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Ultrasound-irradiated Michael addition of amines to ferrocenylenones under solvent-free and catalyst-free conditions at room temperature

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Abstract

A facile Michael addition of ferrocenylenones with aliphatic amines under ultrasound irradiation in the absence of solvent and catalyst at room temperature can afford 1-ferrocenyl-3-amino carbonyl compounds rapidly in high yields, which is also efficient in the aza-Michael reaction of other α,β-unsaturated carbonyl compounds such as chalcone, carboxylic ester, etc. However, aromatic amines do not undergo the conjugate addition at all, and the reactions under existing methods do not proceed or take place in low yield after a long reaction time. Apart from experimental simplicity, generality and selectivity, the advantages of this methodology are the rapid, environmentally benign and less expensive processes, which will contribute to the progress of green chemistry.

Keywords: Michael addition; Ferrocene, amine; β-amino carbonyl compound; Ultrasound; Solvent-free

1. Introduction

β-Amino carbonyl compounds are versatile intermediates for a large number of organic compounds, as exemplified in the preparation of γ-amino alcohols, diamines, β-amino acid derivatives and chiral auxiliaries [1], many of which are present as a segment of biologically important natural products such as alkaloids and polyketides [2]. Other applications of this type of compounds are in the fine chemical and pharmaceutical fields [3]. As a result of this vast range of applications, synthesis of β-amino carbonyl compounds has remained an important objective for a number of years, and the development of efficient synthetic methods leading to β-amino carbonyl compounds and derivatives has attracted much attention in organic synthesis [4]. Among the traditional methods for generating β-amino carbonyl compounds, Mannich-reaction, the reactions of enolates with imines, are established processes for the synthesis of these moieties through carbon–carbon bond formation [5] (Scheme 1). However, due to the harsh reactions and the long reaction time, the classic Mannich reaction presents serious disadvantages [6]. Alternatively, the Michael reaction, acid- or base-induced conjugate addition of nucleophiles to α,β-unsaturated compounds, can be used to create carbon–heteroatom bonds by reaction of α,β-unsaturated carbonyl compounds with amines [7] (Scheme 1). To avoid many of disadvantages of stoichiometric addition of a Lewis acid-mediated ($AlCl_3$, $SnCl_4$, or $TiCl_4$) conjugate addition reaction, a number of reactions that use catalytic quantities of minimally toxic, readily available, economic reagent have been

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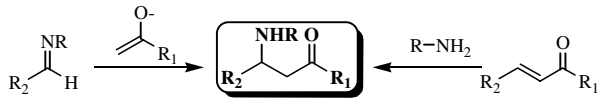


Scheme 1. Synthesis of β-amino carbonyl compounds.

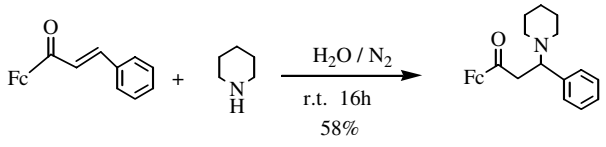
studied in the past few years. To the best of our knowledge, palladium [8], $InCl_3$ [9], $CeCl_3$/NaI [10], $Bi(NO_3)_3$ [11], $Bi(OTf)_3$ [12], copper salts [13], and other acids (Brønsted acids [14], or acidic clays [15]) have been used successfully in aza-Michael addition. Although recent advances have made this route more attractive, development of cheaper, simpler, more efficient and environmentally benign processes is highly desirable.

The derivatives of ferrocene have being attracted the attention of scientists all over the word because of their numerous applications in chemical sensing, asymmetric catalysis, material science and medical chemistry [16]. As a part of program aiming at the synthesis of potential biological or pharmacological active compounds such as ferrocene- or indole-containing fragments and with the increasing interest of our group in efficient, economic and environmentally friendly reactions mediated by metals and their salts, ionic liquids, or under solvent-free conditions [17], now we wish to search an optimized route to 1-ferrocenyl-3-amino carbonyl compounds by Michael-type reaction of amines to ferrocenylenones, which surprisingly no other references available in the literature reported to date.

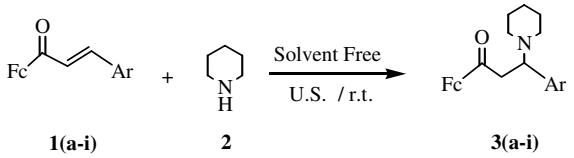
2. Results and discussion

Traditionally, only simple primary amines can reacted with α,β-unsaturated compounds with special activation, such as high temperature [18], high pressure [19], the use of appropriate catalysts, etc. [20]. Recently, Meyers reported that, water assist the *N*-conjugate addition of amines to unsaturated bicyclic lactams [21]. And Matloubi Moghaddam found water can promote Michael addition of secondary amines to α,β-unsaturated carbonyl compounds under microwave irradiation [22]. Chun-Gu Xia also discovered copper-catalyzed conjugate addition of aliphatic amines to α,β-unsaturated compounds in water [13]. These methods are really very fascinating to us because the processes are less expensive and performed in green aqueous solvent, water. The previous findings prompted us to develop a new protocol that employs water as medium in the aza-Michael reaction under mild condition. The starting point of this work was an examination of the generality of these reactions. Primary experiments revealed several features for the optimization of the Michael reaction of amines to ferrocenylenones: (a) the presence of a small amount of water was really helpful to drive the amine addition to completion in accordance with the literature results [22]. However, more water stopped the reactions, and copper salts failed to catalyze the reaction. (b) At least 10 mol equivalent of amines were required. (c) High temperature, microwave and acidic media were all disadvantageous to this reaction, and even induced some unwanted side reactions such as polymerization of vinyl ketones, oxidization of amine moieties or ferrocene fragments, and cleavage of β-amino ketones as desired products. In a typical reaction, ferrocenylenone (0.1 mol), piperidine (1 mol) and water (1 mol) were mixed and stirred at room temperature for 16 h under nitrogen atmosphere. The progress of the reaction was monitored with TLC. After conventional work-up a 58% yield of the 1,4-adduct was obtained (Scheme 2). For demonstrating the generality of this methodology different amines and Michael acceptors were used (Table 3, stir). But the results did not satisfy our interest of the reaction due to undesirable yields and long reaction time.

Recently, ultrasound has been utilized in organic synthesis as a new reaction media. Compared with traditional heating methods, this approach is more convenient, efficient and can be controlled easily. It has been reported that a large number of organic reactions could be facilitated by ultrasound irradiation with high yields, shorter reaction time and milder conditions [23]. Currently, our research group has also demonstrated the efficiency of this methodology for different reactions [24]. We have, therefore, decided to apply this technique to the above-mentioned reactions. Effectiveness of ultrasound to promote this conversion was tested for the reaction of ferrocenylenone and piperidine at ambient temperature in aqueous medium. To our satisfaction, the addition products were obtained in almost quantitative yield (98%) in a very short reaction time (1 h). Encouraged by this result, we carried out the reaction under solvent-free condition (Scheme 3). To our

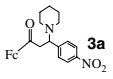
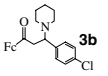
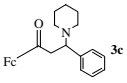
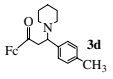
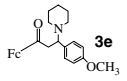
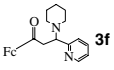
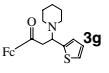
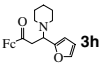
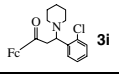


Scheme 2. Water-assisted Michael reaction of amines to ferrocenylenones.



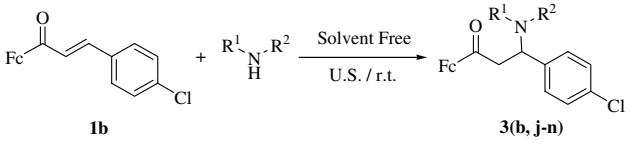
Scheme 3.

Table 1
Ultrasound irradiated Michael additions of ferrocenylenones with piperidine under solvent free condition at room temperature

Entry	Reactant Ar	Product	Time (h)	Yield [a] (%)
1	4-NO_2-C_6H_4 **1a**	 **3a**	0.5	98
2	4-Cl-C_6H_4 **1b**	 **3b**	0.5	98
3	C_6H_5 **1c**	 **3c**	1	98
4	4-CH_3-C_6H_4 **1d**	 **3d**	1.5	96
5	4-OCH_3-C_6H_4 **1e**	 **3e**	1.5	97
6	2-C_5H_4N **1f**	 **3f**	2	90
7	2-C_4H_3S **1g**	 **3g**	2	98
8	2-C_4H_3O **1h**	 **3h**	2	82
9	2-Cl-C_6H_4 **1i**	 **3i**	2	32[b]

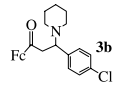
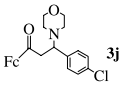
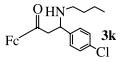
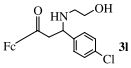
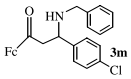
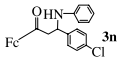
[a] Isolated yields.
[b] Without isolating pure product, the yield resulted from HPLC. The reaction proceeded incompletely, and the existence of chalcone has been tested with TLC.

surprise, the result was satisfactory all the same without any loss of yield. Apart from experimental simplicity, the advantages of this methodology are that the reaction mediated by ultrasound without solvent can proceed well even if the mixture of reactants, one of which is a liquid, is thick slurry. So the quantities of amines can be used minimally. The new findings promoted us to further utilize this new method of ultrasound irradiated aza-Michael addition to different ferrocenylenones (Scheme 3, Table 1) and different amines (Scheme 4, Table 2).



Scheme 4.

Table 2
Ultrasound irradiated Michael additions of amines to 1-ferrocenyl-3-(4-chlorophenyl)prop-2-en-1-one under solvent free condition at room temperature

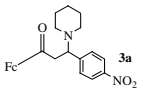
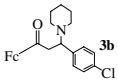
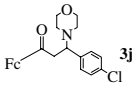
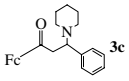
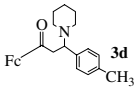
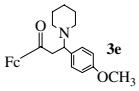
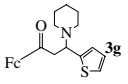
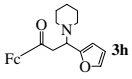
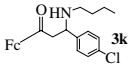
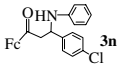
Entry	Amine	Product	Time (h)	Yield[a] (%)
1		 **3b**	0.5	98
2		 **3j**	1	91
3		 **3k**	2	85
4		 **3l**	2	83
5		 **3m**	2	83
6		 **3n**	3	Trace

[a] Isolated yields.

In Table 1 our results from ultrasound irradiated reactions of piperidine to different ferrocenylenones under solvent-free condition (Scheme 3) reveal that in all cases the 1,4-adducts are observed as the exclusive products of the reaction and the yields are good to excellent within 2 h, except for the less reactive Michael acceptor (Table 1, Entry 9) that reacts poorly due to steric influence.

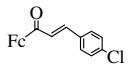
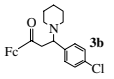
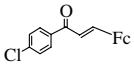
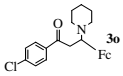
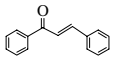
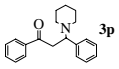
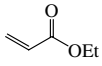
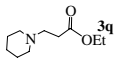
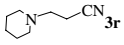
As is shown in Table 2, several different types of amines were subjected for this reaction under the same conditions (Scheme 4). All the aliphatic amines gave excellent yields within 2 h such as piperidine and morpholine (Table 2, Entries 1–2), which added better than other primary amines (Table 2, Entries 3–5) in accordance with their stronger nucleophilicities. However, aniline (Table 2, Entry 6) did not undergo the conjugate addition at all. It is easily found that the new approach is suitable only to active aliphatic amines and failed for less nucleophilic aromatic amines. So this selectivity could be useful to discriminate the two types of amines for synthetic applications. Interestingly, when the primary amines such as *n*-butylamine, ethanolamine, or benzylamine were treated with ferrocenylenones, highly chemo-selectivity occurred in this reaction, only mono-addition products were obtained (Table 2, Entries 3–5). So we established a condition in aza-Michael reactions for selective preparation of mono- and bis-addition products, which could also be useful in the synthesis of β-amino carbonyl compounds.

Table 3
Water-assisted or ultrasound-irradiated aza-Michael reactions of amines to ferrocenylenones at room temperature

Entry	Product	Stir[b]		U.S.[c]	
		Time (h)	Yield[a] (%)	Time (h)	Yield[a] (%)
1	 **3a**	16	73	0.5	98
2	 **3b**	16	77	0.5	98
3	 **3j**	18	54	1	91
4	 **3c**	16	58	1	98
5	 **3d**	18	68	1.5	96
6	 **3e**	18	81	1.5	97
7	 **3g**	18	63	2	98
8	 **3h**	20	57	2	82
9	 **3k**	20	52	2	85
10	 **3n**	20	Trace	3	Trace

[a] Isolated yields.
[b] The reactions proceeded in the presence of water at r.t.
[c] The reactions were performed under sonication conditions at r.t.

Table 4
Ultrasound irradiated Michael additions of piperidine to α,β-unsaturated carbonyl compounds under solvent free condition at room temperature

Entry	Unsaturated Compound	Product	Time (h)	Yield[a] (%)
1		 **3b**	0.5	98
2		 **3o**	2	83
3		 **3p**	0.5	99
4		 **3q**	0.5	98
5		 **3r**	0.5	98

[a] Isolated yields.

Table 3 compares the results from ultrasound-irradiated reaction and those obtained from water-assisted reaction. The reaction proceeded smoothly, giving **3a** in 98% yield under ultrasound condition for 30 minutes. However, only 73% **3a** was obtained in the presence of water by stir for 16 h (Table 3, Entry 1). Ultrasound irradiated aza-Michael addition are advantageous not only in terms of reactivity and simplicity, but also regarding waste disposal and cost. Furthermore, development of organic reactions under solvent-free condition will contribute to the progress of green chemistry. Surprisingly, however, there are few reports on conjugate addition of amines to α,β-unsaturated carbonyl compounds under solvent-free condition.

We also reasoned that this new approach could be versatile and universal for the intermolecular aza-Michael reaction. It was possible to extend the scope of the reaction to acceptors other than 1-ferrocenyl chalcones. Further experiments revealed that the same concept could be applied successfully to 3-ferrocenyl chalcones, chalcones, ethylacrylates or acrylonitriles (Table 4, Entries 2–5), which gave corresponding aza-Michael adducts rapidly in high yields by using ultrasound irradiation under solvent free condition. **3q–r** (Table 4, Entries 4–5) are direct precursors of β-aminoacids. This pathway, therefore, offers a possible route to β-aminoacid derivatives.

3. Conclusion

In conclusion, we have first developed a new methodology using ultrasound irradiation for an intermolecular aza-Michael addition of aliphatic amines to α,β-unsaturated carbonyl compounds under solvent-free and catalyst-free condition at room temperature. In contrast to the existing methods, this technique is very efficient, general, simple, high yielding, environmentally friendly, and oxygen and moisture tolerant. The neat, clean, and green process, Therefore, opens a novel entry to synthesis of β-amino carbonyl compounds and finally bodes well for the development of industrialization. Fur-

ther exploration of addition reactions with complex structure of the biological significance is in progress.

4. Experimental

Melting points were determined on a XT-5A digital melting points apparatus and uncorrected. IR Spectra were obtained on a Nicolet FT-IR500 spectrophotometer using KBr pellets. Elemental analyses were performed on a Carlo-Erba 1110 Elemental analysis instrument. ^{1}H NMR was recorded on Varian Inova 400 MHz NMR spectrometer in $CDCl_3$. High resolution mass spectra were obtained using GCT-TOF instrument. HPLC (LC-8A Waters 515). Ultrasonication was performed in a KQ-250E ultrasonic cleaner with a frequency of 40 kHz and a normal power of 250 W. Ferrocenylenones **1** were prepared as previously reported [24a]. Other reagents were obtained from commercial sources and used without purification.

4.1. General procedure for water-assisted Michael addition of amines to ferrocenylenones

Ferrocenylenones **1** (0.1 mmol), amines **2** (1 mmol) and water (1 ml) were mixed and stirred at room temperature for a specific time under nitrogen atmosphere as shown in Table 3. After the completion of the reaction (monitored by TLC), 30 mL water was added to the crude products and stirred for a while. After filtered and dried under reduced pressure, the excess of amines and water were removed. Further purification was accomplished by crystallization (~10% EtOAc in light petroleum ether) to get pure products **3**, and the isolated yields were described in Table 3.

4.2. General procedure for ultrasound-irradiated Michael addition of amines to ferrocenylenones

The mixture of α,β-unsaturated carbonyl compounds **1** (0.5 mmol) and amines **2** (0.5–5 mmol) was added to a flask which was immersed into the water bath of an ultrasonic cleaner at room temperature controlled by circulated water for a specific time as shown in Tables 1–4. After completion of the reaction, the crude product was washed with petroleum ether to remove the excess of amines and few unreacted α,β-unsaturated carbonyl compounds which can be recycled, and the final product could be obtained if the reactants were pure enough. Otherwise, further purification as described above could have been employed to afford products **3**, and the yields were described in Tables 1–4. The analytical data of compounds **3q**–**r** were in accordance with the reported values [22], and the spectral data of new compounds are following:

1-Ferrocenyl-3-(4-nitrophenyl)-3-(piperidin-1-yl)propan-1-one (***3a***): yellow solid; m.p.: 161–163 °C; IR(KBr): *v* 2932, 1661, 1514, 1456, 1346, 1107, 857, 707, 499 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 7.55–8.22(m, 4H), 4.76(d, J = 6.0 Hz, 2H), 4.51(s, 2H), 4.30(m, 1H), 4.10(s, 5H), 3.27(dd, J_1 = 67.6 Hz, J_2 = 16.4 Hz, 2H), 2.41(s, 4H), 1.40–1.61(m, 6H); HRMS [Found: *m/z*, 446.1292 (M^+); Calc. for $C_{24}H_{26}FeN_2O_3$: M, 446.1293].

1-Ferrocenyl-3-(4-chlorophenyl)-3-(piperidin-1-yl)-propan-1-one (***3b***): yellow solid; m.p.: 143–145 °C; IR(KBr): *v* 2932, 1656, 1491, 1455, 1380,1250, 1093, 820, 494 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 7.28–7.31(m, 4H), 4.75(s, 2H),4.49(s, 2H), 4.17(m, 1H), 4.08(s, 5H), 3.25(dd, J_1 = 40.0 Hz, J_2 = 10.0 Hz, 2H), 2.40(s, 4H), 1.38–1.57(m, 6H); HRMS [Found: *m/z*, 435.1060 (M^+); Calc. for $C_{24}H_{26}ClFeNO$: M, 435.1052].

1-Ferrocenyl-3-phenyl-3-(piperidin-1-yl)propan-1-one (***3c***): yellow solid; m.p.:137–139 °C; IR(KBr): *v* 2931, 1660, 1454, 1380, 1094, 821, 706, 496 cm^{-1}; ^{1}H NMR(400 MHz, $CDCl_3$) δ ppm: 7.25–7.36(m, 5H), 4.75(d, J = 5.2 Hz, 2H), 4.47(s, 2H), 4.19(t, J_1 = J_2 = 6.4 Hz, 1H), 4.03(s, 5H), 3.25–3.28(m, 2H), 2.42(s, 4H), 1.37–1.58(m, 6H); Anal. Calc. for $C_{24}H_{27}FeNO$: C 71.83, H 6.78, N 3.49, Found: C 71.86, H 6.72, N 3.41.

1-Ferrocenyl-3-(4-methylphenyl)-3-(piperidin-1-yl)-propan-1-one (***3d***): yellow solid; m.p.: 139–141 °C; IR(KBr): *v* 2933, 1656, 1454, 1380, 1247, 1106, 815, 496 cm^{-1}; ^{1}H NMR(400 MHz, $CDCl_3$) δ ppm: 7.13–7.27(m, 4H), 4.75(s, 2H), 4.46(s, 2H), 4.18(m, 1H), 4.05(s, 5H), 3.27(s, 2H), 2.42(s, 4H), 2.31(s,3H), 1.36–1.57(m, 6H); Anal. Calc. for C_{25} H_{29} FeNO: C 72.29, H 7.04, N 3.37, Found: C 72.38, H 6.79, N 3.46.

1-Ferrocenyl-3-(4-methoxyphenyl)-3-(piperidin-1-yl)-propan-1-one (***3e***): yellow solid; m.p.: 133–135 °C; IR(KBr): *v* 2933, 1656, 1607, 1509, 1453, 1380, 1254, 1106, 824, 499 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 6.86–7.27(m, 4H), 4.75(s, 2H), 4.46(s, 2H), 4.15(m, 1H), 4.05(s, 5H), 3.77(s, 3H), 3.27(s, 2H), 2.42(s, 4H), 1.25–1.58(m, 6H); Anal. Calc. for $C_{25}H_{29}FeNO_2$: C 69.61, H 6.78, N 3.25, Found: C 69.35, H 6.59, N 3.34.

1-Ferrocenyl-3-(piperidin-1-yl)-3-(pyridin-2-yl)propan-1-one (***3f***): yellow solid; m.p.: 114–116 °C; IR(KBr): *v* 2930, 1665, 1590, 1456, 1379, 1247, 1104, 823, 747, 493 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 7.16–8.58(m, 4H), 4.79(s, 2H), 4.46(s, 2H), 4.38(m, 1H), 4.11(s, 5H), 3.85(dd, J_1 = 17.2 Hz, J_2 = 9.2 Hz, 1H), 3.21(d, J = 17.2 Hz, 1H), 2.49(s, 4H), 1.38–1.59(m, 6H); HRMS [Found: *m/z*, 402.1333 (M^+); Calc. for $C_{23}H_{26}FeN_2O$: M, 402.1395].

1-Ferrocenyl-3-(piperidin-1-yl)-3-(thiophen-2-yl)propan-1-one (***3g***): yellow solid; m.p.: 124–126 °C; IR(KBr): *v* 2932, 1658, 1456, 1412, 1252, 1105, 880, 715, 497 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 6.97–7.24(m, 3H), 4.79(d, J = 10.0 Hz, 2H), 4.64(m, 1H), 4.50(s, 2H),

4.12(s, 5H), 3.27(s, 2H), 2.52(s, 4H), 1.40–1.61(m, 6H); Anal. Calc. for $C_{22}H_{25}FeNOS$: C 64.87, H 6.19, N 3.44, Found: C 64.94, H 6.40, N 3.33.

1-Ferrocenyl-3-(furan-2-yl)-3-(piperidin-1-yl)propan-1-one (**3h**): yellow solid; m.p.: 105–107 °C; IR(KBr): *v* 2933, 1660, 1456, 1380, 1252, 1103, 1004, 824, 735, 499 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 7.39(s, 1H), 6.34(s, 1H), 6.24(s, 1H), 4.80(s, 2H), 4.50(s, 2H), 4.39(dd, $J_1 = 8.4$ Hz, $J_2 = 4.8$ Hz, 1H), 4.14(s, 5H), 3.42(dd, $J_1 = 16.4$ Hz, $J_2 = 8.8$ Hz, 1H), 3.18(d, $J = 15.2$ Hz, 1H), 2.40-2.54(m, 4H), 1.38–1.60(m, 6H); Anal. Calc. for $C_{22}H_{25}FeNO_2$: C 67.53, H 6.44, N 3.58, Found: C 67.47, H 6.47, N 3.40.

1-Ferrocenyl-3-(4-chlorophenyl)-3-morpholinopropan-1-one (**3j**): yellow solid; m.p.: 173–175 °C; IR(KBr): *v* 2846, 1662, 1491, 1454, 1266, 1115,1005, 823, 500 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 7.27–7.32(m, 4H), 4.72(d, $J = 10.4$ Hz, 2H), 4.49(s, 2H), 4.05(m, 1H), 4.04(s, 5H), 3.68(s, 4H), 3.18(d, $J = 53.0$ Hz, 2H), 2.44(s, 4H); HRMS [Found: *m/z*, 437.0828 (M^+); Calc. for $C_{23}H_{24}ClFeNO_2$: M, 437.0845].

1-Ferrocenyl-3-(butylamino)-3-(4-chlorophenyl)propan-1-one (**3k**): yellow solid; m.p.: 79–81 °C; IR(KBr): *v* 3304, 2922, 1661, 1491, 1456, 1378, 1090, 826, 498 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 7.35–7.40(m, 4H), 4.73(d, $J = 9.6$ Hz, 2H), 4.51(s, 2H), 4.25(s, 1H), 4.13(s, 5H), 3.05(s, 2H), 2.41–2.47(m, 2H), 1.46(m, 2H), 1.32(m, 2H), 0.88(m, 3H); HRMS [Found: *m/z*, 423.1031 (M^+); Calc. for $C_{23}H_{26}ClFeNO$: M, 423.1052].

1-Ferrocenyl-3-(2-hydroxyethylamino)-3-(4-chlorophenyl)propan-1-one (**3l**): yellow solid; m.p.: 143–145 °C; IR(KBr): *v* 3292, 3183, 3122, 2838, 1655, 1493, 1457, 1380, 1079, 832, 500 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 7.34–7.40(m, 4H), 4.74(d, $J = 7.2$ Hz, 2H), 4.53(s, 2H), 4.30(t, $J = 6.4$ Hz, 1H), 4.14(s, 5H), 3.63(d, $J = 66.8$ Hz, 2H), 3.05(t, $J = 4.0$Hz, 2H), 2.62–2.65(m, 2H); HRMS [Found: *m/z*, 411.0675 (M^+); Calc. for $C_{21}H_{22}ClFeNO_2$: M, 411.0688].

1-Ferrocenyl-3-(benzylamino)-3-(4-chlorophenyl)propan-1-one (**3m**): yellow solid; m.p.: 113–114 °C; IR(KBr): *v* 3314, 2832, 1658, 1456, 1378, 1107, 821, 738, 701, 482 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 7.27–7.46(m, 9H), 4.72(d, $J = 11.2$ Hz, 2H), 4.50(s, 2H), 4.30(s, 1H), 4.12(s, 5H), 3.62(dd, $J_1 = 38.0$ Hz, $J_2 = 13.6$ Hz, 2H), 3.06(s, 2H); HRMS [Found: *m/z*, 457.0889 (M^+); Calc. for $C_{26}H_{24}ClFeNO$: M, 457.0896].

1-(4-Chlorophenyl)-3-ferrocenyl-3-(piperidin-1-yl)-propan-1-one (**3o**): 128–130 °C; IR(KBr): *v* 2938, 1679, 1589, 1401, 1273, 1095, 982, 829, 758, 487 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 7.97(d, $J = 7.4$ Hz, 2H), 7.49(d, $J = 7.4$ Hz, 2H), 4.17(s, 4H), 4.11(s, 5H), 4.10(m, 1H), 3.48(d, $J = 96.0$ Hz, 2H), 2.40(s, 2H), 2.01–2.06(m, 2H), 1.22–1.34(m, 6H); HRMS [Found: *m/z*, 435.1050 (M^+); Calc. for $C_{24}H_{26}ClFeNO$: M, 435.1052].

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