–13]. There is still scope, therefore, for an improved method for the synthesis of β -amino carbonyl compounds which can avoid the use of expensive and sensitive catalysts.

Furthermore, the use of inorganic solid supported reagents provides an attractive procedure due to their

characteristic properties such as enhanced reactivity and selectivity, simple workup procedure, and milder reaction conditions [14–17]. Among these inorganic supported reagents, iodine supported on dehydrated neutral alumina has found wide application because of its property to form activated iodonium ion [16]. Therefore, we decided to use activated iodonium ion produced from iodine adsorbed on neutral alumina for the coupling reactions of aldehydes, enolizable ketones or 1,3-dicarbonyls with methyl carbamate or aromatic amines using microwave as an energy source, which is superior to conventional methods [18–20] in terms of shorter reaction time and minimization of reaction byproducts. Recently, a method using molecular iodine as the catalyst has been reported for the synthesis of β -amino carbonyl compounds *via* a three-component reaction involving aldehydes, ketones, and benzyl carbamates with good yields. However, this method has the disadvantage of longer reaction time [21].

As a part of our ongoing research in the use of solid support reagents [22], we wanted to expand the scope of iodine-alumina (I_2 - Al_2O_3) as the catalyst for the synthesis of β -amino carbonyl compounds. We, therefore, report herein an efficient and time-saving one-pot protocol for

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the three-component condensation between an aldehyde, a substituted ketone, or 1,3-dicarbonyl compounds with substituted aniline using iodine-alumina ($I_2-Al_2O_3$) as a catalyst under microwave irradiation. This protocol was subsequently extended to the condensation with the less reactive methyl carbamate as a nitrogen source to give β -amino carbonyl compounds which can be easily deprotected to 1,3-amino alcohols or β -amino acids [20] (Scheme 1).

In the initial experiment, a mixture of 4-chlorobenzaldehyde (1a), acetophenone (2a), and 3-chloroaniline (3a) was refluxed in ethanol in presence of $I_2-Al_2O_3$ (20 mol%). On completion of the reaction (8 h, monitored by TLC), workup and subsequent purification by column chromatography afforded the product 4a in 60% yield. The same reaction under microwave irradiation led to the formation of the desired β -amino carbonyl compound 4a (12 min) in 92% yield. In a typical experiment, when a mixture of 3-chloroaniline (3a) (3.91 mmol), 4-chlorobenzaldehyde (1a) (3.56 mmol), and acetophenone (2a) (3.91 mmol) was heated for 12 min in a microwave using $I_2-Al_2O_3$ (0.71 mmol of iodine adsorbed on 1.8 g of neutral alumina, that is, 20 mol% arrived at after optimization is shown in Table 1) as a catalyst in dry ethanol at 100 °C, 4a was obtained in 92% yield.

In another attempt, the same reaction mixture in neat condition under microwave irradiation in presence of $I_2-Al_2O_3$ (20 mol%) catalyst yielded only 46% of compound 4a. Later, the optimized reaction condition was extended for the condensation of methyl carbamate (3f) (3.91 mmol) with benzaldehyde (1e) (3.55 mmol) and acetophenone (2a) (3.91 mmol) in presence of $I_2-Al_2O_3$ (20 mol%) in ethanol in a microwave. The reaction furnished the desired product 4f in 13 min with 75% yield. To study the generality of this methodology, reactions with a number of substituted aromatic aldehydes, substituted aromatic ketones, or 1,3-dicarbonyl compounds and methyl carbamate or substituted anilines were carried out. Irrespective of the substitutions on the aromatic aldehydes, acetophenones or anilines by electron withdrawing or donating groups in either *ortho*, *meta*, or *para* position the reaction proceeded smoothly to give the corresponding products in good to excellent yields (Table 2). However, aldehyde having nitro group substitution failed to give the desired product, where as *para*-nitro acetophenone (2e) condenses readily with aniline

(3b) and benzaldehyde (1e) to afford the product 4e (entry 5, Table 2). On the other hand, benzaldehyde (1e) when reacted with dicarbonyl compounds such as diethyl malonate (2t) and 3-chloroaniline (3a), compound 4t was obtained in 9 min with 89% yield (entry 20, Table 2). All the β -amino carbonyl compounds (4a–4t) obtained after simple workup and purification by column chromatography was characterized by 1H , ^{13}C NMR and IR analyses, and the results are summarized in Table 2.

It is to be noted that the effect of the $I_2-Al_2O_3$ as compared to molecular iodine as a catalyst is more superior as is evident from the fact that, when the reaction is carried out with *meta*-substituted aldehyde, such as 3-methoxybenzaldehyde, it was found that $I_2-Al_2O_3$ successfully gave the products 4h, 4l, 4r, and 4s whereas the reported method using molecular iodine alone as a catalyst failed to yield the desired products [21]. Significantly, no iodination (for compound 4q) was observed at the allylic double bond.

The formation of the β -amino carbonyl compounds may be explained as follows: alumina polarizes the iodine molecule and acts as an activating agent to produce a strongly electrophilic I^+ species. The I^+ species then catalyses *in situ* generation of acylimines which is subsequently attacked by the enolizable ketone to provide the desired compound.

2. Conclusion

In summary, we have established a convenient and environmentally benign protocol for the synthesis of β -amino carbonyl compounds by using $I_2-Al_2O_3$ as a catalyst. In addition, this catalytic protocol has the advantages of mild reaction condition, simple workup procedure, and purification to afford the products in good yields. Due to its operational simplicity, this facile method is expected to have wider application for the preparation of β -amino carbonyl compounds.

3. Experimental Section

All commercially available chemicals and reagents were purchased from Aldrich and used without further purification. IR spectra were recorded on a Perkin-Elmer FT-IR instrument. The 1H - and ^{13}C -NMR spectrum were recorded on a Bruker Avance II 400 NMR machine. Unless otherwise specified, $CDCl_3$ was used as solvent. Mass spectra were recorded with a Water ZQ-4000 equipped with ESI and APCI mass detector and CHN was done on Perkin-Elmer PE 2400 Series II. The $I_2-Al_2O_3$ catalyst was prepared by the procedure reported in reference [24].

General Procedure 4(a–t). A prestirred mixture of aldehyde (3.56 mmol), acetophenone, methyl acetoacetate, or diethyl malonate (3.91 mmol) and methyl carbamate or aniline (3.91 mmol) in dry ethanol (3 mL) was irradiated in a Chem Discover microwave reactor at 100 °C (power 200 W), for 10–15 min, in the presence of $I_2-Al_2O_3$ (20 mol%). The completion of the reaction was monitored by thin layer chromatography. The reaction mixture was filtered through a bed of celite and washed the residue with ethyl acetate (3×5 mL). The filtrate was then washed with aqueous

TABLE 1: Optimization of the amount of I₂-Al₂O₃ catalyst.

Substrate 1 R ¹	Substrate 2 R ²	Substrate 3 R ⁵	I ₂ -Al ₂ O ₃ (mol %)	Time (min)	Product 4	Yield ^a /(%)
4-ClC ₆ H ₄	C ₆ H ₅	3-ClC ₆ H ₄	10	12	4a	57
4-ClC ₆ H ₄	C ₆ H ₅	3-ClC ₆ H ₄	20	12	4a	92
4-ClC ₆ H ₄	C ₆ H ₅	3-ClC ₆ H ₄	20	20	4a	90
4-ClC ₆ H ₄	C ₆ H ₅	3-ClC ₆ H ₄	40	12	4a	91

^a Isolated yields.TABLE 2: I₂-Al₂O₃ catalyzed multicomponent reaction for the preparation of β-amino carbonyl compounds.

Entry	Substrate 1 R ¹	Substrate 2 (R ²)/5 (R ³ , R ⁴)	Substrate 3 R ⁵	Time (min)	Product 4 ^b	Yield ^a /(%) ^c
1	4-ClC ₆ H ₄	R ² = C ₆ H ₅	3-ClC ₆ H ₄	12	4a	92
2	4-MeOC ₆ H ₄	R ² = C ₆ H ₅	C ₆ H ₅	11	4b	90 [23]
3	2-ClC ₆ H ₄	R ² = C ₆ H ₅	4-NO ₂ C ₆ H ₄	15	4c	90
4	3-BrC ₆ H ₄	R ² = C ₆ H ₅	4-MeC ₆ H ₄	10	4d	86
5	C ₆ H ₅	R ² = 4-NO ₂ C ₆ H ₄	C ₆ H ₅	12	4e	89
6	C ₆ H ₅	R ² = C ₆ H ₅		13	4f	75
7	4-MeC ₆ H ₄	R ² = C ₆ H ₅		12	4g	65
8	3-MeOC ₆ H ₄	R ² = C ₆ H ₅		11	4h	75
9	4-MeOC ₆ H ₄	R ² = C ₆ H ₅		12	4i	75
10	4-ClC ₆ H ₄	R ² = C ₆ H ₅		13	4j	70
11	4-OHC ₆ H ₄	R ² = C ₆ H ₅		13	4k	96
12	3,4-(MeO) ₂ C ₆ H ₃	R ² = C ₆ H ₅		10	4l	73
13	4-ClC ₆ H ₄	R ² = 2-MeC ₆ H ₄		15	4m	70
14	4-ClC ₆ H ₄	R ² = 4-MeOC ₆ H ₄		10	4n	65
15	4-ClC ₆ H ₄	R ² = 4-BrC ₆ H ₄		14	4o	72
16	4-ClC ₆ H ₄	R ² = 4-OHC ₆ H ₄		15	4p	69
17		R ² = C ₆ H ₅		14	4q	68
18	3,4-(MeO) ₂ C ₆ H ₃	R ³ = Me R ⁴ = Me		9	4r	75
19	3,4,5-(MeO) ₃ C ₆ H ₂	R ³ = Me R ⁴ = Me		15	4s	67
20	C ₆ H ₅	R ³ = OEt R ⁴ = Et	3-ClC ₆ H ₄	9	4t	89

^a Isolated yields. ^b Products were characterized by ¹H, ¹³C NMR and IR analyses. ^c Reference.

sodium thiosulfate (5%) followed by brine. The organic layer was dried over anhydrous Na_2SO_4 and concentrated in *vacuo* to give the crude mass. The crude compound was then purified by silica gel column chromatography, using ethyl acetate and hexane as eluents, to afford the β -amino carbonyl compounds in pure form.

3-(4-Chlorophenyl)-3-((3-chlorophenyl)amino)-1-phenylpropan-1-one (4a, Table 2). Off white solid; mp 98–100°C; ^1H NMR (400 MHz, $\text{DMSO}-d_6$): δ 3.07 (1H, dd, $J = 4, 17.2$ Hz, CH_2), 3.41 (1H, dd, $J = 8.8, 17.2$ Hz, CH_2), 4.75–4.80 (1H, m, CH), 6.23 (2H, t, $J = 6$ Hz, Ar-H), 6.27 (1H, d, $J = 1.2$ Hz, NH), 6.38 (1H, d, $J = 7.2$ Hz, Ar-H), 6.75 (1H, t, $J = 8$ Hz, Ar-H), 7.13 (2H, d, $J = 8.4$ Hz, Ar-H), 7.19–7.40 (5H, m, Ar-H), 7.73 (2H, d, $J = 7.2$ Hz, Ar-H) ppm; ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$): δ 46.1, 51.9, 111.4, 111.9, 115.4, 128.0, 128.3, 128.5, 128.7, 130.3, 131.4, 133.4, 136.5, 142.5, 149.1, 196.7 ppm; IR. ν_{max} (KBr): 3398, 3062, 2925, 2900, 2853, 1676, 1599, 1518, 1489, 1293, 1089 cm^{-1} ; Elemental analysis for $\text{C}_{21}\text{H}_{17}\text{Cl}_2\text{NO}$ Calcd. C, 68.12; H, 4.63; N, 3.78; Found: C, 67.96; H, 4.70; N, 3.68.

3-(4-Methoxyphenyl)-1-phenyl-3-(phenylamino)propan-1-one (4b, Table 2). The spectroscopic data is in full agreement with the literature data [23].

3-(2-Chlorophenyl)-3-((4-nitrophenyl)amino)-1-phenylpropan-1-one (4c, Table 2). Yellow solid; mp 135–137°C; ^1H NMR (400 MHz, CDCl_3): δ 3.49 (2H, d, $J = 6.2$ Hz, CH_2), 5.38 (1H, m, CH), 5.48 (1H, d, $J = 6.0$ Hz, NH), 6.40 (2H, d, $J = 9.2$ Hz, Ar-H), 7.20–7.50 (7H, m, Ar-H), 7.67 (2H, d, $J = 7.2$ Hz, Ar-H), 7.91 (2H, d, $J = 9.0$ Hz, Ar-H) ppm; ^{13}C NMR (100 MHz, CDCl_3): δ 42.8, 51.6, 112.4, 126.2, 127.7, 127.8, 128.4, 128.9, 129.2, 130.2, 132.4, 134.0, 136.2, 137.7, 138.7, 151.6, 198.2 ppm; IR. ν_{max} (KBr): 3369, 3062, 2925, 2854, 1691, 1598, 1532, 1503, 1471, 1449, 1308, 1291, 1113 cm^{-1} ; Elemental analysis for $\text{C}_{21}\text{H}_{17}\text{ClN}_2\text{O}_3$ Calcd. C, 66.23; H, 4.50; N, 7.36; Found: C 66.45; H 4.43; N 7.41.

3-(3-Bromophenyl)-1-phenyl-3-(p-tolylamino)propan-1-one (4d, Table 2). White solid; mp 107–111°C; ^1H NMR (400 MHz, CDCl_3): δ 2.14 (3H, s, CH_3), 3.39 (2H, dd, $J = 6, 18$ Hz, CH_2), 3.61 (1H, d, $J = 5.6$ Hz, NH), 4.87 (1H, t, $J = 6.4$ Hz, CH), 6.61 (2H, d, $J = 7.6$ Hz, Ar-H), 6.88 (2H, d, $J = 8$ Hz, Ar-H), 7.02–7.52 (6H, m, Ar-H), 7.78 (2H, d, $J = 7.6$ Hz, Ar-H), 7.87 (1H, d, $J = 8.4$ Hz, Ar-H) ppm; ^{13}C NMR (100 MHz, CDCl_3): δ 20.6, 44.8, 59.5, 117.0, 122.9, 127.0, 128.1, 128.2, 128.7, 128.8, 129.5, 129.9, 130.4, 130.4, 131.1, 131.3, 131.6, 133.6, 136.3, 197.0 ppm; IR. ν_{max} (KBr): 3403, 2924, 2854, 1678, 1620, 1597, 1523, 1366, 1289 cm^{-1} ; Elemental analysis for $\text{C}_{22}\text{H}_{20}\text{BrNO}$ Calcd. C, 67.01; H, 5.11; N, 3.55; Found C, 67.23; H, 5.55; N, 3.24.

1-(4-nitrophenyl)-3-phenyl-3-(phenylamino)propan-1-one (4e, Table 2). White Solid; mp 145–147°C; ^1H NMR (400 MHz, CDCl_3): δ 3.40–3.58 (2H, m, CH_2), 5.16 (1H, t, CH), 6.69 (2H, d, $J = 6.4$ Hz, Ar-H), 6.63–6.70 (2H, m, Ar-H), 6.79–6.89 (1H, m, Ar-H), 7.14 (2H, d, $J = 7.6$ Hz, Ar-H), 7.26–7.29

(1H, m, Ar-H), 7.31–7.35 (2H, m, Ar-H), 7.66 (2H, d, $J = 6.4$ Hz, Ar-H); 7.90 (2H, d, $J = 7.2$ Hz, Ar-H) ppm; ^{13}C NMR (100 MHz, CDCl_3): δ 46.0, 53.5, 110.0, 114.8, 122.9, 124.0, 126.1, 128.0, 128.3, 128.9, 142.7, 141.3, 151.1, 196.5 ppm; IR. ν_{max} (KBr): 3400, 3099, 3064, 2985, 2925, 2872, 1678, 1600, 1538, 1352, 1214, 1204 cm^{-1} ; Elemental analysis for $\text{C}_{21}\text{H}_{18}\text{N}_2\text{O}_3$: Calcd. C, 72.82; H, 5.24; N, 8.09; Found: C, 72.96; H, 5.34; N, 8.11.

Methyl (3-oxo-1,3-diphenylpropyl)carbamate (4f, Table 2). Off white solid; mp 115–120°C; ^1H NMR (400 MHz, CDCl_3): δ 3.43–3.49 (2H, m, CH_2), 3.66 (3H, s, COOCH_3), 5.29–5.31 (1H, m, CH), 5.77 (1H, s, NH), 7.22–7.46 (7H, m, Ar-H), 7.56 (1H, t, $J = 7.2$ Hz, Ar-H), 7.90 (2H, d, $J = 7.6$ Hz, Ar-H) ppm; ^{13}C NMR (100 MHz, CDCl_3): δ 30.9, 43.9, 51.7, 52.2, 126.3, 127.4, 128.1, 128.6, 128.7, 133.4, 136.6, 141.4, 156.4, 197.8 ppm; IR. ν_{max} (KBr): 3369, 2955, 2924, 2853, 1733, 1683, 1521, 1294, 1030 cm^{-1} ; Elemental analysis for $\text{C}_{17}\text{H}_{17}\text{NO}_3$: Calcd. C, 72.07; H, 6.05; N, 4.94; Found C, 72.27; H, 6.17; N, 4.86.

Methyl (3-oxo-3-phenyl-1-(p-tolyl)propyl)carbamate (4g, Table 2). Brownish solid; mp 90–94°C; ^1H NMR (400 MHz, CDCl_3): δ 2.30 (3H, s, CH_3), 3.44 (2H, dd, $J = 6, 16.8$ Hz, CH_2), 3.66 (3H, s, COOCH_3), 5.25–5.29 (1H, m, CH), 5.72 (1H, s, NH), 7.12 (2H, d, $J = 7.6$ Hz, Ar-H), 7.24 (2H, d, $J = 8$ Hz, Ar-H), 7.45 (1H, t, $J = 7.6$ Hz, Ar-H), 7.55 (2H, d, $J = 7.6$ Hz, Ar-H), 7.91 (2H, d, $J = 7.6$ Hz, Ar-H) ppm; ^{13}C NMR (100 MHz, CDCl_3): δ 21.0, 44.0, 51.5, 52.2, 126.3, 128.1, 128.7, 129.3, 133.4, 136.6, 137.1, 138.3, 156.3 ppm; IR. ν_{max} (KBr): 3305, 3068, 3013, 2994, 2947, 2923, 2909, 1714, 1690, 1551, 1276, 1050, 763 cm^{-1} ; Elemental analysis for $\text{C}_{18}\text{H}_{19}\text{NO}_3$ Calcd. C, 72.71; H, 6.44; N, 4.71; Found C, 72.91; H, 6.36; N, 4.68.

Methyl (1-(3-methoxyphenyl)-3-oxo-3-phenylpropyl)carbamate (4h, Table 2). Yellowish solid; mp 100–104°C; ^1H NMR (400 MHz, CDCl_3): δ 3.43 (2H, dd, $J = 4.8, 16.4$ Hz, CH_2), 3.68 (3H, s, COOCH_3), 3.78 (3H, s, COCH_3), 5.25–5.30 (1H, m, CH), 5.88 (1H, d, $J = 6.4$ Hz, NH), 6.78 (2H, d, $J = 8$ Hz, Ar-H), 6.90–7.27 (2H, m, Ar-H), 7.44 (2H, t, $J = 7.6$ Hz, Ar-H), 7.56 (1H, t, $J = 7.2$ Hz, Ar-H), 7.90 (2H, d, $J = 7.6$ Hz, Ar-H) ppm; ^{13}C NMR (100 MHz, CDCl_3): δ 43.9, 51.7, 52.3, 55.2, 112.3, 112.6, 118.5, 128.1, 128.7, 129.7, 133.4, 136.6, 156.4, 157.6, 159.7 ppm; IR. ν_{max} (KBr): 3362, 3080, 3047, 3007, 2962, 2925, 2852, 1728, 1683, 1598, 1518, 1491, 1295, 1167, 1022 cm^{-1} ; Elemental analysis for $\text{C}_{18}\text{H}_{19}\text{NO}_4$ Calcd. C, 68.99; H, 6.11; N, 4.47; Found C, 69.12; H, 6.15; N, 4.31.

Methyl (1-(4-methoxyphenyl)-3-oxo-3-phenylpropyl)carbamate (4i, Table 2). Yellowish solid; mp 145–148°C; ^1H NMR (400 MHz, CDCl_3): δ 3.43 (2H, dd, $J = 6.4, 16.8$ Hz, CH_2), 3.66 (3H, s, COOCH_3), 3.77 (3H, s, COCH_3), 5.24–5.25 (1H, m, CH), 5.66 (1H, s, NH), 6.84 (2H, d, $J = 8.8$ Hz, Ar-H), 7.26–7.28 (2H, m, Ar-H), 7.43–7.46 (2H, m, Ar-H), 7.55 (1H, t, $J = 7.6$ Hz, Ar-H), 7.90 (2H, d, $J = 9.6$ Hz, Ar-H) ppm; ^{13}C NMR (100 MHz, CDCl_3): δ 51.4, 52.2, 55.3, 114.0, 127.6, 128.1, 128.7, 133.4, 136.7, 156.3, 158.9 ppm; IR. ν_{max} (KBr):

3296, 3074, 3022, 2994, 2966, 2948, 2906, 2844, 1709, 1687, 1555, 1513, 1280, 1251, 1048, 762 cm⁻¹; Elemental Analysis for C₁₈H₁₉NO₄ Calcd. C, 68.99; H, 6.11; N, 4.47; Found C, 68.89; H, 6.16; N, 4.39.

Methyl (1-(4-chlorophenyl)-3-oxo-3-phenylpropyl)carbamate (4j, Table 2). Off white solid; mp 109–112°C; ¹H NMR (400 MHz, CDCl₃): δ 3.45–3.47 (2H, m, CH₂), 3.66 (3H, s, COOCH₃), 5.25–5.29 (1H, m, CH), 5.86 (1H, s, NH), 7.26–7.47 (6H, m, Ar-H), 7.58 (1H, t, *J* = 7.6 Hz, Ar-H), 7.89 (2H, d, *J* = 7.6 Hz, Ar-H) ppm; IR. ν_{max} (KBr): 3311, 3061, 2953, 2853, 1693, 1545, 1274, 1052, 761 cm⁻¹; Elemental Analysis for C₁₇H₁₆ClNO₃ Calcd. C, 64.26; H, 5.08; N, 4.41; Found C, 64.29; H, 5.12; N, 4.53.

Methyl (1-(4-hydroxyphenyl)-3-oxo-3-phenylpropyl)carbamate (4k, Table 2). Brownish liquid; ¹H NMR (400 MHz, CDCl₃): δ 3.40 (2H, dd, *J* = 6, 16.8 Hz, CH₂), 3.67 (3H, s, COOCH₃), 5.20–5.21 (1H, m, CH), 5.78 (1H, s, NH), 6.69 (2H, d, *J* = 8 Hz, Ar-H), 7.15 (2H, d, *J* = 8 Hz, Ar-H), 7.42–7.46 (2H, m, Ar-H), 7.56 (1H, t, *J* = 7.2 Hz, Ar-H), 7.90 (2H, d, *J* = 7.6 Hz, Ar-H) ppm; ¹³C NMR (100 MHz, CDCl₃): δ 44.1, 51.5, 52.4, 115.5, 115.9, 127.6, 128.2, 128.7, 133.5, 136.5, 155.4, 156.6 ppm; IR. ν_{max} (KBr): 3438, 3019, 1716, 1600, 1514, 1215, 1018, 768 cm⁻¹; Elemental Analysis for C₁₇H₁₇NO₄ Calcd. C, 68.21; H, 5.72; N, 4.68; Found C, 68.36; H, 5.63; N, 4.72.

Methyl (1-(3,4-dimethoxyphenyl)-3-oxo-3-phenylpropyl)carbamate (4l, Table 2). White solid; mp 117–120°C; ¹H NMR (400 MHz, CDCl₃): δ 3.42 (2H, dd, *J* = 6, 16.4 Hz, CH₂), 3.65 (3H, s, COOCH₃), 3.83 (3H, s, COCH₃), 3.84 (3H, s, COCH₃), 5.25 (1H, br, CH), 5.79 (1H, s, NH), 6.79 (1H, d, *J* = 8.4 Hz, Ar-H), 6.88 (1H, d, *J* = 4.8 Hz, Ar-H), 7.42–7.46 (3H, m, Ar-H), 7.56 (1H, t, *J* = 7.2 Hz, Ar-H), 7.90 (2H, d, *J* = 7.6 Hz, Ar-H) ppm; ¹³C NMR (100 MHz, CDCl₃): δ 44.1, 51.7, 52.2, 55.9, 110.0, 111.1, 118.3, 128.1, 128.7, 133.4, 136.7, 148.3, 149.0, 156.4, 198.1 ppm; IR. ν_{max} (KBr): 3379, 3078, 2994, 2959, 2924, 2852, 1728, 1676, 1592, 1535, 1522, 1452, 1295, 1264, 1025, 757 cm⁻¹; Elemental Analysis for C₁₉H₂₁NO₅ Calcd. C, 66.46; H, 6.16; N, 4.08; Found C, 66.59; H, 6.23; N, 4.16.

Methyl (1-(4-chlorophenyl)-3-oxo-3-(o-tolyl)propyl)carbamate (4m, Table 2). Off white solid; mp 110–114°C; ¹H NMR (400 MHz, CDCl₃): δ 2.36 (3H, s, CH₃), 3.36 (2H, dd, *J* = 5.6, 16.4 Hz, CH₂), 3.67 (3H, s, COOCH₃), 5.20–5.22 (1H, m, CH), 5.84 (1H, s, NH), 7.21–7.39 (7H, m, Ar-H), 7.53 (1H, d, *J* = 7.6 Hz, Ar-H) ppm; ¹³C NMR (100 MHz, CDCl₃): δ 21.2, 31.0, 51.4, 52.3, 125.8, 127.8, 128.5, 128.8, 131.9, 132.2, 133.3, 137.2, 138.5, 139.9, 154.5, 194.3 ppm; IR. ν_{max} (KBr): 3319, 3062, 3027, 2951, 2930, 2853, 1690, 1678, 1547, 1491, 1345, 1273, 1053 cm⁻¹; Elemental Analysis for C₁₈H₁₈ClNO₃ Calcd. C, 65.16; H, 5.47; N, 4.22; Found C, 65.21; H, 5.53; N, 4.26.

Methyl (1-(4-chlorophenyl)-3-(4-methoxyphenyl)-3-oxopropyl)carbamate (4n, Table 2). White solid; mp 120–124°C; ¹H

NMR (400 MHz, CDCl₃): δ 3.36 (2H, dd, *J* = 6, 16.8 Hz, CH₂), 3.66 (3H, s, COOCH₃), 3.86 (3H, s, COCH₃), 5.21–5.26 (1H, m, CH), 5.94 (1H, s, NH), 6.91 (2H, d, *J* = 8.8 Hz, Ar-H), 7.25–7.30 (4H, m, Ar-H), 7.86 (2H, d, *J* = 9.2 Hz, Ar-H) ppm; ¹³C NMR (100 MHz, CDCl₃): δ 43.2, 51.3, 52.3, 55.5, 113.9, 127.8, 128.7, 129.6, 130.4, 133.1, 140.1, 156.4, 163.9 ppm; IR. ν_{max} (KBr): 3307, 3061, 3008, 2951, 2840, 1685, 1668, 1604, 1540, 1421, 1260, 1045 cm⁻¹; Elemental Analysis for C₁₈H₁₈ClNO₄ Calcd. C, 62.16; H, 5.22; N, 4.03; Found C, 62.13; H, 5.24; N, 4.11.

Methyl (3-(4-bromophenyl)-1-(4-chlorophenyl)-3-oxopropyl)carbamate (4o, Table 2). White solid; mp 87–91°C; ¹H NMR (400 MHz, CDCl₃): δ 3.4 (2H, dd, *J* = 6, 17.2 Hz, CH₂), 3.67 (3H, s, COOCH₃), 5.23–5.28 (1H, m, CH), 5.75 (1H, s, NH), 7.23–7.29 (4H, m, Ar-H), 7.59 (2H, d, *J* = 8.8 Hz, Ar-H), 7.75 (2H, d, *J* = 8.8 Hz, Ar-H) ppm; ¹³C NMR (100 MHz, CDCl₃): δ 45.7, 51.1, 52.3, 127.8, 128.8, 128.9, 129.6, 130.9, 132.1, 133.3, 135.1, 156.3, 190.9 ppm; IR. ν_{max} (KBr): 3319, 3072, 2926, 2853, 1688, 1586, 1540, 1264, 1199, 1012 cm⁻¹; Elemental Analysis for C₁₇H₁₅BrClNO₃ Calcd. C, 51.47; H, 3.81; N, 3.53; Found C, 51.39; H, 3.76; N, 3.58.

Methyl (1-(4-chlorophenyl)-3-(4-hydroxyphenyl)-3-oxopropyl)carbamate (4p, Table 2). Off white solid; mp 100–104°C; ¹H NMR (400 MHz, CDCl₃): δ 3.36–3.51 (2H, m, CH₂), 3.65 (3H, s, COOCH₃), 5.23 (1H, s, CH), 6.85 (2H, d, *J* = 8.4 Hz, Ar-H), 7.27–7.30 (2H, m, Ar-H), 7.52 (2H, d, *J* = 8 Hz, Ar-H), 7.78 (2H, d, *J* = 8.4 Hz, Ar-H) ppm; ¹³C NMR (100 MHz, CDCl₃): δ 52.4, 65.9, 115.5, 127.8, 128.7, 129.5, 130.7, 130.9, 132.2, 133.1, 156.6, 161.3, 190.9 ppm; IR. ν_{max} (KBr): 3321, 2955, 2925, 2853, 1693, 1669, 1598, 1540, 1278, 1169, 835 cm⁻¹; Elemental Analysis for C₁₇H₁₆ClNO₄ Calcd. C, 61.18; H, 4.83; N, 4.20; Found C, 61.13; H, 4.77; N, 4.13.

(E)-Methyl (5-oxo-1,5-diphenylpent-1-en-3-yl)carbamate (4q, Table 2). Brownish viscous liquid; ¹H NMR (400 MHz, CDCl₃): δ 3.34 (2H, dd, *J* = 5.6, 17.2 Hz, CH₂), 3.67 (3H, s, COOCH₃), 4.85–4.88 (1H, m, CH), 5.69 (1H, s, NH), 6.33 (1H, dd, *J* = 6.4, 16 Hz, CH=), 6.57 (1H, d, *J* = 16 Hz, CH=), 7.19–7.41 (5H, m, Ar-H), 7.46 (1H, t, *J* = 7.6 Hz, Ar-H), 7.56 (2H, d, *J* = 7.6 Hz, Ar-H), 7.95 (2H, d, *J* = 7.2 Hz, Ph) ppm; ¹³C NMR (100 MHz, CDCl₃): δ 43.1, 50.0, 52.2, 126.5, 127.7, 128.1, 128.5, 128.7, 131.1, 133.5, 136.4, 136.7, 156.4, 195.6 ppm; IR. ν_{max} (KBr): 3434, 3023, 2977, 2895, 1712, 1686, 1519, 1424, 1221, 1045 cm⁻¹; MS (ES⁺) for C₁₉H₁₉NO₃ m/z (M + H)⁺ 310.14, found (M + H)⁺ 310.5; Elemental Analysis for C₁₉H₁₉NO₃ Calcd. C, 73.77; H, 6.19; N, 4.53; Found C, 73.71; H, 6.21; N, 4.57.

Methyl 2-((3,4-dimethoxyphenyl)((methoxycarbonyl)amino)methyl)-3-oxobutanoate (4r, Table 2). White solid; mp 140–144°C; ¹H NMR (400 MHz, (CD₃)₂CO-d₆): δ 2.11 (3H, s, COCH₃), 3.40 (3H, s, COOCH₃), 3.65 (3H, s, COOCH₃), 3.67 (6H, s, COCH₃), 4.11–4.12 (1H, m, CH), 5.21–5.26 (1H, m, CH), 6.7–6.94 (3H, m, Ar-H) ppm; ¹³C NMR (100 MHz, (CD₃)₂CO-d₆): δ 30.2, 49.8, 52.3, 52.4, 52.5, 63.3, 108.9, 110.4, 111.1, 118.6, 126.9, 130.1, 132.0, 156.3, 167.7,

190.9 ppm; IR. $\nu_{\max}$ (KBr): 3366, 3050, 3002, 2960, 2839, 1714, 1594, 1519, 1441, 1026 cm^{-1} ; Elemental Analysis for $\text{C}_{16}\text{H}_{21}\text{NO}_7$ Calcd. C, 56.63; H, 6.24; N, 4.13; Found C, 56.53; H, 6.28; N, 4.18.

Methyl 2-(((methoxycarbonyl)amino)(3,4,5-trimethoxyphenyl)methyl)-3-oxobutanoate (4s, Table 2). White solid; mp 157–160°C; ^1H NMR (400 MHz, CDCl_3): δ 2.18 (3H, s, CH_3), 3.67 (3H, s, COOCH_3), 3.72 (3H, s, COOCH_3), 3.81 (3H, s, COCH_3), 3.85 (6H, s, COCH_3), 4.01 (1H, d, $J = 5.2$ Hz, CH), 5.37–5.40 (1H, m, CH), 6.16 (1H, d, $J = 8.8$ Hz, NH), 6.50 (2H, s, Ar-H) ppm; ^{13}C NMR (100 MHz, CDCl_3): δ 31.0, 52.4, 52.9, 54.7, 56.3, 60.8, 62.9, 103.6, 106.7, 135.2, 137.5, 153.3, 167.6, 203.4 ppm; IR. $\nu_{\max}$ (KBr): 3370, 2995, 2956, 2927, 2851, 1728, 1711, 1592, 1540, 1297, 1127 cm^{-1} ; MS (ES^+) for $\text{C}_{17}\text{H}_{23}\text{NO}_8$ m/z ($M + \text{Na}$) $^+$ 392.14, found ($M + \text{Na}$) $^+$ 392.4; Elemental Analysis for $\text{C}_{17}\text{H}_{23}\text{NO}_8$ Calcd. C, 55.28; H, 6.28; N, 3.79; Found C, 55.31; H, 6.24; N, 3.83.

Diethyl 2-((3-chlorophenylamino)(phenyl)methyl)malonate (4t, Table 2). White solid; mp 113–114°C; ^1H NMR (400 MHz, CDCl_3): δ 1.09 (3H, t, $J = 7.2$ Hz, CH_3), 1.16 (3H, t, $J = 7.2$ Hz, CH_3), 3.86 (1H, d, $J = 5.2$ Hz, CH), 4.12 (2H, q, $J = 7.2$ Hz, CH_2), 4.04 (2H, q, $J = 7.2$ Hz, CH_2), 5.22 (1H, d, $J = 5.6$ Hz, CH), 5.64 (1H, br. s, NH), 6.49 (1H, d, $J = 8.8$ Hz, Ar-H), 6.59 (1H, s, Ar-H), 6.70 (1H, d, $J = 8.8$ Hz, Ar-H), 7.00 (1H, t, $J = 8.8$ Hz, Ar-H), 7.26–7.35 (5H, m, Ar-H) ppm; ^{13}C NMR (100 MHz, CDCl_3): δ 13.8, 14.0, 56.7, 57.8, 61.5, 61.8, 111.8, 113.3, 117.6, 126.5, 127.8, 128.6, 130.0, 134.9, 139.0, 147.8, 167.0, 168.0 ppm; IR. $\nu_{\max}$ (KBr): 3376, 2990, 2980, 2933, 2800, 1753, 1568, 1540, 1309, 1196 cm^{-1} ; Elemental analysis for $\text{C}_{20}\text{H}_{22}\text{ClNO}_4$ Calcd. C 63.91; H 5.90; N 3.73; Found C 63.71; H 5.83; N 3.61.

Acknowledgments

M. Rajbangshi thanks the UGC-RGNF for financial assistance and SAIF and NEHU for providing analytical supports.

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