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VISIBLE LIGHT-INDUCED, ATOM-ECONOMIC, HIGHLY EFFICIENT AND GREEN SYNTHESIS OF β-AMINO CARBONYL DERIVATIVES UNDER SOLVENT-FREE CONDITIONS

ASMA RANI[a] AND JAGGI LAL[b1]

[ab]Department of Chemistry, Sanskriti University, Mathura, Uttar Pradesh, India

ABSTRACT

Despite various prior reports of effective catalytic and non-catalytic approaches towards the β-aminocarbonyl; a simple, efficient and green synthetic protocol for the synthesis of β-amino carbonyl derivatives via Mannich reaction under visible light under solvent-free conditions has been described. No use of hazardous solvents in the protocol, hence making this process environment friendly. In view of green chemistry perspectives, various parameters including atom economy, atom-efficiency, carbon efficiency, reaction mass efficiency and optimum efficiency have been calculated and described for the newly developed procedure.

KEYWORDS: Visible-light, Atom Economic, β-amino carbonyl derivatives, Highly-efficient, Green Chemistry Metrics

Visible light is a very powerful tool to construct a complex molecule in one-pot system. Now a day, the aim of scientists is to discourage the procedures that involved the hazardous solvents, catalysts and other chemicals. In the search of green source of energy for the organic transformation, visible light may be an attractive candidate because in recent past, light has been utilized as one the most important and powerful tool to achieve organic transformation. In chemical transformations, the solvent and catalysts are critical source of chemical waste and therefore, removal of such harmful and toxic solvents and catalysts are an important point in designing a green and environmentally benign protocol for the synthesis of targeted molecule. Furthermore, in academic and industrial research laboratories, solvent-free and catalyst-free protocol for organic transformation have attracted interest for the reduction of cost, minimization of hazardous waste, operational simplicity and easiness of purification (Maity *et. al.* 2012). For organic and medicinal chemistry researchers one-pot multicomponent reactions (MCRs) are very efficient and effective tool to generate new products in a single operation. Among the multi-component reactions, three-component reaction is an extremely economical reaction. Such reactions (Ghashghaei *et. al.* 2019) have obtained valuable attention in drug design and drug discovery because of their efficiency, simplicity and high selectivity. A reaction in which at least three different simple substrates react in one-pot to give the target product is known as multicomponent reaction. Such type of processes can reduce the number of steps and present advantages such as little to no waste production and low energy consumption, leading to desired environmentally benign protocols. There are a lot of multi-component reactions such as Biginelli, Passerini, Hantzsch, Robinson, Passerini, Burcherer-Bergs, Asinger, Ugi and Gewald reactions are reported in literature and Mannich reaction is one of the most important C-C bonds forming reaction (Shi *et. al.* 2018). Using Mannich reaction β-aminocarbonyl compounds and 1,2-amino alcohols may be synthesized. Several methods have been reported for the important modifications of the given reaction. However, literature survey demonstrated that the reported methods have suffered various drawbacks such as long reaction time, low yield of the product, use of hazardous solvents, metal catalysts, no reusable catalysts, higher catalyst loading and relatively higher temperature. The limitations of ionic liquids are their solubility in water and cannot be removed easily by distillation after the reaction. They are very expensive and have acute toxicity for aquatic organisms and human ((Matzke *et. al.* 2007). In addition to explore role of visible light for the synthesis of β-amino carbonyl, various green chemistry credentials indices have been calculated by using the working formulas reported in literature (Abou-Shehada *et. al.* 2017).

In the literature, various methods have been developed by using various catalysts systems like ZnI_2, rt (Azizi *et. al.* 2009), $ZrOCl_2.8H_2O$ (Abaee *et. al.* 2012), (Bromodimethyl)sulfonium bromide (Shailaja *et. al.* 2010), HPA/ionic liquid (Sasalkar *et. al.* 2007), Boric acid (Mukhopadhyay *et. al.* 2009), YCl_3 (Yekkirala *et. al.* 2014), Lipase (Li *et. al.* 2009), $CeCl_3.7H_2O$ (Kidwai *et. al.* 2010), $AuCl_3$-PPh_3 (Xu *et. al.* 2004), I_2 (Kataki *et. al.*

[1]Corresponding author

2006), $FePO_4$ (Behbahani *et. al.* 2013), $Bi(OTf)_3.4H_2O$ (Ollevier *et. al.* 2004), Cu-np (Kidwai *et. al.* 2009), Fe_3O_4-L-proline NPs (Safaei-Ghomi *et. al.* 2015), MgO/ZrO_2 (Nagrik *et. al.* 2010), Nano ZrO_2 (Abaee *et. al.* 2014), $Bi(OTf)_3.xH_2O$ (Ollevier *et. al.* 2006), $Fe(O_2CCF_3)_3$ (Zhang *et. al.* 2012), Camphor-10-sulfonic acid (Kundu *et. al.* 2012), SiO_2-$OAlCl_2$ (Li *et. al.* 2007), Carbon-based solid acid (Davoodnia *et. al.* 2011), $NbCl_5$ (Wang *et. al.* 2007), Sulfamic acid (Luo et. al. 2009), Silica based tin(II) (Sharma *et. al.* 2012). Very recently such type of analogues is also used in the leather retanning process (Jianzhong *et. al.* 2024).

Mannich reaction plays an important role in the synthesis of bioactive skeletal used in the synthesis of various bioactive molecules having broad range of biological as pharmaceutical activities (Figure 1), such as hypnotic drug (Sumalatha *et. al.* 2009), analgesic (Abou-Shehada *et. al.* 2017), vasorelaxing property (Ferlin *et. al.* 2002), antimicrobial agent (Barmee *et. al.* 2006), anti-inflammatory drugs (Malinka *et. al.* 2005) and antiparkinsonic agent (Arend *et. al.* 1998) etc. in addition to this Mannich reaction is also used for the synthesis of some alkaloid-like molecules (Chernov *et. al.* 2003). In contamination of our research interest (Lal *et. al.* 2020, 2020, 2016, 2012, 2012, 2015, 2022), in the present research paper, we have developed new method for the synthesis of β-amino carbonyl derivatives. To the best of our knowledge, this is the first report to use visible light for such synthesis.

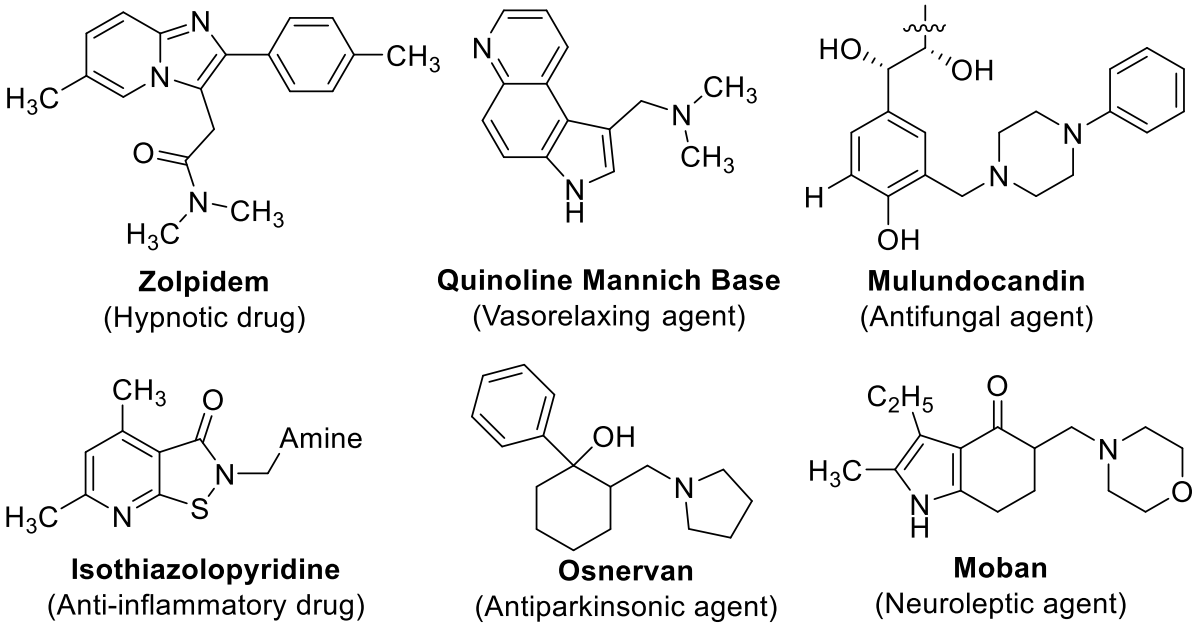


Figure 1: β-amino carbonyl derived biologically active molecules

RESULTS AND DISCUSSION

The schematic representation for the synthesis of β-amino carbonyl derivatives substituted acetophenone, substituted aromatic aldehydes and substituted aromatic amines in the presence of visible light is depicted in Scheme 1. Our investigation started with the three component condensation of acetophenone 1, benzaldehyde 2 and aniline 3 in the presence of visible light in acetonitrile at ambient temperature. To our delight, the desired product was obtained in 62% yield (table 1, entry 1). However, when reaction was prolonged, the yield of the product was decreased may be due to the decomposition of the synthesized product.

When the reaction was carried out on heating at about 60 °C, the desired product is obtained in trace amount reaction in 120 min., which is a positive intimation for us to carry the reaction at ambient temperature (Table 1, entry 2). By encouraged these results, we further carried out the reaction using different solvent systems and concluded that better yield of the desired product is obtained under solvent-free conditions (Table 1, entry 11).

After the screening of the solvent system for the reaction, further, we have screened the various sources of visible light (Table 2, entry 1-10), for this, a series of experiments were performed using visible lights of different intensities (like, blue LED, white LED with or without oxidant). From the experiment, it was observed that maximum yield of product was obtained when photo reactors was used in 20 min. (Table 2, entry 1).

Table 1: Optimization of solvent system for the synthesis of β-amino carbonyl derivatives[a]

Entry	Solvent system	Time (min.)	Yield[b] (%)
1	Acetonitrile	30	62
2	Acetonitrile[c]	120 min.	28
3	Ethanol	30	78
4	Ethanol-water (1:1)	35	51
5	Methanol	35	60
6	Methanol-water (1:1)	35	41
7	Ethanol-methanol (1:1)	35	56
8	Toluene	35	22
9	DMSO	40	Trace
10	DMF	40	Trace
11	Neat	20	96
12	Neat[d]	20	64

[a]Reaction conditions: Acetophenone : benzaldehyde : aniline 1 : 1 : 1 (mmol ratio) in presence/absence of solvent under open air at room temperature using visible light photo reactor (2 CFL's of 9 watt each) in 20 min. [b]Isolated yield.; [c]Under heating at 60 °C for 120 min.; [d]In closed vessel.

When, three and 4 CFL's were used in the photoreactor, no significant enhancement in yield was observed (table 2, entry 2), when CFL's increases in the photoreactor, yields of the product decreased by 2% (Table 2, entry 3), the next experiment was performed in the presence of oxidants (0.1 mol%) of TBHP or DTBP (table 2, entry 6) but no significant effect was observed in the product yield. However, the same reaction was performed under N_2 and in dark (table 2, entry 7 & 8) no product was formed. Further, no significant effect was observed in the yield of the product when the reaction was performed in day light, in the absence or presence of air (table 2, entry 9).

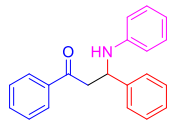
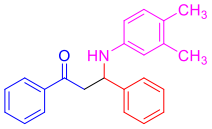
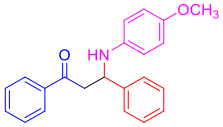
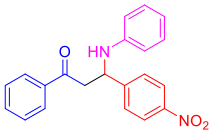
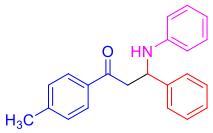
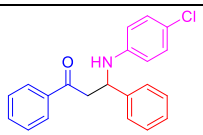
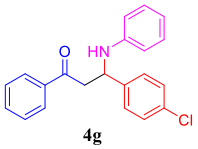
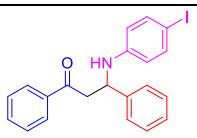
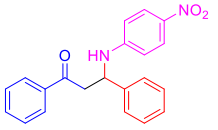
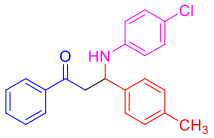
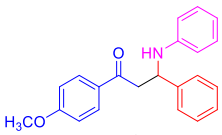
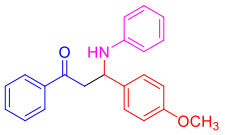
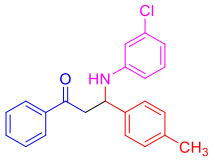
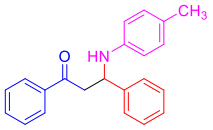
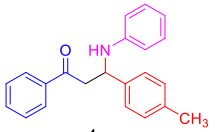
Table 2: Optimization of reaction conditions for the reaction[a]

Entry	Reaction conditions	Time (min.)	Yield[b] (%)
1	2 CFL's	20	96
2	3 CFL's	20	96
3	4 CFL's	20	94
4	White LED (9 w)	60	89
5	Blue LED (4 w)	60	72
6	2 CFL's, oxidants (0.1 mol%)	20	26[c], 32[d]
7	2 CFL's, under N_2	60	NR
8	Dark	60	NR
9	Day light	120	22[e], 48[f]

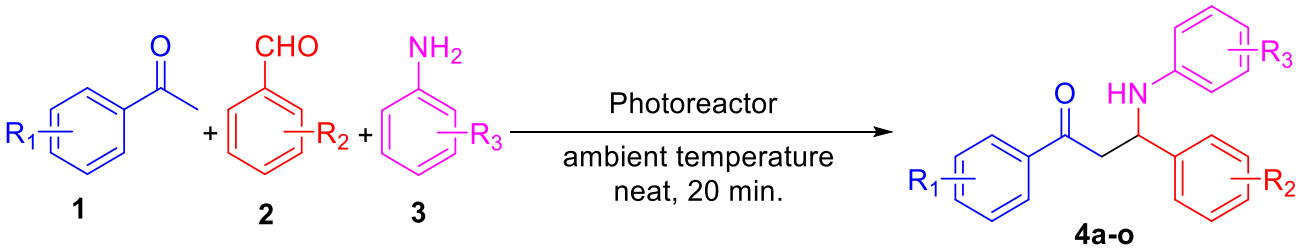
[a]Reaction conditions: Acetophenone : benzaldehyde : aniline 1 : 1 : 1 (mmol ratio) in presence/absence of solvent under open air at room temperature using visible light photo reactor (2 CFL's of 9 watt each) in 20 min. [b]Isolated yield.; [c]TBHP.; [d]DTBP.; [e]Under open air; [f]In the absence of air.; NR - No Reaction.

The optimized reaction conditions in hand we have synthesized 15 (4a-o) products with various electron donating and electron withdrawing substituents and no significant effect was observed on electron withdrawing and electron donating groups. All the reactions proceeds smoothly and products were formed in good to excellent yield in all cases (Table 3). Chromatography is not needed for the separation of the products, which makes our protocol more advantages to reported method.

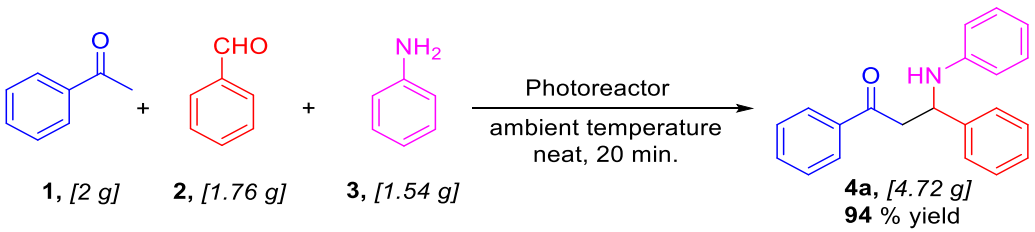
Table 3: Substrate scope and green chemistry metrics for the synthesized compounds[a]

Compound	Green chemistry metrics analysis	Compound	Green chemistry metrics analysis	Compound	Green chemistry metrics analysis
 **4a** **96** % yield 20 min.	[a]**AE** = 94.36 % [b]**AEf** = 90.58 % [c]**CE** = 92 % [d]**RME** = 90.23 % [e]**OE** = 0.96 % **E-factor** = 0.11 g/g	 **4b** **95** % yield 20 min.	**AE** = 94.82 % **AEf** = 89.13 % **CE** = 92 % **RME** = 90.91 % **OE** = 0.96 % **E-factor** = 0.12 g/g	 **4c** **94** % yield 20 min.	**AE** = 94.85 % **AEf** = 89.16 % **CE** = 92 % **RME** = 89.66 % **OE** = 0.95 % **E-factor** = 0.12 g/g
 **4d** **93** % yield 20 min.	**AE** = 95.06 % **AEf** = 88.41 % **CE** = 92 % **RME** = 93.06 % **OE** = 0.98 % **E-factor** = 0.13 g/g	 **4e** **94** % yield 20 min.	**AE** = 94.60 % **AEf** = 88.92 % **CE** = 96 % **RME** = 89.21 % **OE** = 0.94 % **E-factor** = 0.12 g/g	 **4f** **94** % yield 20 min.	**AE** = 94.91 % **AEf** = 89.22 % **CE** = 92 % **RME** = 89.12 % **OE** = 0.94 % **E-factor** = 0.13 g/g
 **4g** **94** % yield 20 min.	**AE** = 94.91 % **AEf** = 89.22 % **CE** = 92 % **RME** = 89.80 % **OE** = 0.95 % **E-factor** = 0.11 g/g	 **4h** **93** % yield 20 min.	**AE** = 95.48 % **AEf** = 88.80 % **CE** = 92 % **RME** = 86.91 % **OE** = 0.91 % **E-factor** = 0.15 g/g	 **4i** **94** % yield 20 min.	**AE** = 95.06 % **AEf** = 88.41 % **CE** = 92 % **RME** = 90.06 % **OE** = 0.95 % **E-factor** = 0.11 g/g
 **4j** **94** % yield 20 min.	**AE** = 95.12 % **AEf** = 89.39 % **CE** = 87 % **RME** = 89.54 % **OE** = 0.94 % **E-factor** = 0.12 g/g	 **4k** **96** % yield 20 min.	**AE** = 94.86 % **AEf** = 91.07 % **CE** = 96 % **RME** = 91.03 % **OE** = 0.96 % **E-factor** = 0.12 g/g	 **4l** **96** % yield 20 min.	**AE** = 94.85 % **AEf** = 91.06 % **CE** = 96 % **RME** = 91.09 % **OE** = 0.96 % **E-factor** = 0.12 g/g
 **4m** **94** % yield 20 min.	**AE** = 95.10 % **AEf** = 89.39 % **CE** = 98 % **RME** = 89.54 % **OE** = 0.94 % **E-factor** = 0.12 g/g	 **4n** **95** % yield 20 min.	**AE** = 94.60 % **AEf** = 89.87 % **CE** = 96 % **RME** = 89.93 % **OE** = 0.95 % **E-factor** = 0.11 g/g	 **4o** **96** % yield 20 min.	**AE** = 94.60 % **AEf** = 89.87 % **CE** = 96 % **RME** = 91.97 % **OE** = 97.21 % **E-factor** = 0.11 g/g

[a]Reaction conditions: Substituted acetophenone : substituted benzaldehyde : substituted aniline 1 : 1 : 1 (mmol ratio) in presence/absence of solvent under open air at room temperature using visible light photo reactor (2 CFL's of 9 watt each) in 20 min.; [b]AE (Atom Economy).; [c]AEf (Atom Efficiency).; [d]CE (Carbon Efficiency).; [e]RME (Reaction Mass Efficiency).; [f]OE (Optimum Efficiency).



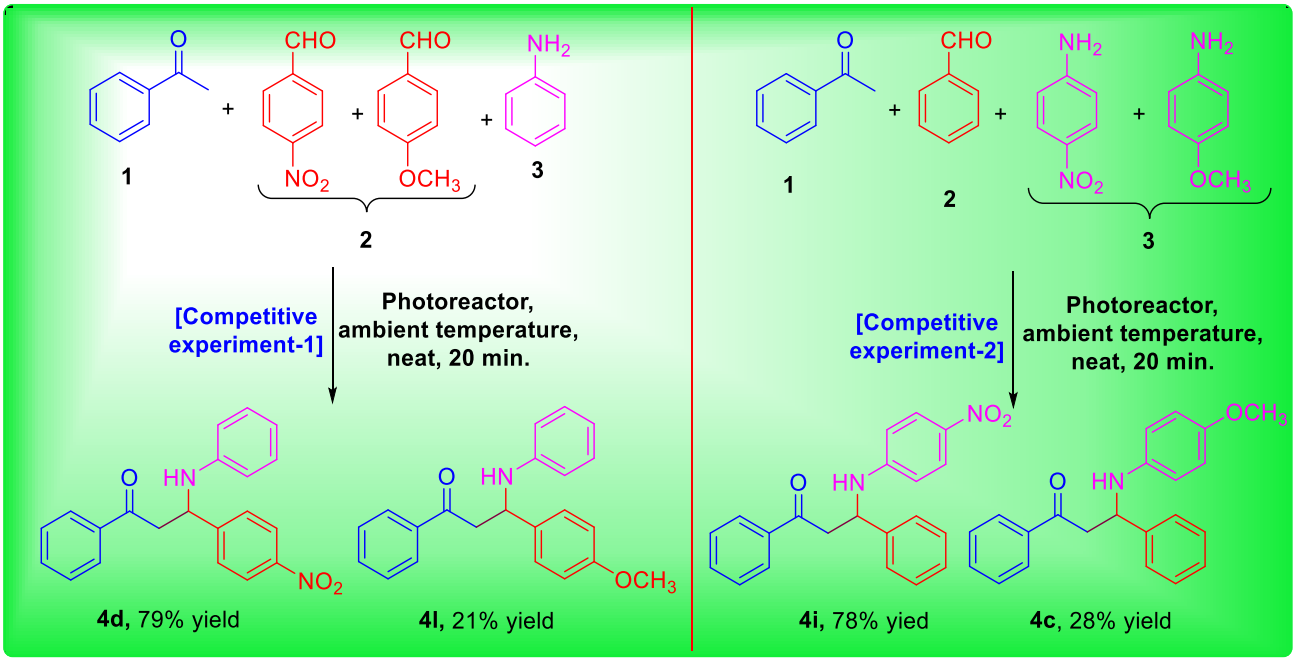
Scheme 1: Visible light mediated synthesis of β-amino carbonyl derivatives



Scheme 2: Gram Scaled-up Reaction

Competitive Experiment

Under optimized reaction conditions (Scheme 3), competitive experiment 1 and 2 were performed to evaluate any change in the starting material may cause any variation in the yields of the products. In *experiment 1*, when acetophenone 1 and aniline 2 were allowed to react with an equimolar mixture of *p*-methoxybenzaldehyde 3 and *p*-nitrobenzaldehyde 3, products 4a and 4b were obtained in 79% and 21% yield respectively. Likewise, in the *experiment 2*, when equal amount of *p*-methoxyaniline (3) and *p*-nitroaniline 3a, were subjected to a reaction with acetophenone and benzaldehyde. Products 4c and 5c were obtained in 78% and 28% yields respectively.

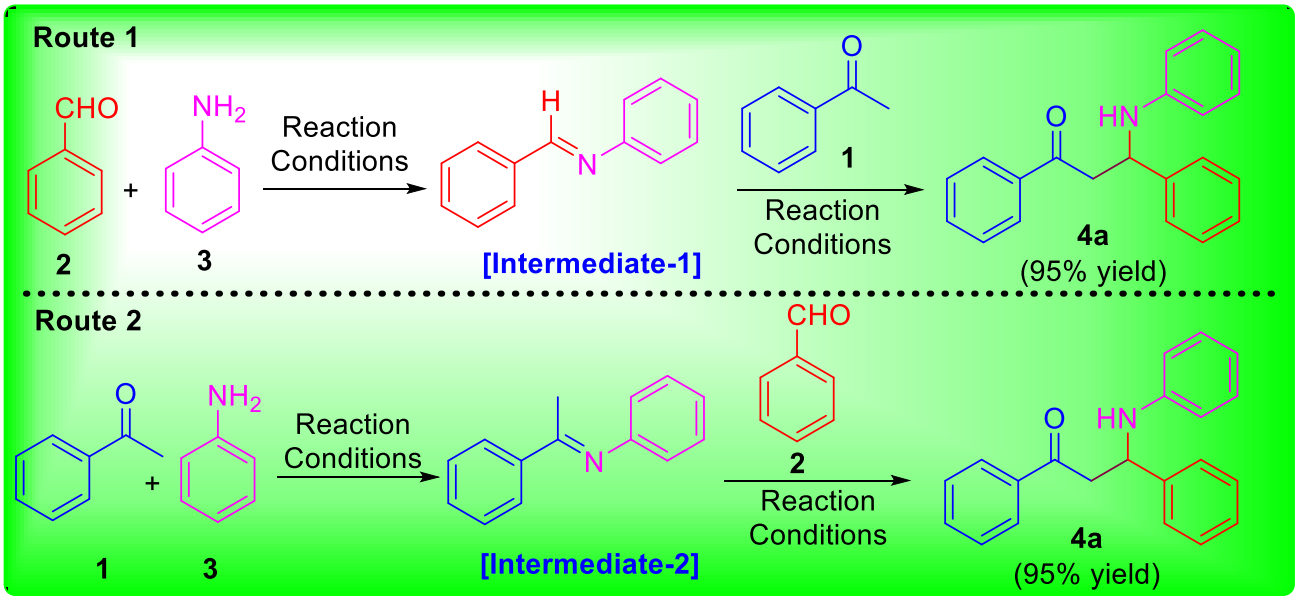


Scheme 3: Competitive experiments

All the results obtained suggest the remarkable selectivity of the reaction favouring electron donating groups over electron withdrawing groups. These experiments also revealed that when the substrates bearing electron donating group were made to react individually, they provided better yields than the substrates bearing electron withdrawing group. However, in the mixture, substrates with electron withdrawing group not only reacted faster, but also resulted in higher yields as compared to substrates having electron donating group.

Mechanistic Study

For the reaction, two routes are possible theoretically. In order to evaluate the routes for the reaction (Scheme 4), two sets of experiments were performed using visible light irradiations at ambient temperature. In the first experiment, the starting materials benzaldehyde 2 and aniline 3 were allowed to react with each other under optimized reaction conditions, which furnish the intermediate-I, which gives final product on reaction with third reagent acetophenone 1. In the second experiment, we have allowed acetophenone 1, to react with aniline 3 as a result intermediate-II was formed which finally reacts with benzaldehyde 2 to furnish the final product. In the reaction it is very interesting to note that, the reaction proceeds smoothly, and concluded that both the reaction routs are feasible there is no significant change in yield of the product and time was observed.



Scheme 4: Mechanistic study of the reaction

Calculation of Green Chemistry Metrics

For the newly developed synthetic protocol, green chemistry metrics (Table 3) like atom economy (AE), atom efficiency (AEf), carbon efficiency (CE), reaction mass efficiency (RME), optimum efficiency (OE) and E-factor have been calculated on the basis of well-established formulas (Sheldon *et. al.* 2018, 2015). For the reaction, atom economy was obtained in the ranges between 94.36-95.48 %, the value of atom efficiency was comes in the range 88.41-91.07, Carbon efficiency for the reaction was obtained in the range between 92-98 %. The process shows a good profile of calculated reaction mass efficiency in ranging between 86-91-93.06 %, which is very useful metric to determine the greenness of a process. To our delight, E-factor for the developed protocol is very low ranging between 0.11-0.15 g/g, which strongly indicates considerable green aspects of the present protocol.

EXPERIMENTAL SECTION

General Remarks

All the chemical reagents used in the experiment were purchased from Himedia, Rankem and Merck chemical companies and used as received. Melting points of the synthesized compounds were determined on electrical thermal melting temperature apparatus as compared with authentic samples. IR spectra of all the synthesized compounds were recorded on Schimadzu Prestise 21 spectrophotometer using KBr discs at room temperature. ^{1}H NMR and ^{13}C-NMR spectra were recorded on BRUKER AVANCE II NMR spectrometer at frequencies 400 MHz and 100 MHz respectively. Mass spectra were recorded on a JEOL-AccuTOF JMS-T100LC Mass spectrometer.

Typical Procedure for The Synthesis of B-Aminocarbonyls

A 10 mL round bottom flask was charged with substituted acetophenones 1 (0.416 mmol), substituted aromatic aldehydes 2 (0.416 mmol), substituted aromatic amines 3 (0.416 mmol) and the content was irradiated under photoreactor (having 2 CFLs of 9 watt each) at ambient temperature for about 20 min. The progress of the reaction was monitored by TLC using petroleum ether/AcOEt = (80:20) ratio as an eluent. After completion of the reaction, the content was added in ice-cooled water and filtered the contents to get the solid product. The product was washed with water and was purified by hot ethanol. All the synthesized compounds reported in the paper are known and were characterized by comparison of their physical and analytical data with those of authentic samples reported in the literature.

Competitive Experiments

A 10 mL round bottom flask was charged with acetophenone 1 (1 mmol), *p*-nitrobenzal-dehyde 2 (0.416 mmol), *p*-methoxy-benzaldehyde 2 (0.416 mmol) and aniline 3 (0.416 mmol) in the first experiment; in the second experiment the sequence and ratio of the reagents are acetophenone 1 (1 mmol), benzaldehyde 2 (0.416 mmol), *p*-nitroaniline 3 (0.416 mmol) and *p*-methoxyaniline 3 (0.416 mmol) the contents of the reactions were irradiated separately under photoreactor (having 2 CFLs of 9 watt each) at ambient temperature for 20 min. The progress of the reaction was monitored

by TLC using petroleum ether/AcOEt = (80:20) ratio as an eluent. After completion of the reaction, the contents of both the reactions were added in ice-cooled water and filtered the contents to get the solid products. The products were washed with water and were purified by hot ethanol.

Gram-Scaled Up Experiment

A 100 mL round bottom flask was charged with acetophenone 1 (16.64 mol), benzaldehyde 2 (16.64 mol), aniline 3 (16.64 mol) and the content was irradiated under photoreactor (having 2 CFLs of 9 watt each) at ambient temperature for about 20 min. The progress of the reaction was monitored by TLC using petroleum ether/AcOEt = (80:20) ratio as an eluent. After completion of the reaction, the content was added in ice-cooled water and filtered the contents to get the solid product. The product was washed with water and was purified by hot ethanol.

Characterization Data of Some Selected Compounds

1,3-Diphenyl-3-phenylamino-propan-1-one (4a)

White coloured solid powder, IR (KBr) λmax/cm^{-1}: 3384, 3096, 3018, 2871, 1669, 1592, 1446, 1350, 1280, 1174, 1008, 746, 682; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.33-3.42 (m, 2H), 4.96 (t, 1H), 6.51 (d, *J* = 8.0 Hz, 2H, Ar-H), 6.61-6.66 (m, 1H, Ar-H). 7.01-7.06 (m, 2H, Ar-H), 7.20 (d, *J* = 6.5 Hz, 2H, Ar-H), 7.24-7.27 (m, 1H, Ar-H), 7.37-7.44 (m, 2H, Ar-H), 7.43-7.52 (m, 1H, Ar-H), 7.51-7.55 (m, 2H, Ar-H), 7.84 (d, *J* 7.8 Hz, 2H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 46.5, 54.4, 115.6, 119.5, 126.6, 128.8, 128.6, 129.4, 132.7, 135.7, 146.6, 197.2; m/z (GC-MS, HRMS): 301.368 (M^+).

3-(3,4-Dimethyl-phenylamino)-1,3-diphenyl-propan-1-one (4b)

White coloured solid; IR (KBr) λmax/cm^{-1}: 3379, 3087, 3012, 2866, 1662, 1589, 1441, 1352, 1283, 1171, 1004, 744, 689; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.34 (s, 6H, -CH_3), 3.10 (d, *J* = 6.1, 2H), 4.52 (t, 1H), 6.32 (s, 1H, Ar-H), 6.29 (d, *J* = 6.8 Hz, 2H, Ar-H), 6.65 (d, *J* = 8.1, 2H, Ar-H), 7.07-7.12 (m, 1H, Ar-H), 7.28 (d, *J* = 6.7 Hz, 2H, Ar-H), 7.26-7.32 (m, 2H, Ar-H), 7.29-7.31 (m, 2H, Ar-H), 7.41-7.46 (m, 1H, Ar-H), 7.93 (d, *J* = 7.8 Hz, 2H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 17.6, 42.8, 55.8, 115.6, 123.6, 126.8, 128.7, 128.7, 129.9, 129.2, 131.4, 137.8, 141.2, 192.4. m/z (GC-MS, HRMS): 327.432 (M^+).

3-(4-Methoxy-phenylamino)-1,3-diphenyl-propan-1-one (4c)

White solid powder; IR (KBr) λmax/cm^{-1}: 3379, 3091, 3015, 2878, 1671, 1596, 1445, 1348, 1279, 1171, 1020, 749, 689; ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.41-3.44 (m, 2H), 3.61 (s, 3H, -OCH_3), 4.81 (t, 1H), 6.52 (d, *J* = 8.6 Hz, 2H, Ar-H), 6.71 (d, *J* = 8.9, 2H, Ar-H), 6.91-7.01 (m, 1H, Ar-H), 7.15 (d, *J* = 8.3 Hz, 2H, Ar-H), 7.26-7.32 (m, 2H, Ar-H), 7.36-7.40 (m, 2H, Ar-H), 7.43-7.51 (m, 1H, Ar-H), 7.82 (d, *J* = 7.5 Hz, 2H, Ar-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 46.5, 55.2, 58.3, 115.4, 122.4, 126.6, 127.4, 128.2, 128.6, 128.1, 129.7, 132.2, 138.1, 141.5, 151.5, 195.1. m/z (GC-MS, HRMS): 332.473 (M^+).

3-(4-Nitro-phenyl)-1-phenyl-3-phenylamino-propan-1-one (4d)

White coloured solid; IR (KBr) λmax/cm^{-1}: 3379, 3091, 3012, 2876, 1661, 1591, 1445, 1352, 1283, 1171, 1002, 745, 681; ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.54 (d, *J* = 6.2 Hz, 2H), 5.16 (t, 1H), 6.58 (d, *J* = 6.6 Hz, 2H, Ar-H), 6.64-6.72 (m, 1H, Ar-H), 7.08-7.13 (m, 2H, Ar-H), 7.39-7.42 (m, 2H, Ar-H), 7.51-7.57 (m, 2H, Ar-H), 7.61 (d, *J* = 7.4 Hz, 2H, Ar-H), 7.86 (d, *J* = 8.0 Hz, 2H, Ar-H), 8.15 (d, *J* = 9.5 Hz, 2H, Ar-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 46.2, 54.2, 112.6, 116.4, 123.3, 128.1, 128.3, 128.2, 129.5, 132.8, 137.2, 140.6, 143.4, 146.1, 198.2. m/z (GC-MS, HRMS): 346.381 (M^+).

3-Phenyl-3-phenylamino-1-p-tolyl-propan-1-one (4e)

White coloured solid; IR (KBr) λmax/cm^{-1}: 3378, 3090, 3014, 2877, 1661, 1587, 1443, 1353, 1278, 1181, 1011, 745, 683; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.41 (s, 3H, -CH_3), 3.43 (d, *J* = 5.9 Hz, 2H), 4.92 (t, 1H), 6.41 (d, *J* = 7.6 Hz, 2H, Ar-H), 6.54 (m, 1H, Ar-H). 6.91 (m, 2H, Ar-H), 7.14 (d, *J* = 6.4 Hz, 2H, Ar-H), 7.23-7.31 (m, 3H, Ar-H), 7.42 (d, 7.7 Hz, 2H, Ar-H), 7.85 (d, *J* = 7.1 Hz, 2H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.8, 44.3, 52.4, 109.3, 113.6, 124.1, 126.4, 127.4, 127.6, 128.2, 128.3, 131.3, 140.4, 141.5, 194.4. m/z (GC-MS, HRMS): 316.374 (M^+).

3-(4-Chloro-phenylamino)-1,3-diphenyl-propan-1-one (4f)

White coloured solid; IR (KBr) λmax/cm^{-1}: 3382, 3097, 3015, 2870, 1665, 1591, 1441, 1359, 1276, 1174, 1020, 741, 689; ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.34-3.51 (m, 2H), 4.98 (t, 1H), 6.34 (d, *J* = 8.4 Hz, 2H, Ar-H), 6.69 (d, *J* = 8.1, 2H, Ar-H), 7.12 (d, *J* = 6.6 Hz, 2H, Ar-H), 7.31-7.26 (m, 2H, Ar-H), 7.32-7.35 (m, 2H, Ar-H), 7.39-7.34 (m, 2H, Ar-H), 7.45-7.53 (m, 1H, Ar-H), 7.87 (d, *J* = 7.8 Hz, 2H, Ar-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 44.11, 55.2, 116.6, 122.7, 125.8, 127.2, 128.1, 128.5, 129.4, 133.9, 137.1, 140.6, 197.3. m/z (GC-MS, HRMS): 335.832 (M^+).

3-(4-Chloro-phenyl)-1-phenyl-3-phenylamino-propan-1-one (4g)

White coloured solid; IR (KBr) λmax/cm^{-1}: 3380, 3091, 3013, 2873, 1663, 1591, 1442, 1358, 1281, 1176, 1001, 749, 683; ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.47 (d, *J* = 5.7 Hz, 2H), 5.21 (t, 1H), 6.61 (d, *J* = 6.3 Hz, 2H, Ar-H), 6.71-6.74 (m, 1H, Ar-H), 7.11-7.15 (m, 2H, Ar-H), 7.29 (d, *J* = 7.6 Hz, 2H, Ar-H), 7.51 (d, *J* = 8.1 Hz, 2H, Ar-H), 7.63-7.69 (m, 2H, Ar-H), 7.72-7.79 (m, 1H, Ar-H), 7.97 (d, *J* = 9.2 Hz, 2H, Ar-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 47.8, 53.4, 111.4, 115.8, 128.2, 128.8, 128.4, 128.6, 129.8, 131.9, 136.4, 141.4, 144.6, 196.2. m/z (GC-MS, HRMS): 337.416 (M^+).

3-(4-Iodo-phenyl)-1-phenyl-3-phenylamino-propan-1-one (4h)

Brown solid, IR (KBr) λmax/cm^{-1}: 3382, 3096, 3011, 2869, 1659, 1596, 1448, 1351, 1277, 1171, 1022, 742, 681; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.96 (d, *J* = 3.1 Hz, 2H), 7.64 (t, 1H), 7.58 (d, *J* = 9.1 Hz, 4H), 7.34 (t, 2H), 7.48 (t, 1H), 7.05 (t, 2H), 6.85 (t, 2H), 6.55 (d, *J* = 9.1 Hz, 1H), 5.03 (d, *J* = 9.1 Hz, 1H), 4.63 (s, 1H), 3.59 (d, *J* = 15 Hz, 1H), 3.44 (d, *J* = 15 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.12, 148.29, 142.37, 136.62, 133.51, 130.56, 128.91, 128.72, 128.24, 127.55, 126.63, 126.21, 122.68, 112.87, 95.12, 77.26, 54.51, 46.12; m/z (GC-MS, HRMS): 428.0 (M^+).

3-(4-Nitro-phenylamino)-1,3-diphenyl-propan-1-one (4i)

White coloured solid; IR (KBr) λmax/cm^{-1}: 3379, 3092, 3021, 2869, 1672, 1590, 1441, 1356, 1282, 1179, 1012, 749, 689; ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.67 (d, *J* = 6.8 Hz, 2H), 5.19 (t, 1H), 6.33 (s, 2H, Ar-H), 6.64 (d, *J* = 6.4, 2H, Ar-H), 7.21-7.29 (m, 1H, Ar-H), 7.27-7.33 (m, 2H, Ar-H), 7.36 (d, *J* = 7.6 Hz, 2H, Ar-H), 7.61-7.68 (m, 1H, Ar-H), 8.02 (d, *J* = 7.2 Hz, 2H, Ar-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 45.6, 53.3, 111.3, 125.2, 126.8, 127.2, 128.5, 128.8, 128.5, 130.7, 132.4, 136.4, 138.3, 140.3, 197.4. m/z (GC-MS, HRMS): 348.637 (M^+).

3-(4-Methoxy-phenyl)-1-phenyl-3-phenylamino-propan-1-one (4l)

White coloured solid; IR (KBr) λmax/cm^{-1}: 3378, 3088, 3016, 2849, 1671, 1579, 1451, 1363, 1239, 1141, 1014, 746, 669; ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.43-3.39 (m, 2H), 3.61 (s, 3H, -OCH_3), 4.94 (t, 1H), 6.44 (d, *J* = 8.1 Hz, 2H, Ar-H), 6.57 (t, 1H, Ar-H), 6.88-6.91 (m, 2H, Ar-H), 7.24 (d, *J* = 8.1 Hz, 2H, Ar-H), 7.29-7.34 (m, 2H, Ar-H), 7.42-7.45 (m, 2H, Ar-H), 7.52-7.55 (m, 1H, Ar-H), 7.88 (d, *J* = 7.6 Hz, 2H, Ar-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 47.7, 54.4, 56.8, 113.7, 113.2, 116.7, 128.3, 128.7, 127.2, 129.6, 132.5, 134.9, 137.2, 160.5, 198.7. m/z (GC-MS, HRMS): 331.423 (M^+).

1,3-Diphenyl-3-p-tolylamino-propan-1-one (4n)

White coloured solid powder; IR (KBr) λmax/cm^{-1}: 3381, 3095, 3016, 2877, 1667, 1587, 1446, 1354, 1282, 1171, 1011, 744, 688; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.48 (s, 3H, -CH_3), 3.63-3.46 (m, 2H), 4.44 (t, 1H), 6.92 (d, *J* = 8.4 Hz, 2H, Ar- H), 6.96 (d, *J* = 7.8, 2H, Ar-H), 7.02-7.09 (m, 2H, Ar-H), 7.12 (d, *J* = 6.4 Hz, 2H, Ar-H), 7.29-7.36 (m, 1H, Ar-H), 7.43-7.48 (m, 2H, Ar-H), 7.61-7.64 (m, 1H, Ar-H), 7.84 (d, *J* = 7.8 Hz, 2H, Ar-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.6, 45.7, 56.1, 113.8, 120.2, 122.1, 128.1, 128.7, 130.3, 133.7, 135.8, 144.2, 196.8. m/z (GC-MS, HRMS): 313.362 (M^+).

1-Phenyl-3-phenylamino-3-p-tolyl-propan-1-one (4o)

White solid powder; IR (KBr) λmax/cm^{-1}: 3380, 3091, 3012, 2879, 1670, 1589, 1453, 1348, 1277, 1178, 1011, 745, 689; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.32 (s, 3H, -CH_3), 3.34-3.41 (m, 2H), 4.86 (t, 1H), 6.76 (d, *J* = 8.1 Hz, 2H, Ar-H), 6.80-6.89 (m, 1H, Ar-H), 7.03-7.06 (m, 2H, Ar-H), 7.11 (d, *J* = 7.8 Hz, 2H, Ar-H), 7.22 (d, *J* = 7.38, 4 Hz, 2H, Ar-H), 7.31-7.39 (m, 2H, Ar-H), 7.46-7.47 (m, 1H, Ar-H), 7.88 (d, *J* = 8.1 Hz, 2H, Ar-H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 21.5, 42.4, 54.9, 111.6, 119.7, 123.8, 127.2, 128.4, 131.8, 132.1, 135.3, 143.9, 190.8. m/z (GC-MS, HRMS): 317.402 (M^+).

CONCLUSIONS

A visible light-induced, efficient, convenient, atom-economic and green protocol has been developed for the synthesis of *β*-aminocarbonyls by the Mannich condensation of substituted acetophenones with substituted aromatic aldehydes and substituted aromatic amines. No use of hazardous solvents and catalyst make the method more advantageous over existing methods. The protocol was found to have good functional group tolerance and a wide range of differently substituted derivatives may be synthesized in good to excellent yield by this method. The developed approach may be seen as an alternate and very attractive pathway to the previously reported methods of this biologically active class of molecule.

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