Brønsted Acid-Catalyzed Mannich-Type Reactions in Aqueous Media

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Abstract: HBF_4-catalyzed Mannich-type reaction of silyl enolates with aldimines took place smoothly in aqueous organic solvent to afford β-aminocarbonyl compounds in high yields. The HBF_4-catalyzed Mannich-type reaction also proceeded smoothly in water without organic solvent in the presence of a surfactant. A three-component synthesis starting from aldehyde, amine, and silyl enolate was successfully realized by means of a Brønsted acid in aqueous media.

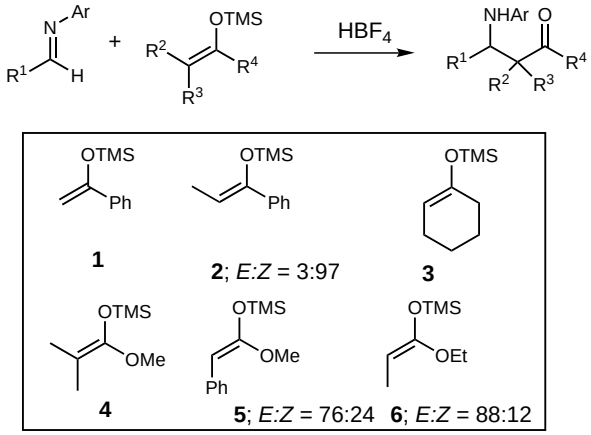
Keywords: aldimine; Brønsted acid; Mannich-type reaction; water as solvent

Introduction

Most Lewis acid-mediated organic reactions have been carried out in organic solvents under strictly anhydrous conditions. In particular, CH_2Cl_2 is the solvent of choice for Lewis acid-catalyzed carbon-carbon bond forming reactions. Because organic compounds are generally harmful to the environment as well as to human beings, it is desirable to reduce the amount of organic solvents employed in synthetic organic reactions. Development of environmentally benign solvents is thus desirable and various kinds of alternative solvents such as $scCO_2$,[1] fluorous media,[2] ionic liquid,[3] and water have been explored. Solvent-free reactions have been also studied.[4] Not only because water is one of the most abundant, cheapest, and environmentally friendly solvents, but also because water exhibits a unique character different from organic solvents, organic reactions in water or aqueous media have attracted much attention of synthetic organic chemists.[5]

The Mannich-type reaction of a silyl enolate with an aldimine constitutes a significant reaction for the preparation of β-aminocarbonyl compounds, which are important intermediates for the synthesis of biologically active nitrogen-containing compounds[6]. Numerous kinds of catalysts have been developed to promote Mannich-type reactions.[7,8,9] Although the original Mannich reaction does not necessarily require anhydrous conditions,[10] most of the Lewis acid-catalyzed Mannich-type reactions are expected to be run under strictly anhydrous conditions. Although water-tolerant Lewis acids such as lanthanide triflate[11] and indium(III) chloride[12] have been developed recently and their potential uses as catalysts in Mannich-type reactions have been studied, there is quite a number of reports on the Mannich-type reaction in aqueous media.[12,13]

As part of our continued interest in reactions leading towards carbon-nitrogen double bonds,[14] we initiated the program to develop Mannich-type reactions in aqueous media. Conventional Lewis acids, such as $TiCl_4$, $SnCl_4$, and $AlCl_3$, are not compatible with aqueous media, and hence, we imagined that a Brønsted acid would be a logical candidate as an activator in aqueous media.[15,16] We report herein that HBF_4 is a quite effective promoter for the Mannich-type reaction of silyl enolates with aldimines, derived from anilines, in aqueous media.[17,18,19] Furthermore, the Brønsted acid-catalyzed Mannich-type reaction proceeded smoothly in water in the presence of a surfactant but free from organic solvents to afford the corresponding β-aminocarbonyl compounds in high yields (Scheme 1). A three-



Scheme 1.

component synthesis starting from aldehyde, amine, and silyl enolate also proceeded successfully.

Results and Discussion

Mannich-Type Reactions in Aqueous Organic Solvent

At the outset, benzylideneaniline and 1-phenyl-1-trimethylsiloxyethene (**1**) (1.5 equiv.) were treated with 0.1 equiv. of Brønsted acid in methanol and the results are shown in Table 1. Aqueous Brønsted acids were diluted with H_2O so that the solvent system consists of methanol:water = 30:1, v/v. It was found that simple addition of diluted aqueous HBF_4 (10 mol %) to the solution of an aldimine and **1** in methanol at 0 °C furnished the β-amino ketone **7a** in 97% yield (entry 6). It was found that a catalytic amount of HBF_4 promoted the Mannich-type reaction smoothly. *p*-TsOH, CF_3SO_3H, and HPF_6 turned out to be effective as promoters, but HCl and HF were less effective.

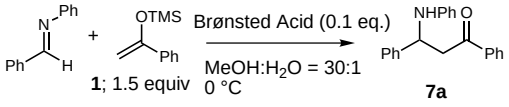
The effect of the solvent was studied and the results are shown in Table 2. Methanol was found to be most effective (entry 1) but polar aprotic solvents such as DMF and CH_3CN also furnished **7a** in good yields. Nonpolar solvents such as toluene was not effective (entry 5). Interestingly, the Mannich-type reaction proceeded smoothly to afford the adduct in high yield even in 20% aqueous methanol, which contains a large amount of water (entry 2). This result encouraged us to investigate the Brønsted acid-catalyzed reaction in water free from organic solvent, which is described later in the article.

We next studied several nucleophiles for the Mannich-type reaction (Table 3). Silyl enol ethers derived from several ketones underwent Mannich-type reactions by means of HBF_4 in aqueous methanol to furnish the corresponding β-aminoketones in high yields. It is noted that ketene silyl acetals, which are considered to be highly sensitive to moisture, also gave the adducts in excellent yields in aqueous isopropyl alcohol at lower temperatures when 3.0 equiv. of the ketene silyl acetals were used (entries 4 – 6). The present Mannich-type reactions showed almost no stereoselectivity (entries 2, 3, 5, and 6).

Next several aldimines were studied and the results are shown in Table 4. Aldimines derived from aliphatic aldehydes, α,β-unsaturated aldehydes, and glyoxylates furnished the adducts in good to excellent yields. An aldimine derived from *p*-methoxybenzaldehyde did not work at all. An aldimine derived from benzylamine did not give a Mannich adduct (entry 9). Use of aldimines bearing *N*-aromatic substituents was found to be requisite to promote the present Mannich-type reactions.

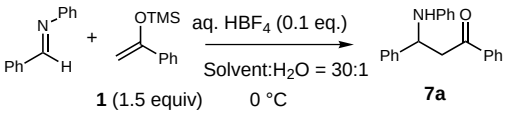
Another characteristic feature of the present addition reaction is high chemoselectivity towards aldimines in preference to aldehydes as shown in Scheme 2. It was found recently that selective activation of imines could be achieved under the influence of lanthanide triflates[20] or transition metal catalysis[21] although conventional Lewis acids activate aldehydes preferentially.[22] Aldehydes did not undergo aldol reaction by means of HBF_4. The high chemoselectivity is rationalized by considering the higher basicity of nitrogen over oxygen.

Table 1. Effects of Brønsted acids.



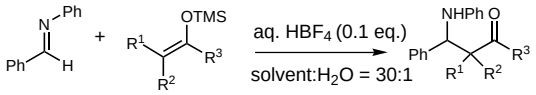
Entry	Brønsted Acid	Time	Yield [%]
1	HCl	2 h	6
2	HF	2 h	9
3	*p*-TsOH	30 min	89
4	CF_3SO_3H	30 min	71
5	HPF_6	2 h	78
6	HBF_4	30 min	97

Table 2. The effects of the solvent.



Entry	Solvent	Time	Yield [%]
1	MeOH	30 min	97
2	MeOH:H_2O = 4:1	2 h	79
3	DMF	2.5 h	82
4	CH_3CN	1.5 h	82
5	Tolune	16 h	3

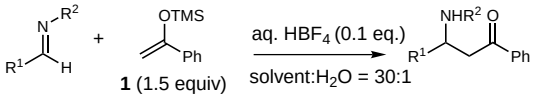
Table 3. Reactions with various silyl enolates.



Entry	Silyl enolate	Solvent	Temp [°C]	Time	Product	Yield [%]	*syn:anti*
1	**1**[a]	MeOH	0	30 min	**7a**	97	-
2	**2**[a]	MeOH	0	3 h	**8a**	83	63:37
3	**3**[a]	MeOH	0	3 h	**9a**	94	50:50
4	**4**[b]	*i*-PrOH	–40	1 h	**10a**	91	-
5	**5**[b]	*i*-PrOH	–40	30 min	**11a**	91	54:46
6	**6**[b]	*i*-PrOH	–20	1.5 h	**12a**	98	54:48

[a] 1.5 equiv. of silyl enol ethers were employed.
[b] 3.0 equiv. of ketene silyl acetals were employed.

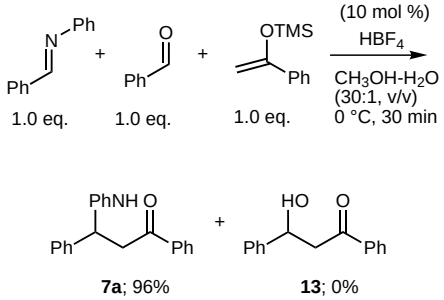
Table 4. Reactions with various aldimines.



1 (1.5 equiv)

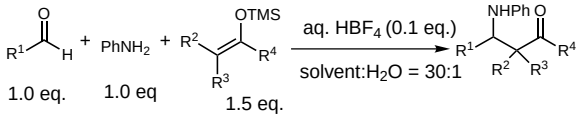
Entry	R^1	R^2	Solvent	Time	Product	Yield [%]
1	Ph	Ph	MeOH	30 min	**7a**	97
2	*p*-$NO_2C_6H_4$	Ph	CH_3CN	1 h	**7b**	89
3	*p*-ClC_6H_4	Ph	MeOH	1 h	**7c**	76
4	*p*-$MeOC_6H_4$	Ph	MeOH	21 h	**7d**	0
5	*p*-MeC_6H_4	Ph	MeOH	30 min	**7e**	85
6	PhCH=CH	Ph	*i*-PrOH	3 h	**7f**	69
7	Ph	*p*-$MeOC_6H_4$	MeOH	1 h	**7g**	88
8	EtOCO	*p*-$MeOC_6H_4$	*i*-PrOH	1 h	**7h**	89
9	Ph	Bn	MeOH	3.5 h	**7i**	0
10	Ph	*p*-$EtOCOC_6H_4$	MeOH	1 h	**7j**	94

Since imines, in particular aliphatic aldimines, are not stable and are difficult to purify, it would be synthetically quite useful if imines, generated *in situ* from aldehyde and amine, would react with silyl enolates to afford β-aminocarbonyl compounds in one vessel. Judging from the high chemoselectivity of the present reaction towards aldimine in preference to aldehyde, we expected that the three-component synthesis of β-aminocarbonyl compounds could be achieved. Results of the one-pot Mannich-type reaction are shown in Table 5. Aliphatic aldimines as well as aromatic aldimines underwent the Mannich-type reaction smoothly to afford the corresponding adducts in good to high yields. It is noted that aldimines were generated quickly even in the presence of water and that silyl enolates were stable enough to react under the present reaction conditions. Phenylglyoxal monohydrate, which possesses water of crystallization, afforded the addition product in 91% yield (entry 5). As the nucleophile, ketene silyl acetals as well as silyl enol ethers were found to be quite effective if the reactions were carried out at lower temperature (entries 10 – 13).



Scheme 2.

Table 5. Results of the three-component syntheses.



Entry	R^1	Silyl enolate[b]	Solvent	Time	Temp [°C]	Product	Yield [%]
1	Ph	**1**	MeOH	1.5 h	0	**7a**	90
2	*p*-$NO_2C_6H_4$	**1**	CH_3CN	2 h	0	**7b**	89
3	*p*-$CH_3C_6H_4$	**1**	MeOH	1.5 h	0	**7d**	84
4	PhCH=CH	**1**	*i*-PrOH	3 h	0	**7f**	69
5	PhCO	**1**	*i*-PrOH	1.5 h	0	**7k**	91
6	EtOCO	**1**	*i*-PrOH	1 h	0	**7l**	55
7	*c*-C_6H_{11}	**1**	CH_3CN	1 h	0	**7m**	79
8	$PhCH_2CH_2$	**1**	*i*-PrOH	6 h	0	**7n**	60
9	$PhCH_2OCH_2$	**1**	*i*-PrOH	2 h	0	**7o**	70
10	Ph	**4**	*i*-PrOH	1 h	–40	**10a**	99
11	*c*-C_6H_{11}	**4**	CH_3CN	1 h	–40	**10b**	89
12	$PhCH_2CH_2$	**4**	*i*-PrOH	1 h	–40	**10c**	80
13	$PhCH_2OCH_2$	**4**	*i*-PrOH	1 h	–40	**10d**	82

[a] 3.0 equiv. of **4** were employed for entries 10 - 13.

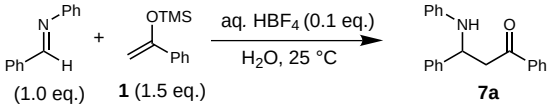
Mannich-Type Reaction in Water in the Presence of a Surfactant

We have found that Brønsted acid-catalyzed Mannich-type reaction took place smoothly in aqueous media. Next, we attempted the Mannich-type reaction in water without an organic solvent. Thus, treatment of *N*-benzylideneaniline and a silyl enol ether (**1**) with 10 mol % HBF_4 in water afforded the corresponding Mannich adduct (**7a**) in less than 5% yield. It is quite reasonable that the organic reaction does not proceed unless substrates are soluble in the solvents. In order to increase the solubility of the substrates in water, several additives were screened and the results are shown in Table 6. Recently, surfactants are being employed to carry out organic reactions in micellar conditions.[23,24] The anionic surfactant SDS (sodium dodecyl sulfate) was found to be quite effective and the adduct was obtained in high yield. A non-ionic surfactant such as Triton X100 is also effective but the cationic surfactant CTAB did not show catalytic activity.

Loading of SDS was studied and the results are shown in Table 7. Although the Mannich-type reaction took place by use of 0.1 equiv. of SDS, use of 0.4 equiv. of SDS gave the best result (entry 3).

The effects of the silyl enolates were studied next and the results are shown in Table 8. Ketene silyl acetals as well as silyl enol ethers were effective as nucleophile in the present Mannich-type reaction and Mannich adducts were obtained in excellent yields. Addition reactions with ketene silyl acetal were faster than those with silyl enol ethers.

Table 6. Effects of additives.



(1.0 eq.) **1** (1.5 eq.) **7a**

Entry	Additive[a]	Time	Yield [%]
1	none	6.5 h	5
2	SDS (0.2 equiv.)	1 h	83
3	TritonX100 (0.2 equiv.)	15 h	68
4	CTAB (0.2 equiv.)	15 h	5
5	DL-Alanine (0.2 equiv.)	1 d	0
6	D-Glucose (0.2 eq.)	1 d	0
7	Starch (70 mg/mL)	1 d	0
8	β-Cyclodextrin (0.2 equiv.)	1 d	0

[a] CTAB = cetyltrimethylammonium bromide;

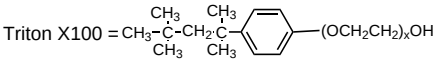
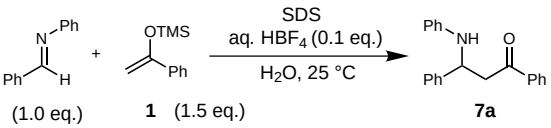


Table 7. Loading of SDS.



(1.0 eq.) **1** (1.5 eq.) **7a**

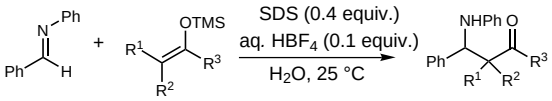
Entry	SDS [equiv.][a]	Time	Yield [%]
1	0.1	30 min	69
2	0.2	1 h	83
3	0.4	1.5 h	90
4	1.0	2 h	88
5	2.0	1.5 h	66

[a] Based on imine.

The Brønsted acid-catalyzed Mannich-type reactions in water were surveyed with several aldimines and the results are shown in Table 9.

Three-component syntheses starting from aldehyde, amine, and silyl enolates were examined in water in the presence of SDS and the results are shown in Table 10. Not only aromatic aldehydes but also aliphatic aldehydes underwent the Mannich-type reaction to afford the corresponding β-aminocarbonyl compounds in good to high yields. Chloral and formaldehyde, which are commercially available as aqueous solutions, also underwent Mannich-type reactions smoothly. Ketene silyl acetals gave the corresponding adducts in higher yields at 0 °C than at 25 °C, probably because the stability of ketene silyl acetals is higher at lower temperatures. Interestingly, initial formation of aldimine before addition of silyl enolate is not required and simple addition of aldehyde, amine, and silyl enolate at the same time led

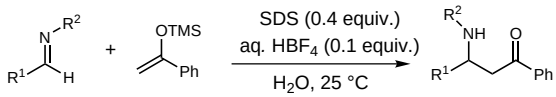
Table 8. Reaction with various silyl enolates.



Entry	Silyl enolate	Time	Product	Yield [%]	*syn:anti*
1	**1**[a]	1.5 h	**7a**	90	-
2	**2**[a]	18 h	**8a**	90	37:63
3	**3**[a]	2 h	**9a**	85	44:56
4	**4**[b]	1 h	**10a**	83	-
5	**5**[b]	1 h	**11a**	92	14:86
6	**6**[b]	1 h	**12a**	89	74:26

[a] 1.5 equiv. of silyl enol ethers were employed.
[b] 3.0 equiv. of ketene silyl ethers were employed.

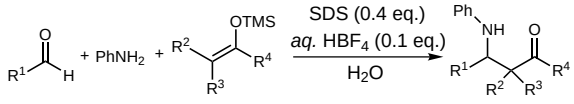
Table 9. Reaction with various imines in water.



(1.0 equiv.) **1** (1.5 equiv.)

Entry	R^1	R^2	Time	Product	Yield [%]
1	*p*-$NO_2C_6H_4$	Ph	2 h	**7b**	75
2	Ph	*p*-$MeOC_6H_4$	1 h	**7g**	79
3	EtOCO	*p*-$MeOC_6H_4$	1 h	**7h**	67

Table 10. Three-component syntheses in water.



(1.0 eq.) (1.0 eq.) (1.5 eq.)

Entry	R^1	Nucleophile	Time	Temp. [°C]	Product	Yield [%]
1	PhCO	**1**	1.5 h	25	**7k**	92
2	*c*-C_6H_{11}	**1**	30 min	25	**7m**	59
3	$BnOCH_2$	**1**	30 min	25	**7o**	54
4	2-Furyl	**1**	30 min	25	**7p**	70
5	2-Thienyl	**1**	3.5 h	25	**7q**	50
6	H	**1**	30 min	25	**7r**	84
7[a]	Ph	**4**	30 min	0	**10a**	89
8[a]	*c*-C_6H_{11}	**4**	1 h	0	**10b**	65
9[a]	$PhCH_2CH_2$	**4**	30 min	0	**10c**	70
10[a]	PhCH=CH	**4**	30 min	0	**10e**	79
11[a]	PhCO	**4**	30 min	25	**10f**	98
12[a]	2-Furyl	**4**	30 min	0	**10g**	85
13[a]	2-Thienyl	**4**	1 h	0	**10h**	91
14[a]	H	**4**	30 min	0	**10i**	75
15[a]	$ClCH_2$	**4**	30 min	0	**10j**	75

[a] 3.0 equiv. of silyl enolate were used for entries 7 –15.

to the smooth formation of the aldimine in water and subsequent addition of silyl enolate resulted in the exclusive formation of the β-aminocarbonyl compounds.[24] Aldol adducts were not observed at all under the reaction conditions.

Conclusion

We have developed Brønsted acid-catalyzed Mannich-type reactions leading to β-aminocarbonyl compounds in aqueous media. Salient features of the present protocols are, 1) aqueous HBF_4 could be used as a catalyst, 2) aldimine may be formed *in situ* in the presence of water, 3) aldimine derived from aliphatic aldehyde worked pretty well, 4) thus, the operation is very simple, 5) use of halogenated solvent is avoided and thus environmentally-conscious.

Experimental Section

General Remarks

^1H (400 MHz) and ^{13}C (125 MHz) NMR spectra were recorded on a Varian Inova 400 spectrometer in $CDCl_3$. Tetramethylsilane (TMS) served as internal standard ($\delta = 0$) for ^1H NMR, and $CDCl_3$ was used as internal standard ($\delta = 77.0$) for ^{13}C NMR. IR spectra were recorded on a Shimadzu FT-IR 8600 spectrometer. Mass spectra were measured by GCMS-QP-5000 (Shimadzu). Purification of the products was performed by column chromatography on silica gel (Fuji sylisia D60L) or preparative TLC on silica gel (Wako gel B-5F). All solvents were purified according to the standard procedures.

Typical Procedure for the Mannich-Type Reaction in Aqueous Organic Solvent for the Preparation of 10a (Table 3, entry 4)

To a solution of *N*-benzylideneaniline (30.6 mg, 0.169 mmol) and the ketene silyl acetal **4** (100 μL, 0.492 mmol) in *i*-PrOH (1.0 mL) was added 4.3% aqueous HBF_4 solution (34.0 μL, 0.0167 mmol) at –40 °C. After being stirred at the temperature for 1 h, the mixture was warmed to 0 °C and was quenched by addition of H_2O. The mixture was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated to dryness. The remaining solid was purified by TLC (SiO_2, hexane:ethyl acetate = 5:1, v/v) to give **10a**; yield: 43.6 mg (0.153 mmol, 91%).

General Procedure for the Mannich-Type Reaction in Water in the Presence of a Surfactant for the Preparation of 10a (Table 8, entry 4)

To a solution of SDS (19.9 mg, 0.069 mmol) in H_2O (1.0 mL) were successively added benzylideneaniline (30.1 mg, 0.166 mmol), the ketene silyl acetal **4** (100 μL, 0.492 mmol), and 4.3 w t% aqueous HBF_4 solution (34.0 μL, 0.0167 mmol) at 0 °C. After being stirred at that temperature for 30 min, Dowex 1-X8 (100 – 200 mesh, Cl^- form) and H_2O were added to quench the reaction, and the reaction mixture was further stirred at that temperature for 10 min. The mixture was extracted with CH_2Cl_2 and the combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated to dryness. The remaining solid was purified by TLC (hexane:ethyl acetate = 5:1, $R_f = 0.3$) to afford the adduct (**10a**); yield 39.0 mg (0.138 mmol, 83%).

Procedure for the Three-Component Synthesis in Water of 10a (Table 10, entry 7)

To a solution of SDS (21.9 mg, 0.0759 mmol) in H_2O (1.0 mL) were successively added aniline (16.0 μL, 0.176 mmol), benzaldehyde (16.0 μL, 0.167 mmol), 1-methoxy-1-trimethylsiloxy-2-methylpropene (0.10 mL, 0.492 mmol), and 4.3 wt % aqueous HBF_4 solution (34.0 μL, 0.0167 mmol) at 0 °C. After being stirred at that temperature for 30 min, Dowex 1-X8 (100 – 200 mesh, Cl^- form) and H_2O were added to quench the reaction, and the reaction mixture was further stirred at the same temperature for 10 min. The mixture was extracted with CH_2Cl_2 and the combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated to dryness. The remaining solid was washed with MeOH to furnish an amino ester as crystals. The MeOH solution was concentrated and purified by preparative TLC (hexane:ethyl acetate = 5:1, $R_f = 0.3$) to afford the second crop; combined yield of the adduct **10a**: 42.1 mg (0.149 mmol, 89%).

1,3-Diphenyl-3-(*N*-phenylamino)propanone (7a)[12]

^1H NMR ($CDCl_3$): $\delta = 7.90$ (d, 2H, $J = 7.1$ Hz), 7.55 (dd, 1H, $J = 7.3$, 7.3 Hz), 7.45 – 7.42 (m, 2H), 7.31 (dd, 2H, $J = 7.9$, 7.9 Hz), 7.22 (dd, 1H, $J = 7.3$, 7.3 Hz), 7.08 (dd, 2H, $J = 8.6$, 7.5 Hz), 6.65 (dd, 1H, $J = 7.3$, 7.3 Hz), 6.55 (dd, 2H, $J = 8.4$, 0.9 Hz), 4.99 (dd, 1H, $J = 7.6$, 5.2 Hz) , 4.54 (s, 1H), 3.50 (dd, 1H, $J = 16.1$, 5.2 Hz), 3.41 (dd, 1H, $J = 16.1$, 7.6 Hz); ^{13}C NMR ($CDCl_3$): $\delta = 198.18$, 146.95, 142.96, 136.68, 133.40, 129.09, 128.81, 128.68, 128.20, 127.34, 126.35, 117.78, 113.80, 54.80, 46.29.

3-(4-Nitrophenyl)-1-phenyl-3-(*N*-phenylamino)-1-propanone (7b)

Mp 107.0 – 110.0 °C (methanol); IR ($CHCl_3$): $\nu = 3429$, 3017, 1670, 1603, 1522, 1506, 1348, 1229 cm^{-1}; ^1H NMR ($CDCl_3$). $\delta =$ 8.16 (d, 2H, $J = 8.8$ Hz), 7.90 (d, 2H, $J = 8.8$ Hz), 7.65 - 7.43 (m, 5H), 7.10 (dd, 2H, $J = 7.7$, 7.3 Hz), 6.70 (dd, 1H, $J = 7.3$, 7.3 Hz), 6.52 (dd, 2H, $J = 7.7$, 0.9 Hz), 5.10 (t, 1H, $J = 6.2$ Hz), 4.67 (s, 1H), 3.51 (d, 2H, $J = 6.0$ Hz); ^{13}C NMR ($CDCl_3$): $\delta = 197.17$, 150.70, 147.16, 146.23, 141.48, 136.25, 133.78, 129.23, 128.80, 128.10, 127.41, 124.05, 118.44, 113.79, 54.13, 45.63; MS (EI): $m/z = 346$ (M^+, 15), 227 (50), 105 (67), 93 (42), 77 (100); Anal. found: C 72.94, H 5.40 N 7.86%; calcd. for $C_{21}H_{18}N_2O_3$: C 72.81, H 5.24, N 8.09%.

3-(4-Chlorophenyl)-1-phenyl-3-(*N*-phenylamino)-1-propanone (7c)

Mp 118.0 – 119.0 °C (methanol); IR ($CHCl_3$): ν = 3420, 3007, 1684, 1603, 1506, 1315, 1285, 1094 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 7.89 (d, 2H, *J* = 8.0 Hz), 7.56 (dd, 1H, *J* = 8.0, 8.0 Hz), 7.44 (dd, 2H, *J* = 8.0, 8.0 Hz), 7.38 (d, 2H, *J* = 8.6 Hz), 7.28 (d, 2H, *J* = 8.6 Hz), 7.08 (dd, 2H, *J* = 8.5, 7.3 Hz), 6.67 (dd, 1H, *J* = 7.3, 7.3 Hz), 6.53 (dd, 2H, *J* = 8.5, 1.1 Hz), 4.97 (dd, 1H, *J* = 7.1, 5.6 Hz), 4.56 (s, 1H), 3.47 (dd, 1H, *J* = 16.2, 5.6 Hz), 3.40 (dd, 1H, *J* = 16.2, 7.1 Hz); ^{13}C NMR ($CDCl_3$): δ = 197.84, 146.66, 141.48, 136.51, 133.54, 132.94, 129.13, 128.94, 128.73, 128.15, 127.76, 118.03, 113.82, 54.13, 46.07; MS (EI): *m/z* = 335 (M^+, 3), 216 (32), 105 (42), 77 (100); Anal. found: C 75.07, H 5.58, N 4.19%: calcd. for $C_{21}H_{18}NOCl$: C 75.11, H 5.40, N 4.17%.

3-(4-Methylphenyl)-1-phenyl-3-(*N*-phenylamino)-1-propanone (7e)

Mp 131.0 – 132.0 °C (methanol); IR ($CHCl_3$): ν = 3420, 3013, 2926, 1684, 1603, 1504, 1317 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 7.90 (d, 2H, *J* = 7.3 Hz), 7.55 (dddd, 1H, *J* = 7.3, 7.3, 1.3, 1.3 Hz), 7.43 (dd, 2H, *J* = 7.3, 7.3 Hz), 7.32 (d, 2H, *J* = 7.9 Hz), 7.12 (d, 2H, *J* = 7.9 Hz), 7.08 (dd, 2H, *J* = 7.3, 7.3 Hz), 6.65 (dd, 1H, *J* = 7.3, 7.3 Hz), 6.55 (dd, 2H, *J* = 8.8, 0.9 Hz), 4.97 (dd, 1H, *J* = 7.5, 5.3 Hz), 4.50 (s, 1H), 3.40 (dd, 1H, *J* = 16.1, 5.3 Hz), 3.48 (dd, 1H, *J* = 16.1, 7.5 Hz), 2.30 (s, 3H); ^{13}C NMR ($CDCl_3$): δ = 198.28, 147.02, 139.92, 136.92, 136.69, 133.35, 129.48, 129.07, 128.66, 128.19, 126.24, 117.68, 113.77, 54.48, 46.33, 21.06.; MS (EI): *m/z* = 315 (M^+, 6), 195 (46), 194 (43), 105 (56), 91 (19), 77 (100); Anal. found: C 83.76, H 6.88, N 4.47%; calcd. for $C_{22}H_{21}NO$: C 83.78, H, 6.71, N 4.46%.

1,5-Diphenyl-3-(*N*-phenylamino)-4-penten-1-one (7f)

Mp 117.0 – 118.0 °C (methanol); IR ($CHCl_3$): ν = 3423, 3011, 1684, 1601, 1506, 1223, 1204 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 7.95 (d, 2H, *J* = 7.5 Hz), 7.57 (dd, 1H, *J* = 7.5, 7.5 Hz), 7.46 (dd, 2H, *J* = 7.5, 7.5 Hz), 7.32 – 7.26 (m, 4H), 7.19 (dd, 1H, *J* = 6.2, 6.2 Hz), 7.15 (dd, 2H, *J* = 7.1, 7.1 Hz), 6.70 (dd, 1H, *J* = 7.1, 7.1 Hz), 6.69 (d, 2H, *J* = 7.1 Hz), 6.64 (d, 1H, *J* = 16.1 Hz), 6.32 (dd, 1H, *J* = 16.1, 6.2 Hz), 4.69 (d, 1H, *J* = 5.9 Hz), 4.27 (s, 1H), 3.39 (d, 2H, *J* = 5.9 Hz). ^{13}C NMR ($CDCl_3$): δ = 198.28, 146.90, 136.86, 136.61, 133.39, 130.71, 130.51, 129.24, 128.70, 128.47, 128.14, 127.53, 126.41, 117.90, 113.87, 52.20, 43.88; MS (EI): *m/z* = 327(M^+, 5), 206 (89), 105 (62), 77 (100); Anal. found: C 84.38, H 6.64, N 4.32%; calcd. for $C_{23}H_{21}NO$: C 84.36, H 6.46, N 4.28%.

3-[*N*-(4-Methoxyphenylamino)]-1,3-diphenyl-1-propanone (7g)

Mp 143.0 – 144.0 °C (methanol); IR ($CHCl_3$): ν = 3429, 3011, 2835, 1684, 1512, 1238, 1205 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 7.90 (dd, 2H, *J* = 7.6, 1.5 Hz), 7.55 (dddd, 1H, *J* = 7.6, 7.6, 1.3, 1.3 Hz), 7.44 (dd, 2H, *J* = 6.2, 6.2 Hz), 7.43 (d, 2H, J = 5.7 Hz), 7.32 (dd, 2H, J = 7.3, 7.3 Hz), 7.23 (dddd, 1H, *J* = 7.3, 7.3, 1.3, 1.3 Hz), 6.68 (dt, 2H, *J* = 9.0, 3.5 Hz), 6.52 (dt, 2H, *J* = 9.0, 2.4 Hz), 4.92 (dd, 1H, *J* = 7.7, 5.0 Hz), 4.29 (s, 1H), 3.68 (s, 3H), 3.48 (dd, 1H, *J* = 16.2, 5.0 Hz), 3.40 (dd, 1H, *J* = 16.2, 7.7 Hz); ^{13}C NMR ($CDCl_3$): δ = 198.32, 152.31, 143.21, 141.16, 136.71, 133.35, 128.77, 128.65, 128.17, 127.28, 126.40, 115.33, 114.67, 55.68, 46.43; MS (EI): *m/z* = 331 (M^+, 7), 212 (47), 211 (56), 196 (77), 167 (24), 105 (69), 77 (100); Anal. found: C 79.74, H 6.66, N 4.28%; calcd. for $C_{22}H_{21}NO_2$: C 79.73, H 6.39, N 4.24%.

Ethyl 2-[*N*-(4-Methoxyphenylamino)]-4-oxo-4-phenylbutanoate (7h)

IR ($CHCl_3$): ν = 3393, 2999, 2937, 1734, 1712, 1686, 1514, 1448, 1367, 1281, 1244, 1180 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 7.94 (dd, 2H, *J* = 7.3, 1.3 Hz), 7.57 (dddd, 1H, *J* = 7.3, 7.3, 1.3, 1.3 Hz), 7.46 (dd, 2H, *J* = 7.3, 7.3 Hz), 6.77 (dt, 2H, *J* = 9.0, 2.4 Hz), 6.68 (dt, 2H, *J* = 9.0, 2.4 Hz), 4.53 (t, 1H, *J* = 4.8 Hz), 4.25 – 4.20 (m, 1H), 4.17 (q, 2H, *J* = 7.1 Hz), 3.73 (s, 3H), 3.53 (d, 2H, *J* = 5.5 Hz), 1.20 (t, 3H, J = 7.1 Hz); ^{13}C NMR ($CDCl_3$): δ 0 198.74, 174.56, 154.37, 141.96, 137.88, 134.87, 130.07, 129.52, 117.10, 116.22, 62.82, 57.06, 55.86, 42.47, 15.18; MS (EI): *m/z* = 327(M^+, 10), 254 (24), 134 (15), 105 (100), 77 (34); Anal. found: C 69.76, H 6.73, N 4.51%; calcd. for $C_{19}H_{21}NO_4$: C 69.69, H 6.46, N 4.28%.

3-[*N*-(4-Ethoxycarbonylamino)]-1,3-diphenyl-1-propanone (7j)

IR ($CHCl_3$): ν = 3422, 3030, 3011, 2984, 1690, 1609, 1522, 1279, 1177, 1109 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 7.88 (d, 2H, *J* = 7.6 Hz), 7.78 (d, 2H, *J* = 8.8 Hz), 7.56 (dd, 1H, *J* = 7.6 Hz), 7.43 (dd, 2H, *J* = 7.6, 7.6 Hz), 7.40 (d, 2H, *J* = 7.2 Hz), 7.31 (dd, 2H, *J* = 7.2, 7.2 Hz), 7.23 (dd, 1H, *J* = 7.2, 7.2 Hz), 6.52 (d, 2H, *J* = 8.8 Hz), 5.12 (s, 1H), 5.07 (dd, 1H, *J* = 6.0, 6.0 Hz), 4.26 (q, 2H, *J* = 7.1 Hz), 3.52 (dd, 1H, *J* = 16.4, 4.9 Hz), 3.46 (dd, 1H, *J* = 16.4, 7.1 Hz), 1.31 (t, 3H, *J* = 7.1 Hz); ^{13}C NMR ($CDCl_3$): δ = 197.93, 166.69, 150.59, 141.95, 136.48, 133.55, 131.29, 128.91, 128.71, 128.15, 127.57, 126.21, 119.19, 112.50, 60.12, 54.18, 45.81, 14.40; MS (EI): *m/z* = 373 (M^+, 9), 254 (100), 208 (48), 120 (30), 105 (78), 77 (78).

1,4-Diphenyl-2-(*N*-phenylamino)-1,4-butanedione (7k)

Mp 133.0 – 134.0 °C (methanol); IR ($CHCl_3$): ν = 3396, 3034, 1684, 1603, 1506 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 7.99 (d, 2H, *J* = 7.7 Hz), 7.85 (d, 2H, *J* = 7.7 Hz), 7.48 (dd, 1H, *J* = 7.7 Hz), 7.40 (dd, 2H, *J* = 7.7 Hz), 7.36 (dd, 2H, *J* = 7.5, 7.5 Hz), 7.12 (dd, 2H, *J* = 8.6, 7.3 Hz), 6.67 – 6.72 (m, 3H), 5.65 (dd, 1H, *J* = 6.3, 5.3 Hz), 4.36 (s, 1H), 3.52 (dd, 1H, *J* = 17.2, 6.3 Hz), 3.40 (dd, 1H, *J* = 17.2, 5.3 Hz); ^{13}C NMR ($CDCl_3$): δ = 198.96, 197.80, 146.20, 136.48, 135.00, 133.61, 129.52, 128.79, 128.63, 128.18, 118.76, 114.00, 54.31, 40.92; MS (EI): *m/z* = 329 (M^+, 1), 224 (23), 105 (100), 77 (62); Anal. found: C 79.76, H 5.82, N 4.31%; calcd. for $C_{22}H_{18}NO_2$: C 80.20, H 6.46, N 4.28%.

Ethyl 2-(*N*-Phenylamino)-4-oxo-4-phenylbutanoate (7l)

IR ($CHCl_3$): ν = 3420, 3030, 3011, 2986, 2930, 1734, 1686, 1603, 1508, 1369, 1283, 1182 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 7.94 (d, 2H, *J* = 7.3 Hz), 7.57 (dddd, 1H, *J* = 7.3, 7.3, 1.3, 1.3 Hz), 7.46 (dd,

2H, $J = 7.3, 7.3$ Hz), 7.18 (dd, 2H, $J = 8.0, 7.3$ Hz), 6.75 (dd, 1H, $J = 7.3, 7.3$ Hz), 6.69 (d, 2H, J = 8.0 Hz), 4.64 – 4.60 (m, 1H), 4.60 – 4.48 (m, 1H), 4.19 (q, 2H, $J = 7.1$ Hz), 3.58 (dd, 1H, $J =$ 17.2, 2.2 Hz), 3.54 (d, 1H, $J = 17.2$, 2.2 Hz), 1.20 (t, 3H, $J =$ 7.1 Hz); ^{13}C NMR ($CDCl_3$) $\delta = 197.26$, 172.81, 146.40, 136.42, 133.50, 129.33, 128.67, 128.11, 119.03, 118.52, 114.01, 113.68, 61.52, 52.99, 40.84, 14.06; MS (EI): $m/z = 297$ (M^+, 14), 224 (16), 105 (100), 77 (63); Anal. found: C 72.66, H 6.61, N 4.68%; calcd. for $C_{18}H_{19}NO_3$: C 72.71, H 6.44, N 4.71%.

3-Cyclohexyl-1-phenyl-3-(*N*-phenylamino)-1-propanone (7m)

IR ($CHCl_3$): $\nu = 3429$, 3034, 3011, 2856, 2934, 1697, 1601, 1506 cm^{-1}; ^{1}H NMR ($CDCl_3$): $\delta = 7.91$ (d, 2H, $J = 7.3$ Hz), 7.54 (dd, 1H, $J = 7.3, 7.3$ Hz), 7.43 (dd, 2H, $J = 7.3, 7.3$ Hz), 7.11 (dd, 2H, $J = 8.4$, 7.3 Hz), 6.63 (dd, 1H, $J = 7.3$, 7.3 Hz), 6.59 (d, 2H, $J =$ 8.4 Hz), 3.91 (ddd, 1H, $J = 5.7, 5.7, 5.7$ Hz), 3.83 (br s, 1H), 3.22 (dd, 1H, $J = 16.7, 5.7$ Hz), 3.10 (dd, 1H, $J = 16.7, 5.7$ Hz), 1.98 – 1.90 (m, 1H), 1.78 – 1.62 (m, 5H), 1.27 – 1.13 (m, 5H); ^{13}C NMR ($CDCl_3$): $\delta = 199.43$, 147.63, 137.11, 133.04, 129.26, 128.55, 128.00, 117.00, 113.13, 54.68, 41.99, 40.28, 29.81, 29.41, 26.81, 26.28, 26.26; MS (EI): $m/z = 307$ (M^+, 6), 224 (21), 203 (35), 105 (100), 93 (36), 77 (71); Anal. found: C 82.36, H 8.45, N 4.67%; calcd. for $C_{21}H_{25}NO$: C 82.04, H 8.20, N 4.56%.

1,5-Diphenyl-3-(*N*-phenylamino)-1-pentanone (7n)

IR ($CHCl_3$): $\nu = 3429$, 3032, 3011, 2928, 2858, 1684, 1601, 1506 cm^{-1}; ^{1}H NMR ($CDCl_3$): $\delta = 7.88$ (d, 2H, $J = 7.3$ Hz), 7.55 (dd, 1H, $J = 7.3, 7.3$ Hz), 7.43 (dd, 2H, $J = 7.3, 7.3$ Hz), 7.25 (dd, 2H, $J = 4.7$, 4.7 Hz), 7.19 – 7.12 (m, 5H), 6.69 (dd, 1H, $J = 7.3$, 7.3 Hz), 6.59 (d, 2H, $J = 8.6$ Hz), 4.08 – 3.98 (m, 1H), 3.85 (br s, 1H), 3.24 (dd, 1H, $J = 16.6$, 4.4 Hz), 3.15 (dd, 1H, $J = 16.6$, 6.6 Hz), 2.87 – 2.61 (m, 2H), 2.06 – 1.19 (m, 2H); ^{13}C NMR ($CDCl_3$): $\delta = 199.30$, 147.09, 141.61, 140.19, 137.10, 133.18, 132.05, 129.55, 129.37, 129.10, 128.58, 128.40, 128.37, 128.28, 127.99, 125.88, 117.49, 113.42, 49.63, 42.52, 40.69, 36.82, 32.69, 26.61; MS (EI): $m/z = 329$ (M^+, 11), 224 (19), 210 (30), 105 (100), 91 (65), 77 (76); Anal. found: C 83.68, H 7.06, N 4.25%; calcd. for $C_{23}H_{23}NO$: C 83.86, H 7.04, N 4.25%.

4-Benzyloxy-1-phenyl-3-(*N*-phenylamino)-1-butanone (7o)

IR ($CHCl_3$): $\nu = 3420$, 3032, 3011, 2866, 1668, 1601, 1502, 1364, 1258 cm^{-1}; ^{1}H NMR ($CDCl_3$): $\delta = 7.94$ (d, 2H, $J = 7.7$ Hz), 7.55 (dd, 1H, $J = 7.5$, 7.5 Hz), 7.44 (dd, 2H, $J = 7.7$, 7.5 Hz), 7.29 – 7.24 (m, 5H), 7.16 (dd, 2H, $J = 8.6, 7.3$ Hz), 6.70 (dd, 1H, $J = 7.3$, 7.3 Hz), 6.64 (d, 2H, $J = 8.6$ Hz), 4.50 (Abq, 1H, $J = 12.1$ Hz), 4.48 (Abq, 1H, $J = 12.1$ Hz), 4.30 – 4.20 (m, 2H), 3.69 – 3.65 (m, 2H), 3.40 (dd, 1H, $J = 16.9$, 7.6 Hz), 3.23 (dd, 1H, $J = 16.9$, 4.0 Hz); ^{13}C NMR ($CDCl_3$) $\delta = 199.38$, 146.64, 137.95, 137.10, 133.18, 129.37, 128.56, 128.38, 128.10, 127.71, 127.68, 117.78, 113.64, 73.33, 71.05, 49.63, 39.19; MS (EI): $m/z = 345$ (M^+, 4), 224 (47), 105 (100), 91 (32), 77 (36); Anal. found: C 79.98, H 6.80, N 4.06%; calcd. for $C_{23}H_{23}NO_2$: C 79.97, H 6.71, N 4.05%.

3-(2-Furyl)-1-phenyl-3-(*N*-phenylamino)-1-propanone (7p)

Mp 98.0 – 99.0 °C (ether-hexane); IR ($CHCl_3$): $\nu = 3420$, 3030, 3013, 1686, 1603, 1504, 1362, 1283 cm^{-1}; ^{1}H NMR ($CDCl_3$): $\delta =$ 7.92 (dd, 2H, $J = 7.7, 1.7$ Hz), 7.44 (dd, 1H, $J = 7.7, 7.7$ Hz), 7.30 (dd, 2H, $J = 1.7$, 0.7 Hz), 7.24 (s, 1H), 7.15 (dd, 2H, $J = 8.6$, 7.5 Hz), 6.72 (ddd, 1H, $J = 7.5$, 7.5, 1.0 Hz), 6.68 (dd, 2H, $J = 8.6, 1.0$ Hz), 6.23 (ddd, 2H, $J = 17.9, 2.4, 0.8$ Hz), 5.22 (t, 1H, $J = 6.2$ Hz), 4.38 (s, 1H), 3.56 (d, 2H, $J = 6.2$ Hz); ^{13}C NMR ($CDCl_3$): $\delta = 197.85$, 154.87, 146.57, 141.57, 136.80, 133.29, 129.22, 128.63, 128.02, 118.32, 113.95, 110.35, 106.41, 48.72, 42.34; MS (EI): $m/z = 291$ (M^+, 13), 172 (68), 105 (100), 77 (78); Anal. found: C 78.19, H 5.68, N 4.98%; calcd. for $C_{19}H_{17}NO_2$: C 78.33, H 5.88, N, 4.81%.

1-Phenyl-3-(*N*-phenylamino)-3-(2-thienyl)-1-propanone (7q)

Mp 116.0 – 117.0 °C (ether-hexane); IR ($CHCl_3$): $\nu = 3414$, 3057, 3032, 3011, 1686, 1603, 1504, 1313, 1284 cm^{-1}; ^{1}H NMR ($CDCl_3$): $\delta = 7.93$ (d, 2H, $J = 7.8$ Hz), 7.53 (dd, 1H, $J = 7.8$, 7.8 Hz), 7.46 (dd, 2H, $J = 7.8$, 7.8 Hz), 7.13 – 7.17 (m, 3H), 7.01 (d, 1H, $J = 3.7$ Hz), 6.92 (dd, 1H, $J = 4.6$, 3.7 Hz), 6.73 (dd, 1H, $J = 7.7$, 7.7 Hz), 6.68 (d, 2H, $J = 7.7$ Hz), 5.38 (d, 1H, $J =$ 6.2 Hz), 4.50 (s, 1H), 3.59 (d, 2H, $J = 6.2$ Hz); ^{13}C NMR ($CDCl_3$): $\delta = 197.75$, 147.63, 146.59, 136.73, 133.44, 129.20, 128.68, 128.12, 126.86, 124.13, 123.89, 118.38, 114.04, 50.71, 45.93; MS (EI): $m/z = 307$ (M^+, 11), 188 (43), 105 (100), 93 (22), 77 (85); Anal. found: C 74.06, H 5.48, N 4.71, S 10.26%; calcd. for $C_{19}H_{17}NOS$: C 74.22, H 5.57, N 4.56, S 10.43%.

1-Phenyl-3-(*N*-phenylamino)-1-propanone (7r)

Mp 111.0 – 112.0 °C (ether/hexane); IR ($CHCl_3$): $\nu = 3414$, 3030, 1711, 1603, 1506, 1364, 1232 cm^{-1}; ^{1}H NMR ($CDCl_3$): $\delta =$ 7.94 (d, 2H, $J = 7.3$ Hz), 7.56 (dd, 1H, $J = 7.3, 7.3$ Hz), 7.45 (dd, 2H, $J = 7.3, 7.3$ Hz), 7.17 (dd, 2H, $J = 7.5, 7.3$ Hz), 6.70 (dd, 1H, $J = 7.3, 7.3$ Hz), 6.64 (d, 2H, $J = 7.5$ Hz), 4.10 (br s, 1H), 3.61 (t, 2H, $J = 6.1$ Hz), 3.28 (t, 2H, $J = 6.1$ Hz); ^{13}C NMR($CDCl_3$): $\delta =$ 199.24, 147.68, 136.71, 133.30, 129.30, 128.63, 128.00, 117.50, 113.01, 38.68, 37.64; MS (EI): $m/z = 225$ (M^+, 23), 106 (100), 105 (20), 93 (10), 77 (52); Anal. found: C 79.71, H 7.01, N 6.30%; calcd. for $C_{15}H_{15}NO$: C 79.95, H 6.71, N 6.22%.

2-Methyl-1,3-diphenyl-3-(*N*-phenylamino)-1-propanone (8a)[12]

IR ($CHCl_3$): $\nu = 3413$, 3059, 3011, 2936, 1680, 1603, 1506, 1317, 1225 cm^{-1}; ^{1}H NMR ($CDCl_3$): $\delta = 7.94 – 7.00$ (m, 12H), 6.62 – 6.44 (m, 3H), 5.07 (major, s, 1H), 4.74 (minor, d, 1H, $J =$ 4.9 Hz), 4.71 (major, d, 1H, $J = 5.9$ Hz), 4.46 (minor, s, 1H), 3.97 (minor, dq, 1H, $J = 6.8$, 3.4 Hz), 3.97 (dq, 1H, $J = 5.9$, 3.2 Hz), 1.29 (major, d, 3H, $J = 7.1$ Hz) , 1.22 (minor, d, 3H, $J =$ 7.0 Hz); ^{13}C NMR ($CDCl_3$): $\delta = 204.04$, 202.57, 147.19, 147.13, 141.85, 141.50, 137.14, 136.18, 133.26, 133.10, 129.02, 128.91, 128.76, 128.61, 128.51, 128.25, 128.13, 127.21, 126.80, 126.72, 117.56, 117.18, 113.77, 113.37, 61.09, 59.16, 46.87, 46.44, 16.71, 11.43.

2-(Phenyl-*N*-phenylaminomethyl)-cyclohexanone (9a)[9a]

^{1}H NMR ($CDCl_3$): δ = 7.20 – 7.00 (m, 7H), 6.63 – 6.45 (m, 3H), 4.80 (major, d, 1H, *J* = 4.5 Hz), 4.61 (minor, d, 1H, *J* = 7.0 Hz), 4.84 – 4.42 (br s, 1H), 2.81 – 2.69 (m, 1H), 2.44 – 2.25 (m, 2H), 2.08 – 1.54 (m, 6H); ^{13}C NMR ($CDCl_3$): δ = 212.76, 211.24, 147.43, 147.17, 141.67, 141.50, 129.01, 129.00, 128.43, 128.33, 127.47, 127.21, 127.12, 126.96, 117.64, 117.45, 114.03, 113.55, 57.98, 57.46, 57.21, 56.57, 42.37, 41.73, 31.25, 28.64, 27.86, 26.98, 24.82, 23.62.

Methyl 2,2-Dimethyl-3-phenyl-3-(*N*-phenylamino)propionate (10a)

Mp 121.0 – 122.0 °C (methanol); IR ($CHCl_3$): ν = 3422, 3009, 2980, 2953, 1724, 1603, 1506, 1317, 1252 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 7.35 – 7.20 (m, 5H), 7.03 (dd, 2H, *J* = 7.3, 7.3 Hz), 6.59 (ddd, 1H, *J* = 7.4, 4.4, 1.1 Hz), 6.49 (dd, 2H, *J* = 7.6, 0.9 Hz), 4.79 (s, 1H), 4.49 (s, 1H), 3.65 (s, 3H), 1.27 (s, 3H), 1.16 (s, 3H); ^{13}C NMR ($CDCl_3$): δ = 176.99, 146.90, 139.21, 129.00, 128.26, 127.99, 127.43, 117.27, 113.37, 64.35, 52.07, 46.99, 24.57, 20.71; MS (EI): *m/z* = 283 (M^+, 8), 182 (100), 104 (28), 77 (28); Anal. found: C 76.42, H 7.31, N 4.74%; calcd. for $C_{18}H_{21}NO_2$: C 76.30, H 7.47, N 4.94%.

Methyl 3-Cyclohexyl-2,2-dimethyl-3-(*N*-phenylamino)propionate (10b)

IR ($CHCl_3$): ν = 3427, 3009, 2930, 2855, 1720, 1600, 1510, 1321, 1256, 1140 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 7.12 (dd, 2H, *J* = 7.7, 7.1 Hz), 6.63 (d, 2H, *J* = 7.7 Hz), 6.61 (dd, 1H, *J* = 7.1, 7.1 Hz), 4.04 (d, 1H, *J* = 10.4 Hz), 3.65 (s, 3H), 3.50 (dd, 1H, *J* = 10.4, 4.0 Hz), 1.70 – 1.50 (m, 6H), 1.22 (s, 3H), 1.19 (s, 3H), 1.26 – 1.00 (m, 5H); ^{13}C NMR($CDCl_3$): δ = 178.05, 149.70, 129.24, 116.33, 112.48, 63.96, 51.72, 47.25, 41.35, 32.91, 28.53, 26.75, 26.38, 26.10, 24.28, 22.61; MS (EI): *m/z* = 289 (M^+, 8), 206 (23), 188 (100), 146 (29), 106 (48); Anal. found: C 74.93, H 9.21, N 4.87%; calcd. for $C_{18}H_{27}NO_2$: C 74.69, H 9.40, N 4.84%.

Methyl 2,2-Dimethyl-5-phenyl-3-(*N*-phenylamino)pentanoate (10c)

IR ($CHCl_3$): ν = 3423, 3030, 3011, 2953, 2860, 1724, 1601, 1497, 1317, 1254, 1134 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 7.24 (dd, 2H, *J* = 8.3, 7.0 Hz), 7.18 – 7.07 (m, 5H), 6.64 (dd, 1H, *J* = 7.7, 7.7 Hz), 6.63 (dd, 2H, *J* = 7.7, 7.7 Hz), 3.73 (s, 1H), 3.64 – 3.60 (m, 1H), 3.55 (s, 3H), 2.77 – 2.84 (m, 1H), 2.59 – 2.52 (m, 1H), 1.93 – 1.85 (m, 1H), 1.64 – 1.54 (m, 1H), 1.19 (s, 3H), 1.17 (s, 3H); ^{13}C NMR ($CDCl_3$): δ = 177.35, 149.02, 141.79, 129.22, 128.46, 128.27, 125.82, 116.80, 112.77, 58.95, 51.67, 47.99, 34.92, 33.10, 22.81, 21.84; MS (EI): *m/z* = 311 (M^+, 5), 210 (100), 117 (13), 91 (70), 77 (11); Anal. found: C 77.32, H 8.05, N 4.63%; calcd. for $C_{20}H_{25}NO_2$: C 77.14, H 8.09, N 4.50%.

Methyl 4-Benzyloxy-2,2-dimethyl-3-(*N*-phenylamino)butanoate (10d)

IR ($CHCl_3$): ν = 3420, 3061, 2953, 2868, 1717, 1601. 1499, 1315, 1275, 1119 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 7.32 – 7.22 (m, 5H), 7.15 (dd, 2H, *J* = 8.6, 8.6 Hz), 6.67 (dd, 1H, *J* = 8.6, 8.6 Hz), 6.66 (dd, 2H, *J* = 8.6, 1.0 Hz), 4.42 (s, 2H), 4.14 (d, 1H, *J* = 7.0 Hz), 3.81 (s, 1H), 3.56 (s, 3H), 3.55 (s, 2H), 1.29 (s, 3H), 1.26 (s, 3H); ^{13}C NMR ($CDCl_3$): δ = 177.29, 148.03, 138.01, 129.14, 128.26, 127.59, 127.54, 117.38, 113.47, 73.36, 70.02, 59.33, 51.76, 45.78, 23.27, 22.58; MS (EI): *m/z* = 327 (M^+, 7), 226 (33), 206 (71), 146 (51), 91 (100), 77 (18); Anal. found: C 73.26, H 7.45, N 4.46%; calcd. for $C_{20}H_{25}NO_3$: C 73.37, H 7.70, N, 4.28%.

Methyl 2,2-Dimethyl-5-phenyl-3-(*N*-phenylamino)-4-pentenoate (10e)

IR ($CHCl_3$): ν = 3422, 3011, 2980, 2953, 2876, 1724, 1600, 1502, 1317, 1252, 1142, 968 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 7.33 – 7.17 (m, 4H), 7.13 (dd, 2H, *J* = 7.5, 7.5 Hz), 6.68 – 6.64 (m, 3H), 6.55 (d, 1H, *J* = 15.7 Hz), 6.19 (dd, 1H, *J* = 15.7, 7.2 Hz), 4.19 (s, 1H), 4.14 (d, 1H, *J* = 7.2 Hz), 3.66 (s, 3H), 1.32 (s, 3H), 1.29 (s, 3H); ^{13}C NMR ($CDCl_3$): δ = 176.96, 147.35, 136.67, 132.79, 129.15, 128.46, 127.54, 127.21, 126.43, 117.53, 113.63, 62.50, 51.98, 47.01, 23.51, 21.56. 199.81, 176.61, 147.21, 137.01, 133.40, 129.38, 128.61, 128.36, 118.62, 114.07, 62.78, 51.96, 46.40, 22.72, 22.41; MS (EI): *m/z* = 309 (M^+, 3), 208 (100), 115 (21), 91 (20), 77 (18); Anal. found: C 77.67, H 7.70, N 4.63%; calcd. for $C_{20}H_{23}NO_2$: C 77.62, H 7.49, N 4.53%.

Methyl 2,2-Dimethyl-4-phenyl-3-(*N*-phenylamino)-4-oxobutanoate (10f)

IR ($CHCl_3$): ν = 3385, 3032, 3011, 1722, 1684, 1601, 1497, 1394, 1229 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 7.91 (d, 2H, *J* = 7.4 Hz), 7.54 (dd, 1H, *J* = 7.4, 7.4 Hz), 7.43 (dd, 2H, *J* = 7.4, 7.4 Hz), 7.17 (dd, 2H, *J* = 7.7, 7.3 Hz), 6.79 (d, 2H, *J* = 7.7 Hz), 6.73 (dd, 1H, *J* = 7.3, 7.3 Hz), 5.28 (s, 1H), 4.77 (s, 1H), 3.55 (s, 3H), 1.32 (s, 3H), 1.22 (s, 3H); ^{13}C NMR ($CDCl_3$): δ = 199.81, 176.61, 147.21, 137.01, 133.40, 129.38, 128.61, 128.36, 118.62, 114.07, 62.78, 51.96, 46.40, 22.72, 22.41; MS (EI): *m/z* = 311 (M^+, 3), 206 (100), 146 (93), 104 (29), 77 (70); Anal. found: C 73.47, H 6.55, N 4.48%; calcd. for $C_{19}H_{21}NO_3$: C 73.27, H 6.80, N 4.52%.

Methyl 3-(2-Furyl)-2,2-dimethyl-3-(*N*-phenylamino)propionate (10g)

Mp 103.0 – 104.0 °C (ether-hexane); IR ($CHCl_3$): ν = 3420, 3030, 3011, 2982, 2953, 1728, 1601, 1502, 1317, 1252, 1148 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 7.30 (s, 1H), 7.11 (dd, 2H, *J* = 7.3, 6.6 Hz), 6.68 (dd, 1H, *J* = 7.3, 7.3 Hz), 6.62 (dd, 2H, *J* = 6.6, 0.9 Hz), 6.25 (dd, 1H, *J* = 3.3, 1.8 Hz), 6.14 (d, 1H, *J* = 3.3 Hz), 4.71 (br s, 1H), 4.47 (br s, 1H), 3.67 (s, 3H), 1.27 (s, 3H), 1.26 (s, 3H); ^{13}C NMR ($CDCl_3$): δ = 176.71, 153.39, 147.07, 141.65, 129.08, 118.06, 113.81, 110.09, 107.88, 58.57, 52.04, 47.23, 23.49, 21.18; MS (EI): *m/z* = 273 (M^+, 5), 172 (100), 104 (27), 77 (40); Anal. found: C 70.26, H 6.75, N 5.14%; calcd. for $C_{16}H_{19}NO_3$: C 70.31, H 7.01, N 5.12%.

Methyl 2,2,-Dimethyl-3-(*N*-phenylamino)-3-(2-thienyl)propionate (10h)

Mp 121.0 – 122.0 °C (ether-hexane); IR ($CHCl_3$): ν = 3420, 3009, 1724, 1603, 1506, 1317, 1252, 1144 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 7.15 (dd, 1H, *J* = 4.8, 1.3 Hz), 7.09 (dd, 2H, *J* = 8.4, 7.3 Hz), 6.90 – 6.94 (m, 2H), 6.66 (dd, 1H, *J* = 7.3, 7.3 Hz), 6.59 (dd, 2H, *J* = 8.4, 1.0 Hz), 4.82 (br s, 1H), 4.64 (br s, 1H), 3.68 (s, 3H), 1.33 (s, 3H), 1.27 (s, 3H); ^{13}C NMR ($CDCl_3$): δ = 176.78, 146.80, 144.15, 129.07, 126.39, 125.96, 124.40, 117.92, 113.59, 60.63, 52.15, 47.39, 23.90, 21.45; MS (EI): *m/z* = 289 (M^+, 3), 188 (100), 104 (25), 77 (29); Anal. found: C 66.26, H 6.35, N 4.83, S 10.87%; calcd. for $C_{16}H_{19}NO_2S$: C 66.41, H 6.62, N 4.84, S 11.08%.

Methyl 2,2-Dimethyl-3-(*N*-phenylamino)propionate (10i)

IR ($CHCl_3$): ν = 3422, 3009, 2955, 2847, 1719, 1603, 1508, 1308, 1256, 1151 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 7.15 (dd, 2H, *J* = 7.7, 7.3 Hz), 6.68 (dd, 1H, *J* = 7.3, 7.3 Hz), 6.62 (d, 2H, *J* = 7.7 Hz), 3.92 (s, 1H), 3.67 (s, 3H), 3.23 (s, 2H), 1.27 (s, 6H); ^{13}C NMR ($CDCl_3$): δ = 177.43, 148.44, 129.18, 117.35, 112.89, 52.67, 51.97, 43.63, 23.53; MS (EI): *m/z* = 207 (M^+, 15), 106 (100), 77 (25); Anal. found: C 69.30, H 8.44, N 7.02%; calcd. for $C_{12}H_{17}NO_2$: C 69.54, H 8.27, N 6.76%.

Methyl 2-Chloro-2,2-dimethyl-3-(*N*-phenylamino)propionate (10j)

IR ($CHCl_3$): ν = 3422, 3032, 3011, 2982, 2955, 1724, 1603, 1506, 1310, 1256, 1142 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 7.17 (dd, 2H, *J* = 7.9, 7.1 Hz), 6.71 (dd, 1H, *J* = 7.1, 7.1 Hz), 6.69 (d, 2H, *J* = 7.9 Hz), 4.14 (d, 1H, *J* = 7.5 Hz), 3.85 – 3.88 (m, 1H), 3.76 (dd, 1H, *J* = 11.5, 6.4 Hz), 3.67 (s, 3H), 3.59 (dd, 1H, *J* = 11.5, 6.4 Hz), 1.32 (s, 3H), 1.30 (s, 3H); ^{13}C NMR ($CDCl_3$): δ = 176.61, 147.65, 129.31, 117.93, 113.50, 61.39, 52.11, 46.88, 45.40, 23.26, 23.07; MS (EI): *m/z* = 255 (M^+, 10), 154 (100), 118 (37), 91 (22), 77 (31); Anal. found: C 60.93, H 7.15, N 5.64%; calcd. for $C_{13}H_{18}NO_2Cl$: C 61.05, H 7.09, N 5.48%.

Methyl 2,3-Diphenyl-3-(*N*-phenylamino)propionate (11a)

Mp 165.0 – 167.0 °C (methanol); IR ($CHCl_3$): ν = 3421, 3032, 3009, 1732, 1603, 1506, 1163 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 7.49 – 7.43 (m, 3H), 7.40 – 7.10 (m, 7H), 7.09 – 6.97 (m, 2H), 6.62 – 6.54 (m, 1H), 6.54 (*syn*, dd, 2H, *J* = 8.6, 1.1 Hz), 6.37 (*anti*, dd, 2H, *J* = 8.6, 0.9 Hz), 4.96 (*anti*, d, 1H, *J* = 9.9 Hz), 4.94 (*syn*, d, 2H, *J* = 7.9 Hz), 3.96 (*syn*, d, 1H, *J* = 7.9 Hz), 3.88 (*anti*, d, 1H, *J* = 9.9 Hz), 3.66 (*syn*, s, 3H), 3.46 (*anti*, s, 3H); ^{13}C NMR ($CDCl_3$): δ = 172.79, 171.85, 147.00, 146.63, 144.47, 140.54, 135.49, 129.74, 129.23, 129.04, 128.99, 128.87, 128.83, 128.71, 128.56, 128.40, 127.65, 127.61, 127.23, 126.83, 117.92, 117.72, 113.92, 113.86, 61.08, 60.16, 60.01, 56.56, 52.17, 52.00; MS (EI): *m/z* = 331 (M^+, 2), 182 (100), 104 (20), 91 (36), 77 (52), 51 (30); Anal. found: C 79.55, H 6.62, N 4.30%; calcd. for $C_{22}H_{21}NO_2$: C 79.73, H 6.39, N 4.23%.

Ethyl 2-Methyl-3-phenyl-3-(*N*-phenylamino)propionate (12a)

IR ($CHCl_3$): ν = 3422, 3032, 2982, 2939, 1719, 1603, 1502, 1182 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 6.58 – 6.52 (m, 1H), 6.47 – 6.43 (m, 2H), 4.72 (*anti*, s, 1H), 4.63 (*syn*, d, 1H, *J* = 4.2 Hz), 4.42 (d, 1H, *J* = 7.3 Hz), 3.99 (q, 2H, *J* = 7.2 Hz), 2.86 (*syn*, dq, 1H, *J* = 7.1, 5.4 Hz), 2.76 (*anti*, dq, 1H, *J* = 7.1, 7.1 Hz), 1.10 (*syn*, d, 3H, *J* = 7.0 Hz), 1.08 (*anti*, d, 3H, *J* = 7.1 Hz), 1.06 (td, 3H, *J* = 7.2, 1.5 Hz); ^{13}C NMR ($CDCl_3$): δ = 174.94, 174.10, 147.01, 146.89, 141.23, 140.65, 129.02, 128.50, 128.42, 127.35, 127.27, 126.89, 126.80, 117.53, 117.30, 113.56, 113.33, 60.72, 60.62, 59.62, 46.75, 46.13, 15.32, 14.10, 14.06, 11.91; MS (EI): *m/z* = 283 (M^+, 4), 182 (100), 77 (27); Anal. found: C 76.15, H 7.77, N 4.82%; calcd. for $C_{18}H_{21}NO_2$: C 76.30, H 7.47, N 4.94%.

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