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Quaternary ammonium salt gemini surfactants containing perfluoroalkyl tails catalyzed one-pot Mannich reactions in aqueous media

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Abstract

A newly prepared quaternary ammonium salt (QAS) gemini fluorosurfactants efficiently catalyze one-pot Mannich reactions of aldehydes, amines and ketones in aqueous media at ambient temperature to afford corresponding β-aminocarbonyl compounds in good to excellent yields. In addition, the gemini fluorosurfactant catalysts were recovered and reused for three times with little loss of their catalytic activities.

Keywords: Quaternary ammonium salt (QAS); Gemini fluorosurfactant; Mannich reaction; β-Aminocarbonyl compound; Lewis acid

1. Introduction

Considerable effort has been made by chemists to obtain a consistent surface tension as low as possible (approximately 20 dyn/cm) [1]. But it resulted in the problem that the surfactants consisting of long hydroalkyl tails [2]. Meanwhile the corresponding value reported for perfluoroalkyl tailed surfactant is from 6 to 13 dyn/cm. It is the $–CF_2–$ especially the $–CF_3$ end group in the molecule that effectively reduces the surface tension to such extent [3]. Since perfluoroalkyl chains are more hydrophobic than their alkyl analogues, the critical micelle concentration (cmc) of perfluoroalkyl surfactants is commonly one to two orders of magnitude lower than that of hydrocarbon surfactants of similar length [4–6].

As antibacterial materials, fluorous QAS surfactants, including gemini QAS fluorosurfactants, attached much attention [7–9]. However, there are few or only limited reports about QAS containing perfluoroalkyl tails used in organic synthesis as catalyst. Heavy fluorous catalysts whose molecules contain more than 60% fluorine by molecular weight had been widely used to provide a facile liquid/liquid separation after reaction [10], but fluorous solvents used are expensive and environmentally troublesome. Meanwhile, QAS containing perfluoroalkyl tails, which shows excellent water solubility and surfactivity, can disperse hydrophobic organic substrate in water homogeneously. As a quaternary ammonium salt, they can also play the role of phase transfer catalyst. Combining these two roles together, fluorous QAS surfactants can be used as a fluorous catalyst soluble in water instead of fluorous solvent.

The use of water as a sole medium for organic reactions would greatly contribute to the development of environmentally friendly processes. Recently, some organic reactions have been realized in water [11]. Among these reactions, Mannich reaction being carried out in water attracted much attention [12]. The main catalysts reported include Lewis acids such as triflates [12d,h] and chlorides [12e], Brønsted acids such as sulfonic acids [12a,b,f,g], hydrochloric acid [12i] and heteropoly acids [12j]. However, when some parent ketones rather than their silyl enolates forms are used directly, some Lewis acids, which results in long reaction time [12e], are not effective catalysts. And there are few reports on effectively catalyzed reaction of anisaldehyde with aniline and acetophenone.

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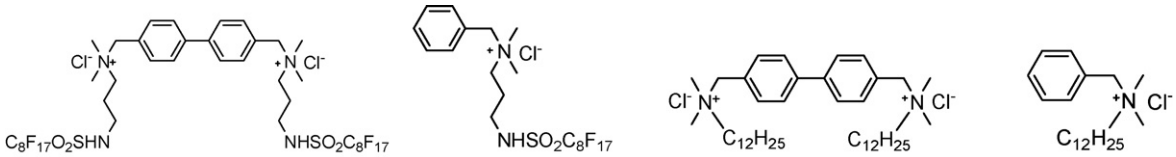


Scheme 1.

Additionally, vigorous stirring was required for the success of these reactions due to the poor solubility of aldehydes, ketones and amines in water. To solve this problem, surfactants were added to form colloidal dispersions as reaction media. Use of surfactants can not only disperse organic substrate in water, but also can make organic synthesis inside substrate-containing particles in water [13]. Our group had reported a facile and efficient method for preparation of β-aminocarbonyl compounds by Mannich reaction of acetophenone with aldehydes and aromatic amines in the presence of rare earth perfluorooctanoate [RE(PFO)$_3$] [14]. Herein, we would like to report a new type of fluorous QAS gemini surfactant (compound **3**) used as a catalyst for one-pot Mannich reaction in water without any organic solvent, and another three QAS surfactants (compound **4**–**6**) have also been prepared for control experiments (Scheme 1).

2. Results and discussion

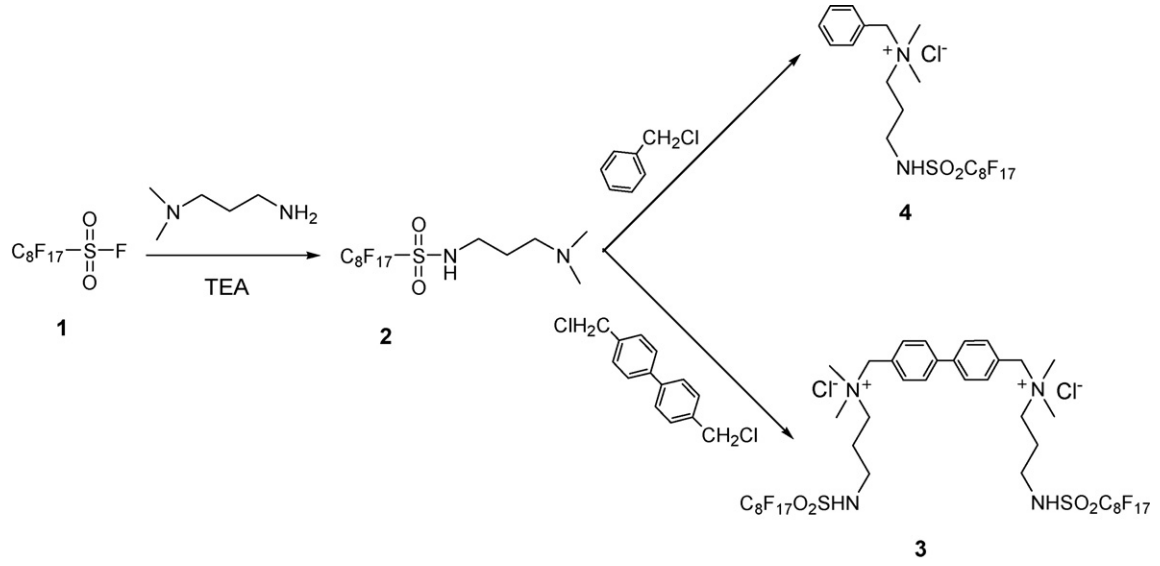
2.1. Synthesis

For our target molecule, biphenyl is chosen as the spacer connecting two amphiphilic moieties, which is more rigid than methylene groups. The strategy to prepare perfluoroalkyl quaternary ammonium compounds **3** and **4** are shown in Scheme 2. Perfluorooctanesulfonyl fluoride **1** is treated with *N*,*N*-dimethylpropyl-1,3-diamine in the presence of triethylamine to afford *N*-(2-(dimethylamino)propyl)-perfluorooctanesulfonamide **2** in 89% yield. Compound **2** can be quaternarized with different alkyl halide in the tertiary amine functional group to form many kinds of QAS. When 4,4′-bis(chloromethyl)-1,1′-biphenyl and benzyl chloride were used as quaternarization reagents, QAS **3** and **4** were obtained from the above reactions in anhydrous EtOH–DMF–$CHCl_3$ system in 67% and 82% yield, respectively. Both of these two QAS **3** and **4** were soluble in water.

2.2. Surface properties of QAS

The partially fluorinated quaternary ammonium salts **3** (GFQAS) and **4** (FQAS) exhibit good solubility in water at room temperature. Fig. 1 shows that the curve of equilibrium surface tension obtained from Wilhelmy plate method as a function of the concentration of gemini surfactant **3** (GFQAS). The value of the cmc obtained by the surface tension curve is consistent with the concentration of break points. The cmc and surface tension values at cmc (γ_{cmc}) of the four QAS are summarized in Table 1.

As shown in Table 1, the fluorinated QAS surfactants exhibit much smaller cmc values than their hydrocarbon counterparts. Moreover, the surface tension at cmc (γ_{cmc}) reduced by fluorinated QAS is much lower than that of hydrocarbon QAS. The cmc of **3** (GFQAS) is one order of magnitude lower than its counterpart **5** (GQAS), which corresponds to the equivalence of



Scheme 2.

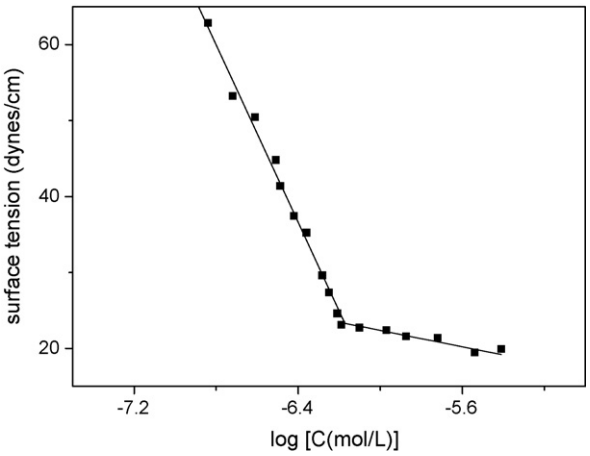


Fig. 1. Surface tension against log (concentration of 3 GFQAS).

Table 1
Cmc of surfactants and surface tension (ST) at each of their cmc at 25 °C

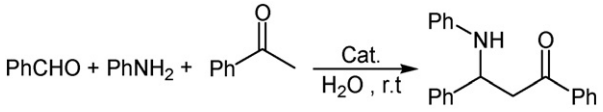
	3 (GFQAS)	**4** (FQAS)	**5** (GQAS)	**6** (TQAS)
cmc (mol/l)	5.54×10^{-7}	3.22×10^{-5}	2.98×10^{-6}	9.35×10^{-4}
ST (dyn/cm)	23.15	23.69	45.06	46.86

1 CF_2 to 1.5 CH_2 units [15]. The excellent surfactivity of **3** (GFQAS) mainly attributes the access to intensive hydrophobic property of the long fluorocarbon chain. Besides, the biphenyl group connecting two amphiphilic moieties more rigidly than methylene groups, can also bring surface tension down to such extent.

2.3. Catalytic activities of QAS

QAS could serve both as a phase transfer catalyst and as a surfactant. Thus, we next investigated their catalytic activities for three-component Mannich-type reactions of benzaldehyde with aniline and acetophenone in water at room temperature. First, the reaction was carried out in the presence of QAS catalyst, and sodium hydroxide (NaOH) was chosen as a Brønsted base (Scheme 3). The results were summarized in Table 2.

It was found that with only 0.2 mol% of the **3** (GFQAS), the reaction gave quite satisfactory yield at room temperature within 6 h. Other QAS, especially the hydrocarbon ones only gave moderate yields, but with more dosage. Furthermore, the phase transfer catalyst triethylbenzylammonium chloride (TEBA), which shows weak emulsification ability, can promote the reaction even more effectively than sodium *p*-dodecylbenzenesulfonate (SDBS). That is, the fluorous QAS gemini



1a **2a**

Scheme 3.

Fig. 2. Photographs of 3 (GFQAS) catalyzed reaction in water. The emulsion of catalyst and reagents formed at the beginning of reaction (I) and the product precipitated after the reaction finished (II). Upper layer: the catalytic mother solution; lower layer: the crude product.

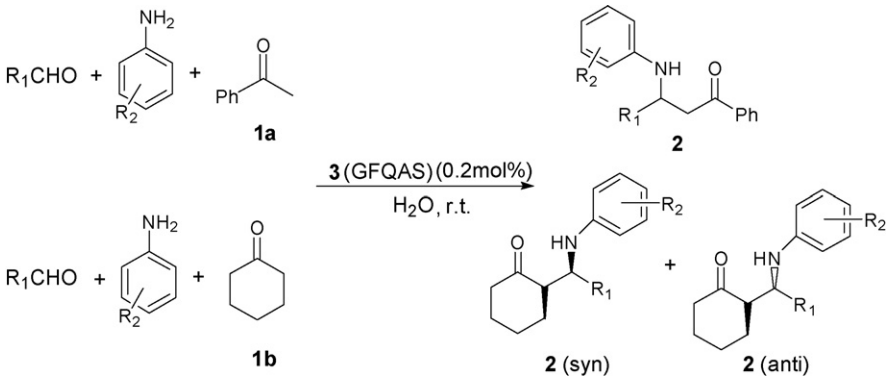
surfactant not only exhibit excellent micelle catalysis but also phase transfer catalysis activity. Studies showed that 1.2×10^{-6} mol% (concentration reached at cmc with this amount) of **3** just afforded poor yield (entry 2, Table 2), while 0.2 mol% of this catalyst gave satisfactory yield. It is mainly because too little amount of 3 could not carry out phase transfer catalysis effectively. After the reaction was completed, the desired product was congregated and precipitated (Fig. 2); hereby it could simply be separated by filtration. As showed in Fig. 2, when the solution of catalyst was mixed with organic substrates such as benzaldehyde, a white emulsion formed through surfactant colloid dispersions (Fig. 2I). Then, after reaction was finished, the product depositing out of the reaction mixture could be isolated by filtration (Fig. 2II). Meanwhile, the catalyst remained in the mother solution, which could be reused for several times without obvious loss of activity (entry 11, Table 2). The yields were obtained from 83% to 78% (with yields of product **2a** being 83%, 81%, and 78% in the first, second and third run, respectively). In view of environmental benign methodologies, recovery and reuse of the reaction media is highly preferable.

The model reaction was also carried out using Brønsted acid-surfactant combined catalysts, where *p*-tolylsulfonic acid (TsOH) was chosen as the Brønsted acid (Table 3). Compared with Brønsted base-surfactant systems, the reactions proceeding under acidic conditions were slow, and the yields were not

Table 2
Mannich-type reactions in the presence of various catalysts under basic aqueous media conditions at room temperature[a]

Entry	Catalyst	Amount (mol%)/ conc. (mol/l)	Time (h)	Yield (%)[b]
1	None	–	6	18
2	**3** (GFQAS)	1.2×10^{-6}/cmc	6	21
3	**3** (GFQAS)	$0.02/1.0 \times 10^{-4}$	6	40
4	**3** (GFQAS)	0.2/0.001	6	83
5	**4** (FQAS)	0.5/0.0025	6	53
6	**5** (GQAS)	1/0.005	6	39
7	**5** (GQAS)	2/0.01	6	56
8	**6** (TQAS)	2/0.01	6	43
9	SDBS	5/0.025	6	39
10	TEBA	5	6	63
11	**3** (GFQAS)	0.2/0.001	6	83, 81, 78[c]

[a] In 10% sodium hydroxide solution.
[b] Isolated yields.
[c] The catalytic mother solution was reused for three times.



Scheme 4.

Table 3
Mannich-type reactions in the presence of various catalysts under acidic aqueous media conditions at room temperature

Entry	Catalyst	Amount (mol%)	Time (h)	Yield (%)[a]
1	TsOH	10	12	Trace
2	**3** (GFQAS) + TsOH	0.2 + 10	12	70
3	**4** (FQAS) + TsOH	0.5 + 10	12	53
4	**5** (GQAS) + TsOH	2 + 10	12	56
5	SDBS + TsOH	5 + 10	12	46

[a] Isolated yields.

as high as above. Nevertheless, it would be noteworthy that the highest yield was achieved by the use of GFQAS **3** as low as 0.2 mol% (entry 2) (Scheme 4).

In order to show the general applicability of the method, the reactions of various aldehydes with aromatic amines and ketones (**1a** or **1b**) were carried out under basic and acidic conditions. It was found that acetophenone in basic conditions gave good to excellent yields, while cyclohexanone afforded no products (Table 4). In acidic conditions both acetophenone and cyclohexanone gave the desired products, but a prolonged time was need for the reaction of acetophenone. It is noteworthy that reaction in basic media proceeded much more quickly than that in acidic media. For example, the reaction of anisaldehyde with aniline and acetophenone proceeded smoothly under basic aqueous conditions to give the product in moderate yield, but it did not provide the product under acidic aqueous conditions (Tables 4 and 5). In general, aromatic aldehydes substituted with electron withdrawing group gave higher yields than that substituted with electron donating group. However, 4-nitrobenzaldehyde provided only imine as the final product, while 3-nitrobenzaldehyde gave the desired product in good yield. In addition, aliphatic aldehydes, such as isobutyaldehyde, showed a relatively lower yield even with prolonged reaction time due to enamine formation.

Table 4
Synthesis of different β-aminocarbonyl compounds using **3** (GFQAS) as catalyst[a]

Entry	R_1	R_2	Ketone	Ketone (equiv.)[b]	Time (h)	Product	Yield (%)[c]
1	C_6H_5	H	**1a**	2	6	**2a**	83
2	C_6H_5	4-CH_3	**1a**	2	6	**2b**	87
3	C_6H_5	4-MeO	**1a**	2	6	**2c**	90
4	4-$NO_2C_6H_4$	H	**1a**	2	6	**2d**	Imine
5	4-FC_6H_4	H	**1a**	2	6	**2e**	61
6	4-ClC_6H_4	H	**1a**	2	6	**2f**	91
7	4-ClC_6H_4	4-Cl	**1a**	2	6	**2g**	85
8	4-$MeOC_6H_4$	H	**1a**	2	10	**2h**	68
9	4-$MeOC_6H_4$	4-Cl	**1a**	2	8	**2i**	80
10	C_6H_5	H	**1b**	5	6	**2j**	Trace
11	3-$NO_2C_6H_4$	H	**1b**	5	6	**2k**	Trace
12	4-$NO_2C_6H_4$	4-Cl	**1b**	5	6	**2l**	Trace
13	4-$MeOC_6H_4$	4-Cl	**1b**	5	6	**2m**	Trace
14	Me_2CH	H	**1b**	5	6	**2n**	Trace
15	2-Furyl	H	**1b**	5	6	**2o**	Trace

[a] All reactions were carried out in 10% NaOH solution at room temperature.
[b] Both of aldehyde and aromatic amine used are 1 equiv.
[c] Isolated yields.

Table 5
Synthesis of different β-aminocarbonyl compounds using **3** (GFQAS) as catalyst[a]

Entry	R_1	R_2	Ketone	Ketone (equiv.)[b]	Time (h)	Product	Yield (%)[c]
1	C_6H_5	H	**1a**	2	12	**2a**	70
2	C_6H_5	4-CH_3	**1a**	2	12	**2b**	74
3	C_6H_5	4-MeO	**1a**	2	12	**2c**	79
4	4-$NO_2C_6H_4$	H	**1a**	2	12	**2d**	Imine
5	4-FC_6H_4	H	**1a**	2	12	**2e**	33
6	4-ClC_6H_4	H	**1a**	2	12	**2f**	79
7	4-ClC_6H_4	4-Cl	**1a**	2	12	**2g**	82
8	4-$MeOC_6H_4$	H	**1a**	2	24	**2h**	trace
9	4-$MeOC_6H_4$	4-Cl	**1a**	2	12	**2i**	72
10	C_6H_5	H	**1b**	5	4	**2j**	83 (44:56)[d,e]
11	3-$NO_2C_6H_4$	H	**1b**	5	4	**2k**	87 (52:48)
12	4-$NO_2C_6H_4$	4-Cl	**1b**	5	12	**2l**	82 (49:51)
13	4-$MeOC_6H_4$	4-Cl	**1b**	5	6	**2m**	73 (43:57)
14	Me_2CH	H	**1b**	5	12	**2n**	45 (–)[f]
15	2-Furyl	H	**1b**	5	12	**2o**	78 (71:29)

[a] All reactions were carried out in the presence of 10 mol% TsOH at room temperature.
[b] Both of aldehyde and aromatic amine used are 1 equiv.
[c] Isolated yields.
[d] *syn*/*anti*-ratio.
[e] *syn*/*anti*-ratio was determined by ^{1}H NMR spectroscopy of the crude products and by comparison with known compounds reported in the literature [12b,f,i,j].
[f] The crude product is a complicated mixture due to enamine formation.

3. Conclusions

In summary, a fluorinated QAS gemini surfactants were prepared and served as a highly effective catalyst for three-component one-pot Mannich reactions in water at room temperature to afford β-aminocarbonyl compounds in good to excellent yields. The method presented an operationally simple, environmentally benign workup procedure without using any organic solvent. Besides, the mother liquid containing catalyst fluorous QAS gemini surfactants could be easily recycled and reused without obvious loss of activities.

4. Experimental

4.1. Methods and apparatus

IR spectra were recorded on a Shimadzu IR-440 spectrometer. ^{1}H NMR spectra were recorded on a BRUKER AM 400 (400 MHz) using TMS as an internal standard. ^{19}F NMR spectra were recorded on a BRUKER WP-500SY (470 MHz) spectrometer and were taken with $CFCl_3$ as an internal standard. Coupling constants (J) are given in Hz. Mass spectra were recorded on a Finnigan-MAT-8430 instrument using EI ionization at 70 eV.

4.2. Preparation of fluorous quaternary ammonium salts

4.2.1. N-(2-(Dimethylamino)ethyl)-perfluorooctanesulfonamide **2**

Perfluorooctanesulfonyl fluoride **1** (13.5 ml, 0.05 mol) was added dropwise to a stirred solution of *N*,*N*-dimethylpropyl-1,3-diamine (7.6 ml, 0.06 mol) in petroleum ether (50 ml) at 0 °C containing triethylamine (10.4 ml, 0.075 mol). The mixture was stirred at room temperature for 4 h and then filtered. The yellow residue was recrystallized from acetone to provide compound **2**.

White solid; 89% yield; mp 117–119 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.76 (m, 2H, CH_2), 2.31 (s, 6H, 2× CH_3), 2.59 (t, 2H, J = 5.6 Hz, CH_2), 3.49 (t, 2H, J = 5.6 Hz, CH_2); ^{19}F NMR (470 MHz, $CDCl_3$): δ = −82.76 (t, 3F, J = 9.4 Hz), −114.49 (t, 2F, J = 14.2 Hz), −122.06 (m, 2F), −123.30 (m, 2F), −123.42 (m, 2F), −123.58 (m, 2F), −124.41 (m, 2F), −127.88 (m, 2F); MS (EI) m/z 584 (M^+). Anal. calcd. for $C_{13}H_{13}F_{17}N_2O_2S$: C, 26.72; H, 2.24. Found: C, 26.73; H, 2.24.

4.2.2. Preparation of **3** (GFQAS)

Compound **2** (6.42 g, 11.0 mmol) and 4,4′-bis(chloromethyl)-1,1′-biphenyl (1.25 g, 5.0 mmol) were added to a solution of EtOH–DMF–$CHCl_3$ (2.5:3:1, 26 ml), followed by stirring at 100 °C for 8 h. After cooling the reaction mixture to room temperature, the resulting suspension precipitated by the addition of Et_2O. The solids were filtered, washed with Et_2O. The crude solid was recrystallized from EtOH and petroleum ether to afford the desired product **3**.

White solid; 67% yield; mp 209–210 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.36 (m, 4H), 2.70 (t, 4H, J = 5.6 Hz), 2.88 (t, 4H, J = 5.6 Hz), 3.01 (s, 12H), 4.58 (d, 4H, J = 8.0 Hz), 7.68 (m, 4H), 7.85 (t, 4H, J = 8.0 Hz); ^{19}F NMR (470 MHz, DMSO-d_6): δ = −82.76 (t, 6F, J = 9.4 Hz), −114.82 (t, 4F, J = 14.2 Hz), −122.09 (m, 4F), −123.31 (m, 4F), −123.44 (m, 4F), −123.59 (m, 4F), −124.40 (m, 4F), −127.88 (m, 4F); MS (EI) m/z 1419 (M^+). Anal. calcd. for $C_{40}H_{38}Cl_2F_{34}N_4O_4S_2$: C, 33.91; H, 2.49. Found: C, 33.94; H, 2.50.

4.2.3. Preparation of **4** (FQAS)

Compound **2** (3.42 g, 5.8 mmol) and chloromethylbenzene (0.76 g, 6.0 mmol) were added to a solution of EtOH–DMF–$CHCl_3$ (2.5:3:1, 18 ml), followed by stirring at 100 °C for 5 h. After cooling the reaction mixture to room temperature, the crude product was precipitated by the addition of Et_2O to the resulting solution. The solid were filtered, washed with Et_2O. The crude product was recrystallized from EtOH and petroleum ether to afford the desired product **4**.

White solid; 82% yield; mp 174–177 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.36 (m, 2H), 2.70 (t, 2H, J = 6.4 Hz), 2.88 (t, 2H, J = 6.4 Hz), 3.11 (s, 6H), 4.60 (s, 2H), 7.34 (s, 2H), 7.53 (m, 1H), 7.76 (s, 2H); ^{19}F NMR (470 MHz, DMSO-d_6): δ = −81.83 (t, 3F, J = 9.4 Hz), −113.18 (t, 2F, J = 14.0 Hz), −121.78 (m, 2F), −122.54 (m, 2F), −122.82 (m, 2F), −123.00 (m, 2F), −123.81 (m, 2F), −127.22 (m, 2F); MS (EI) m/z 710 (M^+). Anal. calcd. for $C_{20}H_{20}ClF_{17}N_2O_2S$: C, 33.79; H, 2.84. Found: C, 33.81; H, 2.86.

4.3. Typical procedure for Mannich reaction catalyzed by **3** (GFQAS) in basic and acidic conditions

3 (GFQAS) (14.2 mg, 0.01 mmol) was dissolved in water (10 ml), and then NaOH (1 g) was added. After the solution was cooled down to room temperature, benzaldehyde (5 mmol), aniline (5 mmol), and acetophenone (10 mmol) were added successively. After being stirred at the same temperature for the period of time listed in the tables, the mixture was placed still and the resulting solid was filtered, washed with water (3× 5 ml) and recrystallized from EtOH to give the pure product.

The filtrate that containing catalyst could be reused directly as reaction media for next run without any treatment.

3 (GFQAS) (14.2 mg, 0.01 mmol) was dissolved in water (10 ml), and then TsOH (95 mg, 0.5 mmol) was added. Benzaldehyde (5 mmol), aniline (5 mmol), and cyclohexanone (25 mmol) were added successively. After being stirred at the same temperature for the period of time listed in the tables, a saturated aq. $NaHCO_3$ solution (10 ml) and brine (10 ml) were added, and the mixture was extracted with ethyl acetate, washed with brine, dried over Na_2SO_4, and concentrated. Purification by silica gel chromatography gave the desired product.

4.4. Spectral characterization of Mannich reaction products

4.4.1. 1,3-Diphenyl-3-phenylamino-propan-1-one (**2a**)

mp 172–173 °C (lit. [12h]: 170–172 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.90–7.88 (m, 2H), 7.56–7.05 (m,

10H), 6.66–6.62 (m, 1H), 6.56–6.53 (m, 1H), 5.00 (dd, 1H, J = 5.2, 7.2 Hz), 4.56 (br, 1H), 3.52 (dd, 1H, J = 5.2, 16 Hz), 3.43 (dd, 1H, J = 7.6, 16 Hz); IR (KBr): 3387, 3021, 1669 cm^{-1}.

*4.4.2. 1,3-Diphenyl-3-p-tolylamino-propan-1-one (**2b**)*

mp 170–172 °C (lit. [16a]: 171 °C); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.89–7.91 (m, 2H), 7.56–7.57 (m, 1H), 7.43 (t, 2H, J = 7.4 Hz), 7.23 (d, 2H, J = 8.2 Hz), 7.08–7.13 (m, 4H), 6.68 (t, 1H, J = 7.4 Hz), 6.64 (d, 2H, J = 8.0 Hz), 4.98 (t, 1H, J = 6.2 Hz), 3.44–3.58 (m, 2H), 2.30 (s, 3H); IR (KBr): 3386, 3020, 2939, 1689 cm^{-1}.

*4.4.3. 3-(4-Methoxy-phenylamino)-1,3-diphenyl-propan-1-one (**2c**)*

mp 124–125 °C (lit. [12h]: 130–132 °C); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.91 (d, 2H, J = 8.0 Hz), 7.56 (t, 1H, J = 7.2 Hz), 7.45 (t, 4H, J = 6.4 Hz), 7.33 (t, 2H, J = 7.4 Hz), 7.24 (s, 1H), 6.69 (d, 2H, J = 8.0 Hz), 6.53 (d, 2H, J = 8.4 Hz), 4.93 (t, 1H, J = 6.8 Hz), 4.30 (br, 1H), 3.70 (s, 3H), 3.51–3.38 (m, 2H); IR (KBr): 3399, 2974, 1672, 1598 cm^{-1}.

*4.4.4. (4-Nitro-benzylidene)-phenyl-amine (**2d**)*

mp 89–91 °C (lit. [16b]: 93 °C); ^1H NMR (400 MHz, $CDCl_3$): δ = 8.57 (s, 1H), 8.36–8.33 (d, 2H, J = 8.8 Hz), 8.11–8.09 (d, 2H, J = 8.8 Hz), 7.47–7.43 (t, 2H, J = 7.8 Hz), 7.33–7.27 (m, 3H); IR (KBr): 3187, 3021, 1678, 1527, 1348 cm^{-1}.

*4.4.5. 3-(4-Fluoro-phenyl)-1-phenyl-3-phenylamino-propan-1-one (**2e**)*

mp 111–113 °C (lit. [16a]: 111–112 °C); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.90 (d, 2H, J = 7.0 Hz), 7.58 (t, 1H, J = 7.0 Hz), 7.48–7.42 (m, 4H), 7.10 (t, 2H, J = 7.2 Hz), 7.01 (t, 2H, J = 8.2 Hz), 6.69 (t, 1H, J = 7.6 Hz), 6.55 (d, 2H, J = 7.6 Hz), 5.00 (t, 1H, J = 7.4 Hz), 4.56 (br, 1H), 3.52–3.40 (m, 2H); IR (KBr): 3376, 3020, 1667 cm^{-1}.

*4.4.6. 3-(4-Chloro-phenyl)-1-phenyl-3-phenylamino-propan-1-one (**2f**)*

mp 116–117 °C (lit. [12h]: 114–115 °C); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.93 (d, 2H, J = 8.0 Hz), 7.60 (t, 2H, J = 7.6 Hz), 7.50–7.40 (m, 2H), 7.05 (t, 2H, J = 8.4 Hz), 6.90 (t, 2H, J = 6.8 Hz), 6.52 (d, 2H, J = 7.6 Hz), 6.30 (t, 2H, J = 7.6 Hz), 4.99 (t, 1H, J = 5.6 Hz), 4.57 (br, 1H), 3.52–3.40 (m, 2H); IR (KBr): 3376, 3020, 1667 cm^{-1}.

*4.4.7. 3-(4-Chloro-phenyl)-3-(4-chloro-phenylamino)-1-phenyl-propan-1-one (**2g**)*

mp 155–157 °C (lit. [16c]: 155 °C); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.94–7.93 (d, 2H, J = 4.6 Hz), 7.63–7.60 (t, 1H, J = 6.4 Hz), 7.51–7.48 (t, 2H, J = 6.0 Hz), 7.44–7.39 (m, 2H), 7.33–7.30 (t, 2H, J = 6.4 Hz), 7.08–7.06 (d, 2H, J = 8.0 Hz), 6.50–6.48 (d, 2H, J = 8.2 Hz), 4.98–4.96 (t, 1H, J = 4.6 Hz), 3.48–3.45 (t, 1H, J = 6.4 Hz), 2.21 (s, 2H); IR (KBr): 3378, 3020, 1668 cm^{-1}.

*4.4.8. 3-(4-Methoxy-phenyl)-1-phenyl-3-phenylamino-propan-1-one (**2h**)*

mp 150–152 °C (lit. [12h]: 150–151 °C); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.87–7.93 (m, 2H), 7.55–7.57 (m, 1H), 7.46 (t, 2H, J = 7.0 Hz), 7.35 (d, 2H, J = 8.4 Hz), 7.07–7.11 (m, 2H), 6.83–6.86 (m, 2H), 6.70 (t, 1H, J = 7.6 Hz), 6.54 (d, 2H, J = 7.6 Hz), 4.96 (t, 1H, J = 6.4 Hz), 3.77 (s, 3H), 3.54 (d, 1H, J = 5.4 Hz), 3.34 (d, 1H, J = 7.6 Hz); IR (KBr): 3387, 3021, 1668 cm^{-1}.

*4.4.9. 3-(4-Chloro-phenylamino)-3-(4-methoxy-phenyl)-1-phenyl-propan-1-one (**2i**)*

mp 149–151 °C (lit. [16c]: 148 °C); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.90–7.88 (t, 2H, J = 6.7 Hz), 7.58–7.54 (t, 1H, J = 7.4 Hz), 7.46–7.42 (t, 2H, J = 8.0 Hz), 7.33–7.31 (m, 2H), 7.04–7.01 (m, 2H), 6.87–6.84 (m, 2H), 6.48–6.45 (m, 2H), 4.91–4.88 (t, 1H, J = 7.4 Hz), 4.57 (br, 1H), 3.77 (s, 3H), 3.50–3.44 (dd, 1H, J = 5.6, 16 Hz), 3.41–3.35 (dd, 1H, J = 7.6, 16 Hz); IR (KBr): 3381, 3020, 1669 cm^{-1}.

*4.4.10. 2-(Phenyl-phenylamino-methyl)-cyclohexanone (**2j**)*

mp 135–137 °C (lit. [16d]: 139–140 °C); ^1H NMR (400 MHz, $CDCl_3$, major/minor = 56:44): δ = 7.39–7.30 (m, 5H), 7.24–7.22 (t, 2H, J = 7.6 Hz), 6.65–6.63 (d, 1H, J = 4.4 Hz), 6.57–6.53 (d, 2H, J = 7.2 Hz), 4.81 (d, 0.44H, J = 4.0 Hz), 4.64 (d, 0.56H, J = 7.2 Hz), 2.75–2.83 (m, 1H), 2.28–2.47 (m, 2H), 1.58–1.94 (m, 6H); IR (KBr): 3386, 2939, 1689, 1500 cm^{-1}.

*4.4.11. 2-[(3-Nitro-phenyl)-phenylamino-methyl]-cyclohexanone (**2k**)*

mp 163–165 °C; ^1H NMR (400 MHz, $CDCl_3$, major/minor = 52/48): δ = 8.26–8.24 (d, 1H, J = 7.6 Hz), 8.09–8.07 (d, 1H, J = 8.0 Hz), 7.80–7.77 (m, 1H), 7.49–7.45 (t, 1H, J = 8.0 Hz), 7.12–7.08 (t, 2H, J = 8.0 Hz), 6.70–6.66 (m, 1H), 6.54–6.52 (d, 2H, J = 8.0 Hz), 4.86 (d, 0.52H, J = 4.0 Hz), 4.84 (d, 0.48H, J = 5.2 Hz), 2.89–2.86 (m, 1H), 2.42–2.34 (m, 2H), 2.08–1.95 (m, 3H), 1.79–1.75 (m, 1H), 1.66–1.58 (m, 2H); IR (KBr): 3386, 3021, 1673, 1527, 1348 cm^{-1}.

*4.4.12. 2-[(4-Chloro-phenylamino)-(4-nitro-phenyl)-methyl]-cyclohexanone (**2l**)*

mp 169–171 °C; ^1H NMR (400 MHz, $CDCl_3$, major/minor = 51/49): δ = 8.18–8.16 (d, 2H, J = 8.8 Hz, Ar), 7.57–7.53 (m, 2H, Ar), 7.05–7.02 (d, 2H, J = 8.8 Hz, Ar), 6.44–6.41 (d, 2H, J = 8.8 Hz, Ar), 4.80 (d, 0.49H, J = 5.8 Hz), 4.64 (d, 0.51H, J = 7.2 Hz), 2.86–2.83 (t, 1H, J = 6.2 Hz), 2.48–2.30 (m, 2H), 2.10–2.01 (m, 2H), 1.95–1.94 (d, 1H, J = 5.6 Hz), 1.80–1.58 (m, 3H); IR (KBr): 3386, 3021, 1673, 1527, 1348 cm^{-1}.

*4.4.13. 2-[(4-Chloro-phenylamino)-(4-methoxy-phenyl)-methyl]-cyclohexanone (**2m**)*

mp 132–134 °C (lit. [16e]: 132–134 °C); ^1H NMR (400 MHz, $CDCl_3$, major/minor = 57/43): δ = 7.27–7.24 (t, 2H, J = 7.4 Hz), 7.01–6.99 (d, 2H, J = 8.2 Hz), 6.85–6.83 (d,

2H, J = 8.2 Hz), 6.46–6.43 (d, 2H, J = 8.2 Hz), 4.75 (d, 0.43H, J = 4.8 Hz), 4.59 (d, 0.57H, J = 6.4 Hz), 3.78 (s, 3H), 2.69–2.68 (m, 1H), 2.42–2.38 (m, 1H), 2.43–2.32 (m, 1H), 1.93–1.81 (m, 4H), 1.68–1.63 (m, 2H); IR (KBr): 3362, 2964, 1703, 1603, 1512 cm^{-1}.

*4.4.14. 2-(2-Methyl-1-phenylamino-propyl)-cyclohexanone (**2n**)*

mp 87–89 °C; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.16–7.12 (t, 2H, J = 8.0 Hz), 6.67–6.61 (m, 3H), 3.91–3.88 (dd, 1H, J = 4.4, 7.6 Hz), 2.49–2.27 (m, 3H), 2.13–1.82 (m, 4H), 1.76–1.59 (m, 3H), 0.96–0.88 (d, 6H, J = 6.4 Hz); IR (KBr): 3386, 2968, 2939, 1689 cm^{-1}.

*4.4.15. 2-(Furan-2-yl-phenylamino-methyl)-cyclohexanone (**2o**)*

mp 120–121 °C; ^1H NMR (400 MHz, $CDCl_3$, major/minor = 71/29): δ = 7.29–7.10 (m, 3H), 6.71–6.61 (m, 3H), 6.26–6.17 (m, 2H), 4.88 (d, 0.71H, J = 4.8 Hz), 4.82 (d, 0.29H, J = 5.4 Hz), 4.5 (br, 1H), 2.99–2.89 (m, 1H), 2.40–1.60 (m, 8H); IR (KBr): 3362, 2938, 1673, 1597, 1500 cm^{-1}.

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References

[1] (a) R. Zhang, L. Zhang, P. Somasundaran, J. Colloid Interf. Sci. 278 (2004) 453–460;
(b) K.D. Danov, S.D. Kralchevska, P.A. Kralchevsky, Langmuir 20 (2004) 5445–5453;
(c) A. Paszternak, E. Kiss, P. Jedlovszky, J. Chem. Phys. 122 (2005) 124704.
[2] M.K. Chaudhury, G.M. Whitesides, Langmuir 7 (1991) 1013–1025, and references found therein.
[3] P. Mach, C.C. Huang, H.T. Nguyen, Langmuir 13 (1997) 6357–6359.
[4] M.P. Krafft, Adv. Drug. Deliv. Rev. 47 (2001) 209–228.
[5] J.G. Riess, Chem. Rev. 101 (2001) 2797–2920.
[6] M.P. Krafft, A. Chittofrati, J.G. Riess, Curr. Opin. Colloid Interf. Sci. 8 (2003) 251–258.
[7] H. Shao, W.D. Meng, F.L. Qing, J. Fluor. Chem. 125 (2004) 721–724.
[8] H.Y. Sun, J. Li, X.L. Qiu, et al. J. Fluor. Chem. 126 (2005) 1425–1431.
[9] Z.L. Shi, K.G. Neoh, E.T. Kang, Ind. Eng. Chem. Res. 46 (2007) 439–445.
[10] (a) J.A. Gladysz, D.P. Curran, Handbook of Fluorous Chemistry, Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim, 2004, pp. 24–40;
(b) W.B. Yi, C. Cai, J. Fluor. Chem. 127 (2006) 1515–1521;
(c) Y. Yin, G. Zhao, J. Fluor. Chem. 128 (2007) 40–45.
[11] (a) C.J. Li, Chem. Rev. 93 (1993) 2023–2035;
(b) A. Lubineau, J. Auge, Y. Queneau, Synthesis (1994) 741–760;
(c) C.J. Li, Tetrahedron 52 (1996) 5643–5668;
(d) C.J. Li, T.H. Chan, Organic Reactions in Aqueous Media, John Wiley, New York, 1997;
(e) P.E. Grieco, Organic Reactions in Water, Blackie Academic & Professional, London, 1998;
(f) U.M. Lindstrom, Chem. Rev. 102 (2002) 2751–2772;
(g) C.J. Li, Chem. Rev. 105 (2005) 3095–3166;
(h) N. Eghbali, C.J. Li, Green Chem. 9 (2007) 213–215.
[12] (a) K. Manabe, Y. Mori, S. Kobayashi, Synlett (1999) 1401–1402;
(b) K. Manabe, S. Kobayashi, Org. Lett. 1 (1999) 1965–1967;
(c) T. Akiyama, J. Takaya, H. Kagoshima, Synlett (1999) 1426–1428;
(d) S. Kobayashi, T. Busujima, S. Nagayama, Synlett (1999) 545–546;
(e) T.P. Loh, S.B. Liung, K.L. Tan, L.L. Wei, Tetrahedron 56 (2000) 3227–3237;
(f) K. Manabe, Y. Mori, S. Kobayashi, Tetrahedron 57 (2001) 2537–2544;
(g) S. Iimura, D. Nobutou, K. Manabe, S. Kobayashi, Chem. Commun. (2003) 1644–1645;
(h) T. Ollevier, E. Nadeau, J. Org. Chem. 69 (2004) 9292–9295;
(i) T. Akiyama, K. Matsuda, K. Fuchibe, Synlett (2005) 322–324;
(j) N. Azizi, L. Torkiyan, M.R. Saidi, Org. Lett. 8 (2006) 2079–2082.
[13] K. Manabe, Y. Mori, T. Wakabayashi, S. Nagayama, S. Kobayashi, J. Am. Chem. Soc. 122 (2000) 7202–7207.
[14] L.M. Wang, J.W. Han, J. Sheng, H. Tian, Z.Y. Fan, Catal. Commun. 6 (2005) 201–204.
[15] T. Yoshimura, A. Ohno, K. Esumi, Langmuir 22 (2006) 4643–4648.
[16] (a) N.G. Kozlov, L.I. Basalaeva, Russ. J. Gen. Chem. 74 (2004) 926–932;
(b) O. Tsuge, S. Iwanami, Bull. Chem. Soc. Jpn. 43 (1970) 3543–3549;
(c) M.E. Mansour, S.K. Sadany, et al. J. Chem. Eng. Data 34 (1989) 368–370;
(d) A.H. Blatt, N. Gross, J. Org. Chem. 29 (1964) 3306–3311;
(e) L. Yi, J.H. Zou, H.S. Lei, X.M. Lin, Org. Prep. Proced. Int. 23 (1991) 673–676.