CHAPTER 3

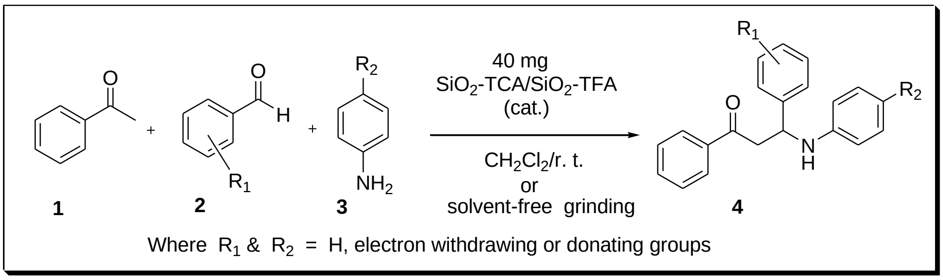
Designing of silica supported organocatalysts from carboxylic acids for the Mannich-type synthesis of β-amino carbonyl compounds

3.1 Introduction

The utilization of organocatalysts in organic synthesis have received considerable attention for production of fine chemicals because of lack of sensitivity to moisture and oxygen, ready availability, low cost and low toxicity as compared to other traditional catalysts [1-3]. However, the capability and applicability of an organocatalyst in organic transformations can be improved if its recovery and reuse procedure become more and more facile [4-5]. The recycling of an organocatalyst simplifies the purification steps, avoiding wastes and gives potential for utilization in large-scale operations [6-8]. The immobilization of organocatalysts on inert supports (such as charcoal, alumina, silica, and polymers etc.) makes them heterogeneous which improves the availability of active sites of catalyst for the synthesis of small molecules under especially simple, mild and more environmentally benign conditions [9-10]. Among the various supports, silica has special position because of its abundant availability, thermal stability and polar surface which can easily bind the polar groups of organic molecules that lead to the generation of more active catalytic sites [11]. The application of such type of heterogeneous catalyst in multicomponent reactions (MCRs) provides an attractive strategy for rapid and efficient library generation of complex molecules with higher atom-economy [12-13].

The synthesis of β-amino carbonyl compounds from acid catalyzed Mannich-type reactions of aldehydes, amines and ketone are widely applicable as synthetic intermediates for various pharmaceuticals and natural product as discussed in **Chapter 1** [14-15]. Several modifications of the classical Mannich reaction have been developed using preformed electrophiles and stable nucleophiles [16-17]. But, the preferred route is the multicomponent strategies that give wide range of structural variations. A variety of Brønsted, Lewis and solid acids have been employed as catalyst for the Mannich-type reactions. Unfortunately, many of them require longer reaction time, excess amount of non-recyclable catalysts, use of expensive heavy metal salts, harsh reaction condition and difficulty in product isolation. Also most of the reported procedures were only applicable to aliphatic amines and failed to work with aromatic amines [18-22]. Although some of the recent protocols made this route attractive, the development of fast, simple and environmentally benign approaches that could be performed at ambient temperature for the Mannich-type reaction is highly desirable.

In this chapter three reusable solid acid catalysts were designed by supporting simple carboxylic acids: trifluoroacetic acid (TFA), trichloroacetic acid (TCA) and acetic acid (AA) on silica by wet impregnation method which were characterized by SEM, EDX, TGA, FT-IR and powder XRD analysis. After observing their thermal stability and surface properties, they were utilized as highly efficient solid acid catalysts for the reaction of acetophenone, arylamines and aryl aldehyde (**Scheme 3.1**) in CH_2Cl_2 solution and solvent-less mechanochemical method at ambient temperature. Since, the use of solvent-free grinding method will display several advantages such as pollution reduction, less energy consumption and less side product [23].



Scheme 3.1 Mannich-type reactions catalyzed by silica supported organic acids

3.2 Results and discussion

3.2.1 Synthesis and characterization of silica supported organocatalysts

3.2.1a Optimization of catalyst loading

The supported acids were prepared by wet impregnation method from the mixture of carboxylic acid ($CF_3COOH/CCl_3COOH/CH_3COOH$) with neutral silica (100-200 mesh) in diethyl ether at room temperature stirring. Loading of each acid on the silica was calculated based on the weight of supported organocatalysts obtained and the weight of silica used. The loading of each supported catalysts was optimized by increasing or decreasing the amount of supports and acids. It has been observed that almost similar amount of acids were loaded on silica support in case of entry 1 and entry 2 (**Table 3.1**). The preparation of catalysts was optimized from the mixture of 4 mmol of carboxylic acids and 10 g of silica.

Table 3.1 Optimization of the catalyst loading

Entry	Silica (neutral) (g)	Carboxylic acids (mmol)	Loading (mmol/g) (a)/(b)/(c)
1	3	10	0.441/0.355/0.346
2	10	4	0.343/0.358/0.365

SiO_2-AA (a), SiO_2-TCA (b), SiO_2-TFA (c)

3.2.1b Characterization of catalyst using FT-IR

The IR spectra of the supported catalysts were shown in **Figure 3.1**.

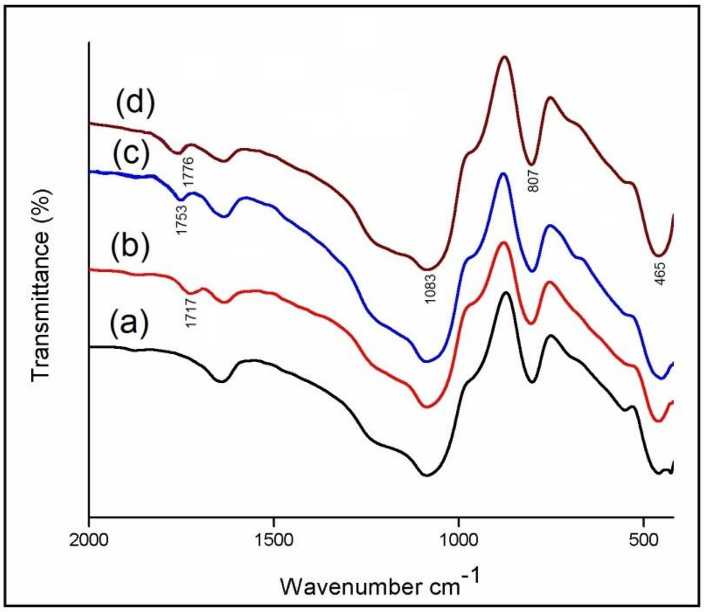


Figure 3.1 FT-IR spectra of SiO_2 (a), SiO_2-AA (b), SiO_2-TCA (c) and SiO_2-TFA (d)

The broad band appears at 1083 cm^{-1} and strong peak at 807 cm^{-1} were assigned to asymmetric and symmetric stretching vibrations of Si–O–Si respectively. Band at 465 cm^{-1} was assigned to Si–O–Si bending vibrations. The carbonyl stretching vibrations of the supported acids were observed in the increasing order at 1717, 1753, 1776 cm^{-1} for CH_3COOH, CCl_3COOH and CF_3COOH respectively.

3.2.1c SEM and EDX analysis

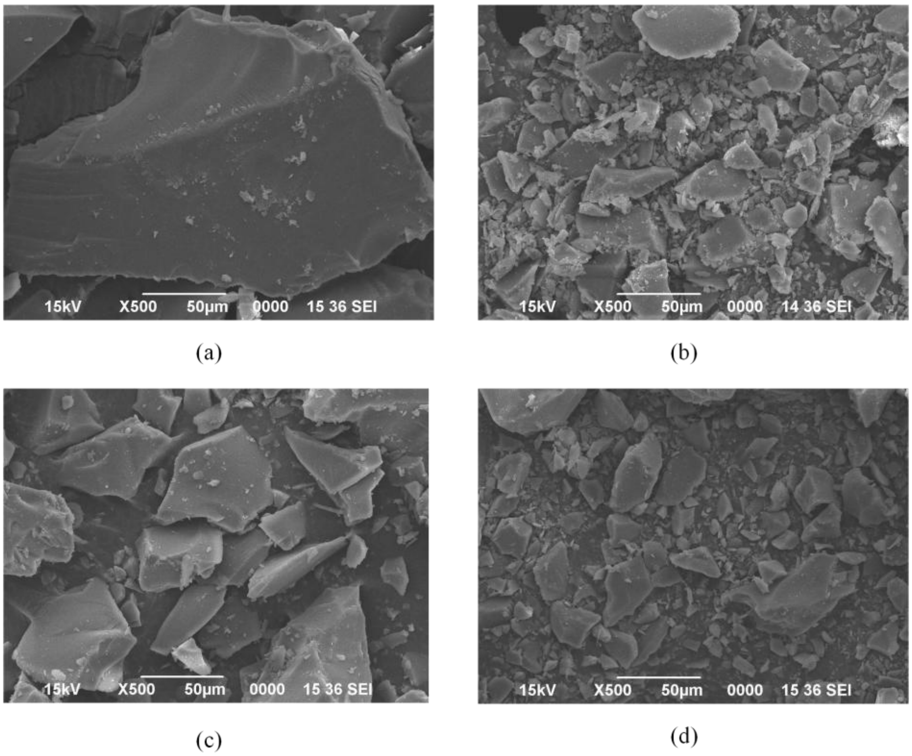
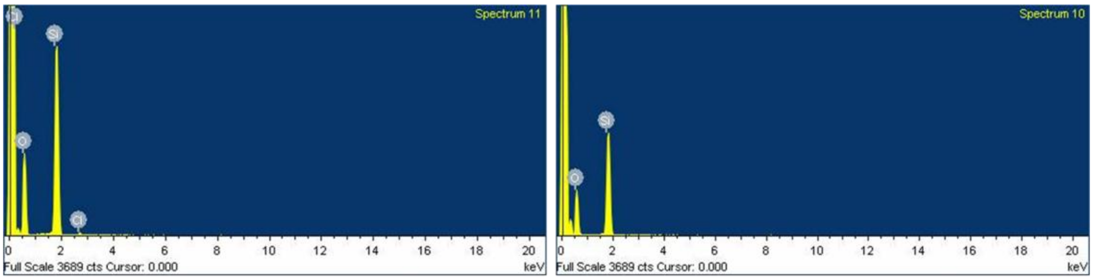

(a) (b) (c) (d)

Figure 3.2 SEM images of silica (a), SiO_2- AA (b), SiO_2-TCA (c) and SiO_2-TFA (d)

The SEM images of organocatalysts (**Figure 3.2**) distinctly expressed the change in the appearance and morphology of silica support. The roughness of silica surface increased through physical interactions with carboxylic acids. All these surfaces had no definite particle sizes. The particle sizes of trichloroacetic acid catalyst were found to be higher than TFA and AcOH catalysts.

The impregnation of trichloroacetic acid on the surface of silica support was confirmed by the presence of Cl atom in EDX spectra (**Figure 3.3**).



(c) (d)

Figure 3.3 EDX spectra of SiO_2-TCA (c) and SiO_2-TFA (d)

The EDX analysis of silica-TFA catalyst didn't identify any F atom on its surface due to fluorine mobility during EDX analysis [24].The lower bond dissociation energy of C-F bond (453kJ/mol) may facilitate the formation of anions or free radicals of fluorine from impregnated CF_3COOH under strong electron beam irradiation. After that the negatively charged F^- anions are slowly migrating away from the irradiated area by the possible repulsive interactions with the accumulated negative charge of electron beam. This ionic mobility of F atom prevents their detection with EDX spectra. The presence of fluoride in the catalyst was further confirmed by the fluoride ion selective electrode (Orion multiparameter kit) using Lassaigne filtrate of SiO_2-TFA catalyst.

3.2.1d Thermal analysis

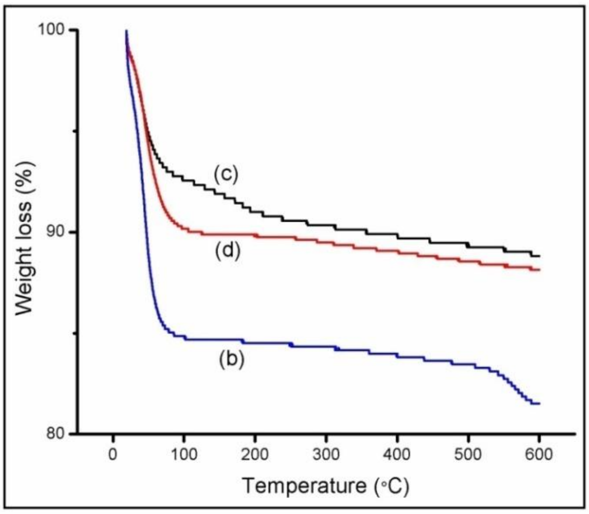


Figure 3.4 TGA curve of SiO_2-AA (b), SiO_2-TCA (c) and SiO_2-TFA (d)

The TGA curves furnished information about the thermal stability of loaded carboxylic acids on silica support (**Figure 3.4**). The weight loss around 80-90 ^{o}C may include loss of surface physisorbed water and some amount of organic acids from SiO_2-AA (b), SiO_2-TCA (c) and SiO_2-TFA (d) catalysts.

3.2.1e Powder XRD analysis

The XRD patterns of supported acids showed slight sharpening of basic broad amorphous peak of silica at 2ɵ= 25^{o} (**Figure 3.5**).

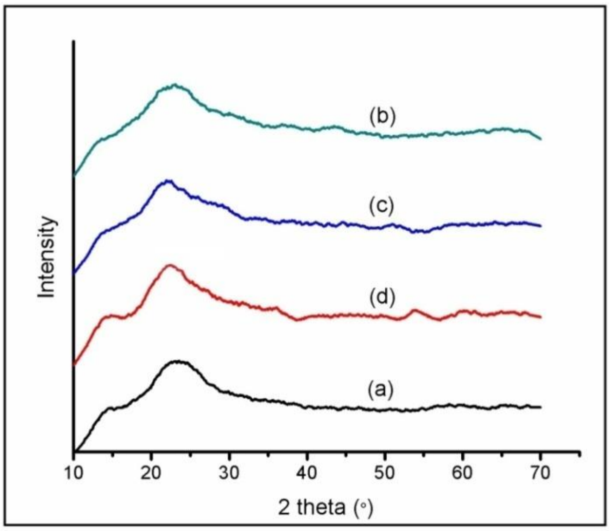


Figure 3.5 Powder XRD of silica (a), SiO_2-AA (b), SiO_2-TCA (c) and SiO_2-TFA (d)

3.2.2 Applications of the catalysts for the Mannich-type reaction

After observing the thermal stability and optimized amount of loading of each carboxylic acid on the surface of silica, the catalytic performance of these organocatalysts were tested for the reaction of benzaldehyde (1 mmol), aniline (1 mmol) and acetophenone (1 mmol) in different solvents at room temperature (**Table 3.2**, entries 5-11). The unsupported carboxylic acids resulted in 20-57% yield of β-amino carbonyl compound during 4-48 h time in solution at room temperature stirring (**Table 3.2**, entries 2-4) [25]. We did not observe any product formation using 40 mg of silica for the same reaction in CH_2Cl_2 (**Table 3.2**, entry 1). The progress of the reactions was monitored by using thin layer chromatography.

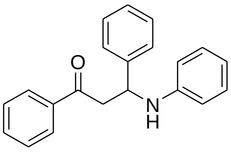
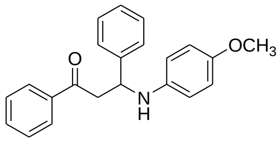
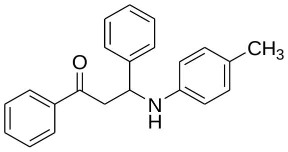
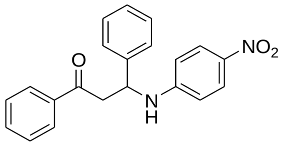
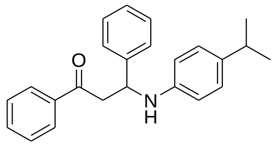
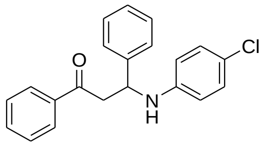
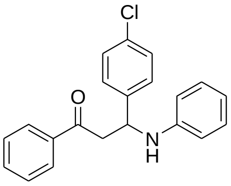
Table 3.2 Optimization of the Mannich-type reaction catalyzed by silica supported acids at room temperature

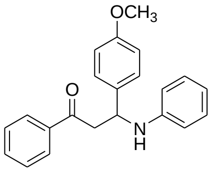
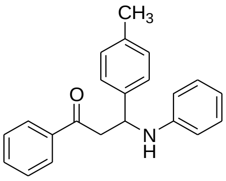
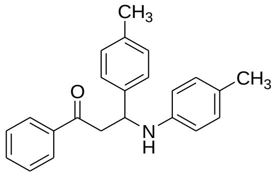
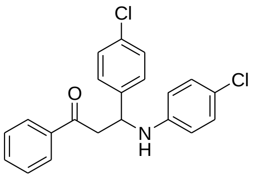
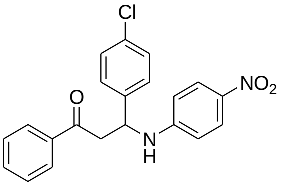
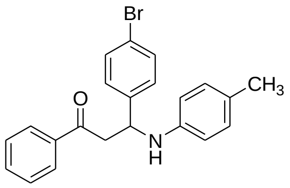
Entry	Catalyst	Catalyst (mg)[a]	Time (min) (b)/(c)/(d)	Solvents	Yield(%)[b] **4a** (b)/(c)/(d)
1	SiO_2	40	10 h	CH_2Cl_2	No reaction
2	TFA	0.5 mmol	4 h	EtOH	57 [25]
3	TCA	0.5 mmol	4 h	EtOH/CH_2Cl_2	50/55
4	AA	0.5 mmol	48 h	EtOH	20
5	(b)/(c)/(d)	20	90	CH_2Cl_2	45/65/70
6	(b)/(c)/(d)	40	70/50/45	CH_2Cl_2	80/87/90
7	(b)/(c)/(d)	62	45	CH_2Cl_2	82/88/93
8	(b)/(c)/(d)	40	60	EtOH	70/83/85
9	(b)/(c)/(d)	40	45	THF	-/35/40
10	(b)/(c)/(d)	40	45	CH_3CN	-/60/70
11	(b)/(c)/(d)	40	120	H_2O	No reaction
12	(b)/(c)/(d)	40	60/25/20	-	82/90/93[c]

[a] Amount of catalyst against 1 mmol of benzaldehyde, aniline and acetophenone; [b] Methods: Using SiO_2-AA (b), SiO_2-TCA (c) and SiO_2-TFA (d); [c] Under solvent-free grinding at room temperature.

The best activity obtained using 40 mg of each catalysts in CH_2Cl_2 (**Table 3.2**, entry 6). The reaction with SiO_2-AA catalyst requires more time as compared to SiO_2-TCA and SiO_2-TFA in CH_2Cl_2. The same reaction could be performed more efficiently in solvent-free mechanochemical method at room temperature using 40 mg of SiO_2-TCA and SiO_2-TFA catalysts (**Table 3.2**, entry 12). Finally, the optimization conditions for the synthesis of β-amino carbonyl compounds were extended for various aromatic aldehydes and aryl amines with 40 mg of SiO_2-TCA and SiO_2-TFA catalysts in solution (**Table 3.3)** and solvent-free grinding methods (**Table 3.4)**.

Table 3.3 Synthesis of β-amino carbonyl compounds **4** catalyzed by SiO_2-TFA and SiO_2-TCA in solution

Entry	**2** R_1	**3** R_2	Product **4**	Yield% (Time in mins) (c)/(d)[a]	Mp. (°C) Found (reported) [ref]
1	H	H	 **4a**	87(50)/90(45)	168.5-169 (169-170) [26]
2	H	4-OCH_3	 **4b**	88(50)/90(50)	164.5-165.3 (164-165) [27]
3	H	4-CH_3	 **4c**	86(50)/92(50)	167.5-168.2 (167-168) [26]
4	H	4-NO_2	 **4d**	82(70)/85(1h)	179.5-181 (179-180) [26]
5	H	4-$(CH_3)_2CH$-	 **4e**	84(50)/87(45)	117.5-119.2 (120) [28]
6	H	4-Cl	 **4f**	90(45)/93(40)	167.7-169.4 (170-171) [26]
7	4-Cl	H	 **4g**	86(50)/90(45)	114.2-114.9 (114-115) [26]

8	4-OCH$_3$	H	 **4h**	83(45)/85(40)	143-145.5 (142-143) [26]
9	4-CH$_3$	H	 **4i**	80(45)/85(45)	133-134.5 (134-135) [26]
10	4-CH$_3$	4-CH$_3$	 **4j**	89(55)/92(45)	137-138.9 (135-136) [26]
11	4-Cl	4-Cl	 **4k**	84(45)/88(45)	120.2-122.7 (118-119) [26]
12	4-Cl	4-NO$_2$	 **4l**	83(55)/87(50)	149.5-151.3 (149-150) [26]
13	3-Br	4-CH$_3$	 **4m**	86(50)/92(50)	109-110.5 (107-111) [29]

[a] Using 40 mg of SiO$_2$-TCA (c) and SiO$_2$-TFA (d) catalysts against 1 molar equivalents of arylaldehyde, arylamine and acetophenone in CH$_2$Cl$_2$ at 25 °C.

Table 3.4 Synthesis of β-amino carbonyl compounds **4** under solvent-free condition

Entry	**2**	**3**	Product	Yield %
	R$_1$	R$_2$	**4**	(Time in mins) (c)/(d)^a

1	H	H	**4a**	90(25)/93(20)
2	H	4-CH_3	**4c**	88(25)/92(20)
3	H	4-NO_2	**4d**	85(34)/85(25)
4	4-OCH_3	H	**4h**	86(22)/85(18)
5	4-CH_3	4-CH_3	**4j**	92(27)/96(15)
6	4-Cl	4-Cl	**4k**	84(33)/88(17)
7	4-Cl	4-NO_2	**4l**	84(30)/89(20)

[a] All the reactions were carried out using grinding method utilizing 40 mg of SiO_2-TCA (c) and SiO_2-TFA (d) catalysts against 1 mmol of arylaldehyde, arylamine and acetophenone.

The nature of aryl substituents had no effects on the yield of products irrespective of electron withdrawing or donating groups (**Table 3.3**). The solvent-free method completed the reactions within 15-25 min reaction time (**Table 3.4**).

3.2.3 Leaching test of the catalysts

The stability of both silica-supported catalysts (SiO_2-TCA and SiO_2-TFA) in solution was examined to evaluate if the carboxylic acid from silica support could be leached out by solvent. In a control experiment, the optimized amount of catalyst (40 mg of SiO_2-TCA or SiO_2-TFA) was stirred at room temperature in 3 mL of dichloromethane for 1 h without addition of reactant and then filtered. A mixture of benzaldehyde (1 mmol), aniline (1 mmol) and acetophenone (1 mmol) was added to the filtrate and then it was continued to stir for 75 min. We didn’t observe any product on thin layer chromatographic plate which clearly confirmed the absence of free acidic species in the reaction medium through leaching. Furthermore, the recovered catalyst amounts after work up process were also identical with the initial amounts of catalysts. The isolated catalysts again utilized to complete one cycle of reaction with the optimized amount of substrates for the preparation of **4a** derivative. This evidence showed that no leaching had occur within the reaction time.

3.2.4 Reusability of supported catalysts

The recyclability of the two more acidic catalysts was tested by conducting the already mentioned model reaction with the reactivated catalysts in CH_2Cl_2 for five cycles. The results obtained were depicted in **Table 3.5**.

Table 3.5 Recycling of SiO_2-TCA (c) and SiO_2-TFA (d) catalysts in CH_2Cl_2

Entry	Cycle	Time (min) (c)/(d)	Product (**4a**) Yield (%) (c)/(d)
1	1st	50/45	87/90
2	2nd	50/45	85/87
3	3rd	65/55	83/85
4	4th	65/55	80/83
5	5th	70/60	78/80

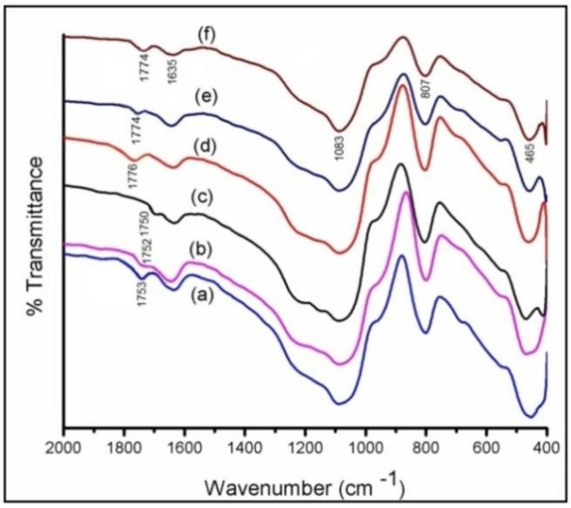
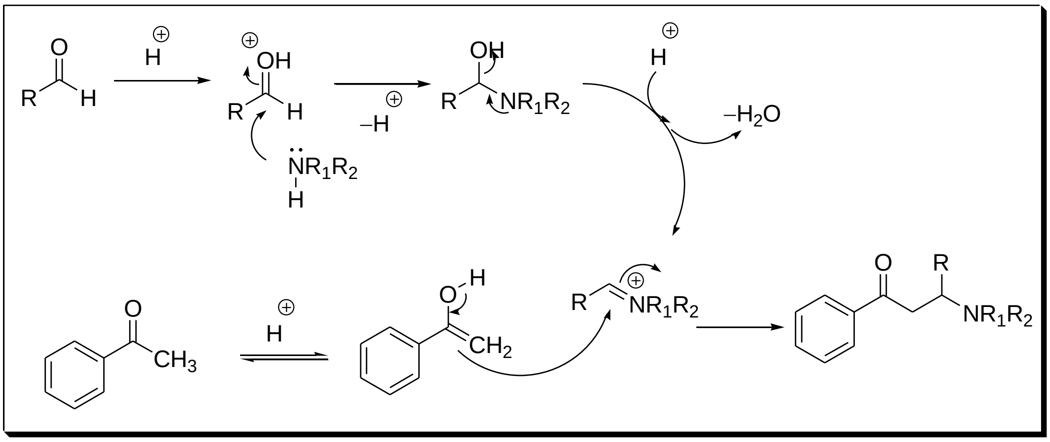


Figure 3.6 FT-IR spectra of SiO_2-TCA (a), SiO_2-TCA 3rd run (b), SiO_2-TCA 5th run (c), SiO_2-TFA (d), SiO_2-TFA 3rd run (e), SiO_2-TFA 5th run (f)

From the results it was clear that the percentage yields of products were similar after subsequent runs and therefore the catalyst can be used up to 5th cycle with small loss of its activity. The reused FT-IR spectra of SiO_2-TCA and SiO_2-TFA (**Figure 3.6**) clearly supported the experimental results of recyclability.

3.2.5 Mechanistic pathway for the synthesis of β-amino carbonyl compounds

The plausible mechanism for the synthesis of β-amino carbonyl compounds catalyzed by silica supported organocatalysts is described in **Scheme 3.2**.



Scheme 3.2 Plausible mechanism for the synthesis of β-amino carbonyl compounds

3.3 Conclusion

In summary, this chapter demonstrates the preparation and characterization of three efficient heterogeneous silica supported organocatalysts from three non-recyclable carboxylic acids. The solid catalysts were characterized in terms of optimization of loading, presence of carboxylic acid, thermal stability, and morphology. The efficiency of the solid catalysts was evaluated for the Mannich-type reactions of acetophenone, aryl amines and aryl aldehydes to β-amino carbonyl compounds in CH_2Cl_2 and solvent-free grinding method at ambient temperature within short time interval which was observed to be several hours in case of many reported methods. The notable advantages of these catalysts are - high catalytic activity at mild condition, simple operation coupled with easy work up procedure, recyclability, and low cost.

3.4 Experimental section

3.4.1 General

Silica (100-200 mesh, neutral) was purchased from Merck. All known β-amino carbonyl compounds **4** were identified by comparison of their melting points, FT-IR, ^{1}H NMR and ^{13}C NMR spectroscopic data with those of authentic compounds (prepared by known method) and literature reported data [26-29]. The detection of fluoride ion was measured on an Orion multiparameter kit (model: 4-Star pH.ISE Benchtop) with a fluoride ion selective electrode.

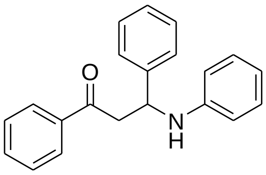
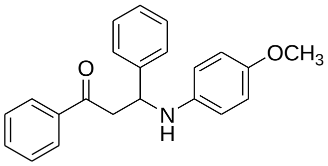
3.4.2 General procedures for the synthesis of silica-supported organocatalysts based on carboxylic acids (SiO_2-TFA, SiO_2-TCA, SiO_2-AA)

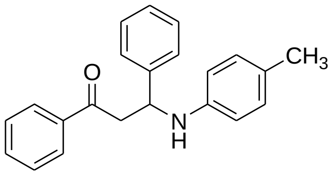
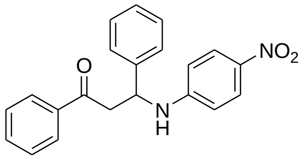
Silica (10 g, 100-200 mesh, neutral) was charged in a 100 mL two necked round bottom flask in anhydrous diethyl ether (50 mL). After that, 4 mmol of the organic acid ($CF_3COOH/CCl_3COOH/CH_3COOH$) was added to the above mixture over a period of 5 min at room temperature. The mixture was stirred for 2 h. Finally, the reaction mixture was filtered and the solid residue was washed with diethylether (2×10 mL), dried at 70 °C for 20 h and silica-supported acid was obtained as a white powder. The loading of acids were observed as 0.365 mmol/g of SiO_2-TFA, 0.357 mmol/g of SiO_2-TCA and 0.343 mmol/g of SiO_2-AA.

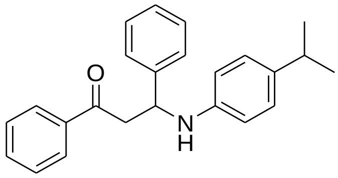
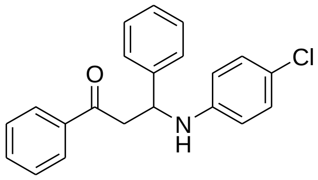
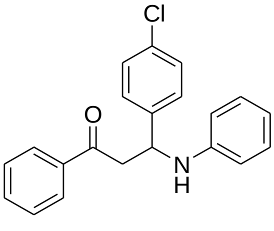
3.4.3 Typical procedure for the synthesis of β-amino carbonyl compound 4

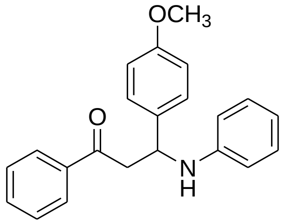
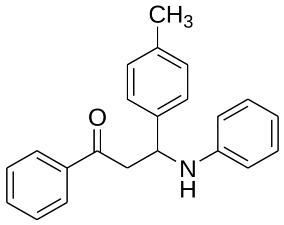
A mixture of arylaldehyde (1 mmol), arylamine (1 mmol) and acetophenone (1 mmol) in dichloromethane (3 mL) was stirred at room temperature (or grinded in mortar with a pestle in absence of solvent) in presence of silica supported organocatalyst (40 mg) for appropriate time. After completion of the reaction, as monitored by TLC, the dichloromethane solution was filtered (or diluted the mixture with 3 mL of CH_2Cl_2 for solvent-free reaction) to separate the solid catalyst from the crude product. The used catalyst was again regenerated after washing with CH_2Cl_2 (3 mL) and dried at 70 °C for 2 h. The filtrate was evaporated under reduced pressure to yield the crude solid product. The product was precipitated in pure state from the solution of hexane (2 mL).

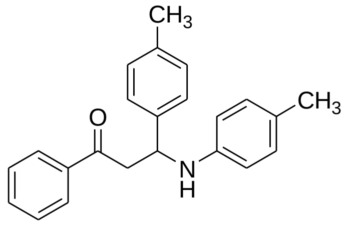
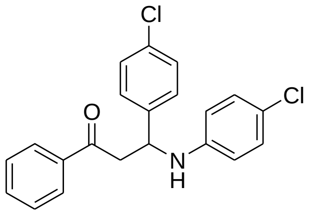
3.5 Spectral and elemental data of synthesized β-amino carbonyl compounds

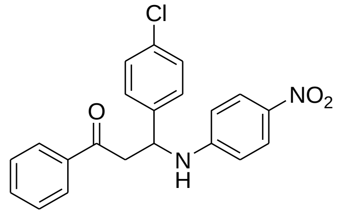
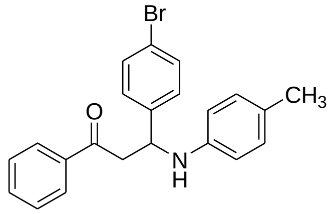
Compound	Spectral Data
 1,3-Diphenyl-3-(phenylamino) propan-1-one **Table-3.4**, entry-1, (**4a**)	White solid, Mp. 168.5-169 °C FT-IR (KBr): 3382, 3020, 2921, 2873, 2372, 1668, 1597, 1506, 1446, 1368, 1291, 1218, 1175, 1072, 993, 858, 746, 689 cm^{-1}; ^1H NMR (400MHz, $CDCl_3$): δ (ppm) = 3.42 (dd, *J* = 7.4, 16Hz, 1H), 3.49 (dd, *J* =5.5, 16Hz, 1H), 5.01 (t, *J* = 5Hz, 1H), 6.57 (d, *J* = 7.8Hz, 2H), 6.66 (t, *J* = 7.4Hz, 1H), 7.07 (t, *J* = 7.8Hz, 2H), 7.19-7.25 (m, 2H), 7.32 (t, *J* = 7.3Hz, 2H), 7.40-7.45 (m, 3H), 7.56 (t, *J* = 7.4Hz, 1H), 7.92 (d, *J* = 7.3Hz, 2H); ^{13}C NMR (100MHz, $CDCl_3$): δ = 46.3, 54.9, 113.9, 117.8, 126.4, 127.4, 128.2, 128.7, 129.1, 133.4, 136.8, 143.0, 147.0, 198.3; Elemental analysis for $C_{21}H_{19}NO$: Cal. C 83.69, H 6.35, N 4.65; Found: C 83.64, H 6.40, N 4.63.
 3-(4-Methoxy phenylamino)-1,3-diphenyl propan-1-one **Table-3.4**, entry-2, (**4b**)	White solid, Mp. 164.5-165.3 °C FT-IR (KBr): 3371, 3062, 2927, 2377, 1665, 1511, 1449, 1406, 1277, 1236, 1096, 1037, 996, 813, $697cm^{-1}$; ^1H NMR (400MHz, $CDCl_3$): δ (ppm) = 3.41 (dd, *J* = 7.8, 16Hz, 1H), 3.47 (dd, *J* = 5, 16Hz, 1H), 3.68 (s, 3H), 4.92 (m, 1H), 6.53 (d, *J* = 6.9Hz, 2H), 6.69 (d, *J* = 6.9Hz, 2H), 7.20-7.24 (m, 3H), 7.34 (t, *J* = 6.9Hz, 2H), 7.46 (t, *J* = 7.8Hz, 2H), 7.57 (t, *J* = 7.8Hz, 1H), 7.92 (d, *J* = 7.3Hz, 2H); ^{13}C

	NMR (100MHz, CDCl$_3$): δ = 46.5, 55.8, 114.8, 115.4, 126.5, 127.4, 128.3, 128.7, 128.9, 133.4, 136.9, 141.3, 143.3, 152.4, 198.5; Elemental analysis for $C_{22}H_{21}NO_2$: Cal. C 79.74, H 6.39 N 4.23; Found: C 79.70, H 6.41, N 4.20
 3-(p-Tolyl amino)-1,3-diphenyl propan-1-one **Table-3.4**, entry-3, (**4c**)	White solid, Mp. 167.5-168.2 °C FT-IR (KBr): 3374, 3015, 2913, 2377, 1667, 1611, 1515, 1447, 1367, 1282, 1212, 1111, 1070, 993, 914, 805, 746, 693 cm^{-1}; ^{1}H NMR (400MHz, CDCl$_3$): δ (ppm) = 2.17 (s, 3H), 3.42 (dd, *J* =7.4, 16Hz, 1H), 3.49 (dd, *J* =5.5, 16Hz, 1H), 5.0 (t, *J* = 5Hz, 1H), 6.48 (d, *J* = 7.8Hz, 2H), 6.88 (d, *J* = 7.8Hz, 2H), 7.19-7.25 (m, 1H), 7.32 (t, *J* = 7.32Hz, 2H), 7.41-7.45 (m, 4H), 7.56 (t, *J* = 7.4Hz, 1H), 7.90 (d, *J* = 7.32Hz, 2H); ^{13}C NMR (100MHz, CDCl$_3$): δ = 20.4, 46.5, 55.2, 114.1, 126.5, 127.1, 127.4, 128.3, 128.9, 129.7, 133.5, 134.0, 141.0, 142.5, 198.4; Elemental analysis for $C_{22}H_{21}NO$: Cal. C 83.78, H 6.71, N 4.44; Found: C 83.75, H 6.74, N 4.42.
 3-[(4-Nitro phenyl)amino]-1,3-diphenyl-1-propanone **Table-3.4**, entry-4, (**4d**)	Yellow solid, Mp. 179.5-181 °C FT-IR (KBr): 3365, 2920, 2855, 1683, 1595, 1520, 1398, 1284, 992, 811, 695 cm^{-1}; ^{1}H NMR (400MHz, CDCl$_3$): δ (ppm) = 3.53 (dd, *J* = 5.1, 16Hz, 1H); 3.61 (dd, *J* = 5, 16.4Hz, 1H), 5.11 (m, 1H), 6.53 (d, *J* = 6.8Hz, 2H), 6.63 (d, *J* = 6.9Hz, 2H), 7.26 (m, 1H), 7.38-7.32 (m,3H), 7.45 (t, *J* = 7.8Hz, 2H), 7.61 (t, *J* = 7.7Hz, 1H), 7.9 (d, *J* = 8.8Hz, 2H), 8.01 (d, *J* = 9.1Hz, 2H); ^{13}C NMR (100MHz, CDCl$_3$): δ = 45.5, 54.4, 112.3, 113.4, 126.4, 127.9, 128.8, 129.2, 129.6, 133.8, 136.8, 137.1, 139.9, 152.4, 197.6; Elemental analysis for $C_{21}H_{18}N_2O_3$: Cal. C 72.82, H 5.24, N 8.09; Found: C 72.75, H 5.28, N 8.05.

 3-(4-Isopropyl phenylamino)-1,3- diphenyl propan-1-one **Table-3.4**, entry-5, (**4e**)	White solid, Mp. 117.5-119.2 °C FT-IR (KBr): 3375, 3032, 2910, 2365, 1665, 1578, 1476, 1356, 1272, 1210, 1062, 990, 810, 767, 656 cm^{-1}; ^{1}H NMR (400MHz, $CDCl_3$): δ (ppm) = 1.16 (d, *J* = 6.9Hz, 6H) 2.76 (d, *J* = 6.9 Hz, 1H), 3.46 (dd, *J* = 7.8, 16Hz, 1H), 3.53 (dd, *J* = 5.52, 16Hz, 1H), 4.96 (t, *J* = 6Hz, 1H), 6.55 (d, *J* = 8.2Hz, 2H), 6.97 (d, *J* = 8.2Hz, 2H), 7.23-7.25 (m, 1H), 7.33 (t, *J* = 7.3Hz, 2H), 7.41-7.46 (m, 4H), 7.55 (t, *J* = 8.3Hz 1H), 7.91 (d, *J* = 8.2Hz, 2H); ^{13}C NMR (100MHz, $CDCl_3$): δ = 24.1, 33.1, 46.2, 55.6, 114.3, 126.6, 127.4, 128.7, 128.8, 133.4, 136.7, 142.1, 144.0, 198.3; Elemental analysis for $C_{24}H_{24}NO$: Cal. C 84.18, H 7.06, N 4.09; Found: C 84.15, H 7.10, N 4.07.
 3-(4-Chloro phenylamino)-1,3-diphenyl propan-1-one **Table-3.4**, entry-6, (**4f**)	White solid, Mp. 167.7-169.4 °C FT-IR (KBr): 3372, 3021, 2914, 2392, 1684, 1563, 1479, 1411, 1270, 1162, 1083, 992, 821, 687 cm^{-1}; ^{1}H NMR (400MHz, $CDCl_3$): δ (ppm) = 3.41 (dd, *J* = 7.4, 16.4Hz, 1H), 3.47 (dd, *J* = 5.1, 16.2Hz, 1H), 4.69 (br, 1H), 5.1 (t, *J* = 5.8Hz, 1H), 6.43 (d, *J* = 8.2Hz, 1H), 6.56 (s, 1H), 6.3 (d, *J* = 7.8Hz, 1H), 6.97 (t, *J* = 8.2Hz, 1H), 7.28 (d, *J* = 7.3Hz, 1H), 7.35 (t, *J*= 7.3Hz, 2H), 7.42-7.48 (m, 4H), 7.59 (t, *J* = 7.3Hz, 1H), 7.84 (d, *J* = 8.3Hz, 2H); ^{13}C NMR (100MHz, $CDCl_3$): δ= 45.6, 54.2, 111.5, 113.1, 117.6, 126.4, 127.5, 128.2, 128.8, 128.9, 130.1, 133.3, 134.7, 136.5, 142.2, 148.1, 197.8; Elemental analysis for $C_{21}H_{18}ClNO$: Cal. C 75.11, H 5.40, N 4.17; Found: C 75.16, H 5.46, N 4.22.
	White solid, Mp. 114.2-114.9 °C FT-IR (KBr): 3398, 3034, 2925, 2378, 1667, 1598, 1499, 1401, 1285, 1216, 1176, 1090, 995, 826, 752, 686 cm^{-1}; ^{1}H NMR (400MHz, $CDCl_3$): δ (ppm) =

3-(4-Chloro phenyl)-1-phenyl-3-(phenylamino) propan-1-one **Table-3.4**, entry-7, (**4g**)	3.42 (dd, J = 7.3, 16Hz, 1H), 3.45 (dd, J = 5.5, 16Hz, 1H), 4.97 (t, J = 5.4Hz, 1H), 6.54 (d, J = 7.8Hz, 2H), 6.69 (t, J = 7.3Hz, 1H), 7.10 (t, J = 8.3Hz, 2H), 7.28 (t, J = 8.3Hz, 2H), 7.38 (d, J = 8.7Hz, 2H), 7.46 (t, J = 7.8Hz, 2H), 7.58 (t, J = 7.3Hz, 1H), 7.89 (d, J = 7.3 Hz, 2H); ^{13}C NMR (100MHz, $CDCl_3$): δ = 46.1, 54.2, 113.9, 118.1, 127.8, 128.2, 128.7, 128.8, 128.9, 129.2, 133..0, 133.6, 136.6, 141.6, 146.7, 197.9; Elemental analysis for $C_{21}H_{18}ClNO$: Cal. C 75.11, H 5.40, N 4.17; Found: C 75.19, H 5.42, N 4.14.
 3-(4-Methoxy phenyl)-1-phenyl-3-(phenylamino) propan-1-one **Table-3.4**, entry-8, (**4h**)	White solid, Mp. 143-145.5 °C FT-IR (KBr): 3374, 2380, 1665, 1602, 1509, 1448, 1369, 1288, 1248, 1174, 1108, 1027, 825, 751, 689 cm^{-1}; ^{1}H NMR (400MHz, $CDCl_3$): δ (ppm) = 3.39 (dd, J = 7.4, 16Hz, 1H), 3.45 (dd, J =5.5, 16Hz, 1H), 3.76 (s, 3H), 4.49 (s, 1H), 4.95 (t, J = 6.4Hz,1H), 6.57 (d, J = 8.2Hz, 2H), 6.67 (t, J = 7.4Hz, 1H), 6.85 (d, J = 6.9Hz, 2H), 7.10 (t, J = 7.3Hz, 2H), 7.35 (d, J = 7.3Hz, 2H),7.45 (t, J = 6.9Hz, 2H), 7.56 (t, J = 7.3Hz, 1H), 7.90 (d, J = 8.2Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 46.4, 54.3, 55.3, 113.9, 114.3, 117.8, 127.5, 128.2, 128.7, 129.2, 133.4, 135.0, 136.9, 147.1, 158.9, 198.5; Elemental analysis for $C_{22}H_{21}NO_2$: Cal. C 79.74, H 6.39, N 4.23; Found: C 79.82, H 6.46, N 4.19.
 1-Phenyl-3-phenyl amino-3-*p*-tolyl-propan-1-one **Table-3.4**, entry-9, (**4i**)	White solid, Mp. 133-134.5 °C FT-IR (KBr): 3372, 2987, 1670, 1525, 1468, 1378, 1248, 1185, 1008, 846, 750, 696 cm^{-1}; ^{1}H NMR (400MHz, $CDCl_3$): δ (ppm) = 2.31 (s, 3H), 3.44 (dd, J = 7.4, 16Hz, 1H), 3.48 (dd, J = 5, 16Hz, 1H), 4.99 (t, J = 5.5Hz, 1H), 6.55 (d, J = 8.2Hz, 2H), 6.66 (t, J = 7.4Hz, 1H),7.08-7.12 (m, 4H), 7.33 (t, J = 8.2Hz, 2H), 7.43 (t, J = 6.9Hz, 2H), 7.55 (d, J = 7.4Hz,1H), 7.91 (d, J = 8.2Hz, 2H); ^{13}C NMR

	(100MHz, $CDCl_3$): δ = 21.2, 46.4, 54.7, 114.0, 117.9, 126.4, 128.3, 128.8, 129.2, 129.6, 133.5, 136.8, 137.1, 139.9, 146.9, 198.4; Elemental analysis for $C_{22}H_{21}NO$: Cal. C 83.78, H 6.71, N 4.44; Found: C 83.87, H 6.79, N 4.51.
 3-(p-Tolyl amino)-1-phenyl-3-p-tolyl propan-1-one **Table-3.4**, entry-10, (**4j**)	White solid, Mp. 137-138.9 °C FT-IR (KBr): 3386, 2920, 2871, 2378, 1671, 1616, 1519, 1446, 1368, 1291, 1215, 1115, 993, 805 cm^{-1}; ^1H NMR (400MHz, $CDCl_3$): δ (ppm) = 2.17 (s, 3H), 2.30 (s, 3H), 3.40 (dd, *J* = 7.3, 16Hz, 1H), 3.47 (dd, *J* =5.5, 16Hz, 1H), 4.94 (t, *J* = 6.4Hz, 1H), 6.50 (d, *J* = 8.7Hz, 2H), 6.89 (d, *J* = 8.2Hz, 2H), 7.12 (d, *J* = 8.2Hz, 2H), 7.30 (d, *J* = 8.3Hz, 2H),7.42 (d, *J* = 7.3Hz, 2H), 7.56 (t, *J* = 7.3Hz, 1H), 7.91 (d, *J* = 7.3Hz, 2H); ^{13}C NMR (100MHz, $CDCl_3$): δ = 20.4, 21.1, 46.4, 55.1, 114.3, 126.4, 128.7, 129.5, 129.7, 133.4, 136.9, 137.0, 140.1, 198.5; Elemental analysis for $C_{23}H_{23}NO$: Cal. C 83.86, H 7.04, N 4.25; Found: C 83.92, H 7.07, N, 4.30.
 3-(4-Chloro phenylamino)-3-(4-chlorophenyl)-1-phenyl propan-1-one **Table-3.4**, entry-11, (**4k**)	White solid, Mp. 119.3-120 °C FT-IR (KBr): 3374, 2978, 1683, 1580, 1515, 1345, 1290, 1085, 990, 857, 780 cm^{-1}; ^1H NMR (400MHz, $CDCl_3$): δ (ppm) = 3.38 (dd, *J* = 7.3, 16Hz, 1H), 3.47 (dd, *J* =5.5, 16Hz, 1H), 4.91 (t, *J*= 5.5Hz, 1H), 6.45 (d, *J* = 6.9Hz, 2H), 7.01 (d, *J* = 8.7Hz, 2H), 7.25-7.29 (m, 2H), 7.35 (d, *J* = 8.7Hz, 2H), 7.44 (t, *J* = 8.2Hz, 2H), 7.55 (t, *J* = 7.3Hz, 1H), 7.89 (d, *J* = 8.2Hz, 2H), 8.04 (d, *J* = 8.7Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$): δ = 46.0, 54.4, 115.1, 122.9, 127.8, 128.2, 128.8, 128.9, 129.0, 129.1, 133.3, 133.7, 136.5, 141.1, 145.4, 197.9; Elemental analysis for $C_{21}H_{17}Cl_2NO$: Cal. C 68.12, H 4.63, N 3.78; Found: C 68.18, H 4.66, N 3.85.

 3-(4-Nitro phenylamino)-3-(4-chlorophenyl)-1 phenyl propan-1-one **Table-3.4**, entry-12, (**4l**)	Yellow solid, Mp. 149.5-151.3 °C FT-IR (KBr): 3359, 3084, 1683, 1584, 1330, 1172, 1093, 842, 757 cm^{-1}; ^1H NMR (400MHz, $CDCl_3$): δ (ppm) = 3.49 (d, *J* = 6.4Hz, 2H), 5.06 (m, 1H), 5.57 (d, *J* = 5.9Hz, 1H), 6.52 (d, *J* = 9.1Hz, 2H), 7.28-7.36 (m, 4H), 7.46 (d, *J* = 8.2Hz, 2H), 7.57 (t, *J* = 7.8Hz, 1H), 7.86 (d, *J* = 7.8Hz,2H), 8.03 (d, *J* = 8.8Hz, 2H); ^{13}C NMR (100MHz, $CDCl_3$): δ = 44.7, 53.8, 113.6, 121.8, 126.7, 128.0, 128.5, 129.4, 129.8, 133.8, 134.4, 136.4, 136.7, 140.5, 152.4, 196.6; Elemental analysis for $C_{21}H_{17}ClN_2O_3$: Cal. C 66.23, H 4.50, N 7.36; Found: C 66.27, H 4.54, N 7.43.
 3-(p-Tolyl amino)-3-(3-bromophenyl)-1-phenyl propan-1-one **Table-3.4**, entry-13, (**4m**)	White solid; Mp. 109-110.5 °C FT-IR (KBr): 3389, 2990, 1696, 1560, 1514, 1225, 1107, 986, 864, 730, 684 cm^{-1}; ^1H NMR (400MHz, $CDCl_3$): δ (ppm) = 2.18 (s, 3H), 3.42 (dd, *J* = 7.8, 16Hz, 1H), 3.46 (dd, *J* = 5.5, 16Hz, 1H), 4.92 (t, *J* = 5.5Hz, 1H), 6.49 (d, *J* = 8.2Hz, 2H), 6.92 (d, *J* = 8.2Hz, 2H), 7.19 (t, *J* = 7.8Hz, 2H), 7.37 (m, 1H), 7.46 (t, *J* = 7.8Hz, 2H), 7.59 (m, 2H), 7.90 (d, *J* = 6.8Hz, 2H); ^{13}C NMR (100MHz, $CDCl_3$): δ = 20.5, 46.2, 55.0, 114.4, 123.0, 125.3, 128.2, 128.8, 129.8, 130.5, 133.6, 144.1, 145.6, 197.8; Elemental analysis for $C_{22}H_{20}BrNO$: Cal. C 67.02, H 5.11, N 3.55; Found: C 67.12, H 5.16, N 3.64.

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